J Occup Health 2007; 49: 205–216

Journal of Occupational Health

# Plasma n-3 Polyunsaturated Fatty Acid and Cardiovascular Disease Risk Factors in Japanese, Korean and Mongolian Workers

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**Abstract: Plasma n-3 Polyunsaturated Fatty Acid and Cardiovascular Disease Risk Factors in Japanese, Korean and Mongolian Workers: Akiko NOGI, *et al*. Department of Environmental and Preventive Medicine, Shimane University School of Medicine**—The favorable role of n-3 polyunsaturated fatty acid (PUFA) in cardiovascular disease (CVD) has been demonstrated in animal experiments and in humans in Western countries, but its effect remains controversial in Asian populations. An observational study of Japanese, Koreans and Mongolians with extended histories of remarkably different frequencies of fish intake was conducted to examine whether differences in plasma n-3 PUFA affects CVD risk factors. We conducted a cross-sectional study in workplace settings and determined body mass index (BMI), blood pressure, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglyceride (TG), glucose, insulin, homeostasis model assessment-insulin resistance (HOMA-IR) and fatty acid composition in plasma. A total of 411 Japanese, 418 Korean and 252 Mongolian workers aged 30–60 yr participated in this study. The Japanese ate fish more frequently and had remarkably higher values of eicosapentaenoic acid, docosahexaenoic acid and n-3 PUFA, and lower values of BMI and HOMA-IR, followed by the Koreans, and then the Mongolians. In age groups, the Japanese and Koreans showed a similar tendency of increase in n-3 PUFA with increasing age. General linear measurement multivariate analysis after adjustment for gender, age, smoking, drinking, exercise habits and BMI showed n-3 PUFA was associated with HDL-C and TG in the Japanese, while it was associated with systolic blood pressure in the Koreans, and TG in the Mongolians. In conclusion, an increase in n-3 PUFA was associated with HDL-C and TG in the Japanese and Mongolians, but these beneficial effects were not constant across the three Asian ethnic groups.
*(J Occup Health 2007; 49: 205–216)*

**Key words:** n-3 PUFA, Fish, Triglyceride, HDL-cholesterol, Insulin resistance, Asian

The identification of major risk factors through epidemiological studies and the control of these risk factors have contributed to a drop in cardiovascular disease (CVD) mortality rates in almost all industrialized countries[1)]. The emergence of a premature CVD epidemic in developing Asian countries during the past two decades has attracted less comment and little public response[2, 3)]. Increasing levels of CVD risk factors in Asian developing countries appear to be related to adverse lifestyle changes accompanying industrialization and urbanization[4)], in particular, the global availability of cheap animal products and a sedentary lifestyle[5)]. There is a clear need to identify major CVD risk factors in each country and to develop cost-effective methods for the management of CVD in the workplace settings. However, most of the data on CVD risk factors are based on studies in Western countries with only limited information derived from Asian populations.

Dietary fatty acids appear to be of significant importance in CVD. Epidemiological data strongly support the relationship between high n-3 polyunsaturated fatty acid (PUFA) intake and lower incidence of CVD[6)]. The reported mechanisms include: lowering of blood pressure; altered lipid profile, especially lowered plasma triglyceride (TG); altered thrombotic tendency; anti-inflammatory effects, anti-arrhythmic effects, relaxation of the blood vessels and reduced insulin resistance[6, 7)].

*Received Aug 11, 2006; Accepted Feb 14, 2007*
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While, the favorable role of n-3 PUFA in CVD has been demonstrated in several animal experiments and in Western populations, it remains less clear in Asians populations[8]. One reason for this is a lack of research reports on Asian populations in developing countries. Another reason is the complex nature of n-3 PUFA in combination with other dietary factors, such as carbohydrates[8, 9], vegetable oil and fiber. While randomized control trials should be used to define treatment recommendations, as potential confounders and biases inherent in observational studies severely limit the strength of their conclusions, such control trials have several limitations[10]. Controversial results of fish oil effects on CVD risk factors in randomized control trials appear to be due to the complex nature of controlled dietary trials, the limited number of subjects, the duration of administration and different intake of fish of subjects at the baseline[10].

In an extended administration of fish oil, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) continued increasing in the erythrocyte membrane during 20 wk of dosing, even after attainment of their extremes with maximum changes in plasma fatty acid composition[11]. Furthermore, a report revealed a diminished effect following a long-term administration of n-3 PUFA[11]. As most clinical trials have administered fish oil for only up to 12 wk because of low subject compliance and high cost[10], such a short duration of administration may be insufficient to induce the full effects of n-3 PUFA. An observation study in populations with different rates of long-term fish intake provides more direct data establishing the effectiveness of fish oil intake in a non-experimental setting, despite potential confounders and biases[10]. The use of n-3 PUFA supplements may induce greater preventative effects on CVD in Western populations, who have a low fish intake (1.4 g/d of α-linolenic acid and 0.1–0.2 g/d of EPA and DHA in the U.S.A.), while the effects of n-3 PUFA may be underestimated in the Japanese who consume a daily average of 2.4–2.9 g of n-3 PUFA[12, 13]. In contrast to the Japanese, Mongolians eat large amounts of meat and dairy products but little fish due to geography and a weak infrastructure for fresh food supply[14]; thus, relatively greater favorable effects on insulin resistance from n-3 PUFA might be anticipated. Our goal was to conduct an observational study of three ethnic Asian groups, relatively close genetically[15, 16], but with remarkably different frequencies of fish intake, to determine whether differences in dietary n-3 PUFA independently affect CVD risk factors, such as dyslipidemia, hypertension, hyperglycemia and insulin resistance.

## Materials and Methods

*Subjects*

A total of 749 Japanese aged 30–60 yr (386 men and 363 women) participated in regular health check-ups at manufacturing factories in Shimane Prefecture, Japan in 1999–2002[17]. From this group, a total of 411 individuals (194 men and 217 women) were randomly chosen and examined for data on fatty acid composition and metabolic measurements of their plasma. A total of 418 Koreans aged 30–60 yr (240 men and 178 women) were recruited during regular health check-ups at various workplaces by the Health Promotion Center of Dong-A University in Busan, Korea in 2003[15]. Additionally, a total of 252 Mongolians aged 30–60 yr (100 men and 152 women) were chosen by random sampling at lists of workers from two large companies (cashmere factory and power plant) in Ulaanbaatar, Mongolia[17]. None of the participants was using prescription medications for diabetes, hyperlipidemia or hypertension. Information on each participant's lifestyle was obtained using a self-reported questionnaire, including habits on smoking, alcohol consumption, exercising for over 20 min twice a week, meat intake more than twice a day and frequency of fish intake per week[17].

The Ethics Committee of Shimane University School of Medicine approved all study protocols, and all subjects gave their written informed consent.

*Measurements*

After an overnight fast, the body weight of each subject while dressed in very light clothing was measured with a standard scale to an accuracy of ± 0.2 kg, and height was measured to an accuracy of ± 0.5 cm using a height bar fixed on a wall, with subjects standing straight with back, buttocks and heels against the wall, as previously described[17]. BMI was calculated as weight (kilograms) divided by squared height (meters squared). Blood pressure was measured at the right arm using a standard sphygmomanometer (Nippon Rinsho Kikikogyo, Tokyo, Japan) with the participants seated.

Venous blood was collected from the antecubital vein after a 12-h overnight fast. Blood samples were separated and transported from Busan or Ulaanbaatar to Shimane, and then frozen at –80°C and used in this study, all within a three-month period. The concentrations of total cholesterol, HDL-cholesterol (HDL-C), TG and glucose were measured using enzymatic assay kits (Cholesterol E-test, HDL Cholesterol E-test, Triglyceride G-test and Glucose CII-test, Wako Pure Chemical, Osaka, Japan) at the Shimane University School of Medicine. The levels of low-density lipoprotein-cholesterol (LDL-C) were calculated with the following formula: total cholesterol (mg/d*l*)–HDL-C (mg/d*l*)–0.20 × TG, in the case of less than 400 mg/d*l* of TG, or total cholesterol (mg/d*l*)–HDL-C (mg/d*l*)–0.16 × TG, in the case of or more than 400 mg/d*l* of TG[18]. The concentration of insulin was measured by the Insulin-EIA test (Wako Pure Chemical, Osaka, Japan). Homoeostasis model assessment-insulin resistance (HOMA-IR) was calculated with the following formula: fasting plasma insulin ($\mu$U/m*l*) × fasting plasma glucose (mg/d*l*)/405[19].

Fatty acid composition was determined using a modification of the one-step analysis[20] as previously described[21] for a good recovery for plasma fatty acid, rather than by the conventional Folch procedure[20]. To 100 $\mu l$ of plasma, 2.0 m*l* methanol-n-octane (4:1, v/v) containing 10 mg tricosanoic acid as an internal standard and 200 $\mu l$ acetyl chloride were added. The mixture was incubated at 100°C for 60 min and cooled, then neutralized with 0.5 N aqueous NaOH containing 10% sodium chloride. The neutralized mixture was shaken for 10 min at room temperature and centrifuged at 1,800 × g for 5 min. The octane phase with the fatty acid methyl esters was directly subjected to gas chromatography. The gas chromatography separation was done on a Model 5890II (Hewlett-Packard, Avondale, PA, U.S.A.) equipped with a flame ionization detector and an automatic sampler Model 7673. A 30 m × 0.25 mm capillary column (DB-WAX P/N 122-7032, J & W Scientific, CA, U.S.A.) was initially maintained at 100°C for 1 min, raised to 180°C at 20°C/min, then raised to 240°C at 2°C/min, and further raised to 260°C at 4°C/min and maintained for 5 min. Fatty acid composition was expressed as molecular percentage/m*l* plasma. Several fatty acid indexes were derived from the primary data: the total percentage of saturated fatty acids, which was calculated as the sum of the percentages of palmitic acid (16:0) and stearic acid (18:0); the total percentage of monounsaturated fatty acids, which was represented as the percentages of oleic acid (18:1); the total percentage of n-3 PUFAs, which was calculated as the sum of the percentages of $\alpha$-linolenic acid (18:3n-3), EPA (20:5n-3), docosapentaenoic acid (22:5n-3, DPA) and DHA (22:6n-3); and, the total percentage of n-6 PUFAs, calculated as the sum of the percentages of linoleic acid (18:2n-6) and arachidonic acid (20:4n-6). The unsaturation index (USI) for each group was calculated by taking the molecular percentage of each fatty acid, and multiplying it by the number of double bonds in the fatty acids.

*Statistical analyses*

Analysis of data was done with SPSS statistical analysis software (Version 14.0J, SPSS Inc, Tokyo, Japan). Results were expressed as means ± SEMs. Since the data for TG, insulin and HOMA-IR were significantly skewed, they were transformed logarithmically before performing a statistical analysis. Subjects of all three ethnic groups were divided into three tertiles, according to absolute plasma n-3 PUFA levels, to directly compare dietary n-3 PUFA intake among three Asian ethnic groups. A general Kendal test was used for the frequency of the age groups, ethnicity or tertiles of plasma n-3 PUFA, and *post hoc* analyses by means of the Kendal test for two independent samples were used for the frequency of each group, using the youngest group, the Japanese group or the lowest tertile of plasma n-3 PUFA as a reference category. One-way ANOVAs for the age groups, ethnicity or tertiles of plasma n-3 PUFA were used to assess the differences in anthropometric and metabolic parameters, and *post hoc* analyses were performed by the Bonferroni test for two independent samples, again using the youngest group, the Japanese group or the lowest tertile of plasma n-3 PUFA as a reference category. To assess the relationships between plasma n-3 PUFA and metabolic parameters, Pearson's correlation coefficients were calculated. General linear measurement multivariate analysis (GLM) was used to compare parameters adjusted for gender, age, smoking, drinking, exercise habits and BMI, and *post hoc* analysis was done using the lowest tertile of n-3 PUFA as a reference category. One-way ANOVA and GLM results for the tertiles of plasma n-3 PUFA with trend analysis were used to assess the dose-response relationship of quantitative metabolic parameters by tertiles of plasma n-3 PUFA levels. A nominal two-sided $p$-value of less than 0.05 was used to assess the significance.

## Results

*Lifestyle, anthropometric and metabolic parameters in the plasma*

Lifestyles of the Japanese, Korean and Mongolian subjects by age group are shown in Table 1. The Japanese had the greatest proportion of blue-collar workers, and the Koreans had a significantly higher frequency of smoking and a higher rate of exercise, relative to the other ethnic groups. The Japanese ate fish more frequently, followed by the Koreans, while the Mongolians consumed meat more frequently. In the age groups, the frequency of smoking and drinking decreased with age in all three ethnic groups, and the proportion of blue-collar workers decreased with age for the Japanese and Mongolians.

Anthropometric and metabolic parameters in plasma for the Japanese, Korean and Mongolian subjects by age are shown in Table 2. The Mongolians had significantly higher values for BMI, followed by the Koreans, and then the Japanese. Similarly, the Mongolians had significantly higher values for blood pressure, followed by the Koreans and Japanese. Relative to the Japanese, metabolic parameters of the Koreans showed significantly lower values for HDL-C and higher values for LDL-C and TG. The Mongolians also had significantly higher values for insulin and HOMA-IR, followed by the Koreans, and then the Japanese.

The oldest group aged 50–60 yr had the highest values of BMI, blood pressure, total cholesterol, LDL-C, TG and glucose levels among all the three ethnic groups, relative to the youngest group aged 30–39 yr. The

**Table 1.** Lifestyle of subjects by age and ethnicity

| Ethnicity / Parameters | Age group (yr) 30–39 | 40–49 | 50–60 | *p* by age | Total | *p* by ethnicity |
|---|---|---|---|---|---|---|
| Japanese | | | | | | |
| Number (Men/Women) | 76 (39/37) | 178 (89/89) | 157 (66/91) | NS | 411 | |
| Age | 37.0 ± 0.2 | 44.9 ± 0.2* | 54.5 ± 0.2* | <0.001 | 47.1 ± 0.3 | <0.001 |
| Blue collar work | 57 (76.0%) | 134 (75.3%) | 103 (65.6%)* | 0.007 | 320 (74.1%) | <0.001 |
| Current smoking | 26 (34.2%) | 62 (35.2%) | 37 (23.6%)* | 0.023 | 125 (30.3%) | <0.001 |
| Current drinking | 38 (50.0%) | 100 (56.8%) | 70 (44.6%) | NS | 208 (50.5%) | NS |
| Exercise (≥ twice a week) | 11 (14.5%) | 22 (12.4%) | 47 (29.9%)* | 0.001 | 80 (19.4%) | <0.001 |
| Meat intake (≥ twice a day) | 83 (58.9%) | 72 (41.9%) | 42 (40.0%) | NS | 197 (47.1%) | <0.001 |
| Fish intake (≥ once a week) | 68 (89.4%) | 168 (94.4%) | 149 (94.9%) | NS | 385 (93.4%) | <0.001 |
| Fish intake (≥ three times a week) | 55 (72.4%) | 105 (59.0%) | 102 (65.0%) | NS | 262 (63.7%) | <0.001 |
| Koreans | | | | | | |
| Number (Men/Women) | 141 (92/49) | 172 (94/78)* | 105 (54/51)* | 0.021 | 418 | |
| Age | 34.9 ± 0.2 | 44.3 ± 0.2* | 54.5 ± 0.3* | <0.001 | 43.7 ± 0.4* | |
| Blue collar work | 48 (34.0%) | 83 (48.3%) | 39 (37.1%) | NS | 170 (40.7%)* | |
| Current smoking | 90 (63.8%) | 88 (51.2%)* | 47 (44.8%) | 0.002 | 225 (53.8%)* | |
| Current drinking | 93 (66.0%) | 102 (59.3%) | 48 (45.7%)* | 0.027 | 193 (46.2%) | |
| Exercise (≥ twice a week) | 57 (40.4%) | 72 (41.9%) | 39 (26.0%) | NS | 168 (40.2%)* | |
| Meat intake (≥ twice a day) | 5 (3.5%) | 15 (8.7%) | 7 (6.7%) | NS | 27 (6.5%)* | |
| Fish intake (≥ once a week) | 137 (97.2%) | 166 (96.5%) | 98 (93.3%) | NS | 401 (95.9%) | |
| Fish intake (≥ three times a week) | 57 (40.4%) | 88 (51.2%) | 56 (53.3%)* | 0.034 | 201 (48.1%)* | |
| Mongolians | | | | | | |
| Number (Men/Women) | 86 (22/64) | 120 (54/66)* | 46 (24/22)* | 0.001 | 252 | |
| Age | 37.1 ± 0.2 | 43.4 ± 0.2* | 53.8 ± 0.4* | <0.001 | 43.2 ± 0.4* | |
| Blue collar work | 48 (55.8%) | 56 (46.7%) | 18 (39.1%) | 0.045 | 123 (48.8%)* | |
| Current smoking | 17 (19.8%) | 39 (32.5%)* | 17 (37.0%)* | 0.023 | 73 (28.9%) | |
| Current drinking | 32 (37.6%) | 63 (52.5%) | 21 (45.7%) | NS | 116 (46.0%) | |
| Exercise (≥ twice a week) | 12 (14.0%) | 13 (10.8%) | 7 (15.2%) | NS | 32 (12.7%) | |
| Meat intake (≥ twice a day) | 73 (84.9%) | 105 (87.5%) | 40 (87.0%) | NS | 218 (86.5%)* | |
| Fish intake (≥ once a week) | 30 (34.9%) | 35 (29.2%) | 10 (21.7%) | NS | 75 (29.8%)* | |
| Fish intake (≥ three times a week) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | NS | 0 (0.0%)* | |

Data are means ± SEMs. The general Kendal test was used for the frequency of each age group, and *post hoc* analyses by means of the Kendal test for two dependent samples were used for the frequency in lifestyle of each group, using the youngest group or the Japanese as a reference category. One-way ANOVA for the age group or three ethnic groups was used to assess the differences in age by age group or ethnicity, and *post hoc* analyses were performed by the Bonferroni test for two independent samples, using the youngest group or the Japanese as a reference category.

Mongolians showed a tendency of higher levels of insulin and HOMA-IR with age, while these levels in the Koreans had a tendency to decrease with age.

*Fatty acid composition in plasma*

Fatty acid composition in plasma for the Japanese, Korean and Mongolian subjects by age is shown in Table 3. In fatty acid composition, the Japanese showed remarkably higher values for EPA, DHA, n-3 PUFA and USI, and lower values for n-6 PUFA/n-3 PUFA, followed by the Koreans, and then the Mongolians. Plasma EPA levels in the Japanese were three times those of the Mongolians, and the DHA and n-3 PUFA levels were twice those of the Mongolians. Plasma EPA, DHA and n-3 PUFA levels of the Koreans fell between those of the Japanese and Mongolians. A wide range of n-3 PUFA in the Japanese (2.35–20.96%) and Koreans (3.10–16.80%) was observed, while the Mongolians had a very narrow range of n-3 PUFA (2.89–7.90%). The Japanese showed significantly lower values for oleic acid and α-linolenic acid, relative to the Mongolians.

In age groups, the Japanese and Koreans showed

**Table 2.** Anthropometric and metabolic charactaristics of subjects by age and ethnicity

| Ethnicity<br>Parameters | Age group (yr)<br>30–39 | <br>40–49 | <br>50–60 | *p*<br>by age | Total | *p*<br>by ethnicity |
|---|---|---|---|---|---|---|
| Japanese | | | | | | |
| Height (cm) | 163.9 ± 1.0 | 161.9 ± 0.6 | 158.6 ± 0.6* | <0.001 | 161.0 ± 0.4 | <0.001 |
| Weight (kg) | 60.6 ± 1.5 | 59.9 ± 0.9 | 58.8 ± 0.8 | NS | 59.6 ± 0.6 | <0.001 |
| BMI (kg/m$^2$) | 22.4 ± 0.5 | 22.7 ± 0.2 | 23.3 ± 0.3 | NS | 22.9 ± 0.2 | <0.001 |
| Systolic BP (mmHg) | 115 ± 1 | 119 ± 1 | 126 ± 2* | <0.001 | 121 ± 1 | 0.001 |
| Diastolic BP (mmHg) | 71 ± 1 | 74 ± 1 | 78 ± 1* | <0.001 | 75 ± 1 | <0.001 |
| Total cholesterol (mg/d*l*) | 196 ± 4 | 201 ± 2 | 217 ± 3* | <0.001 | 206 ± 2 | <0.001 |
| LDL-cholesterol (mg/d*l*) | 121 ± 3 | 125 ± 2 | 139 ± 3* | 0.001 | 129 ± 2 | 0.001 |
| HDL-cholesterol (mg/d*l*) | 58 ± 2 | 56 ± 1 | 54 ± 1 | 0.043 | 56 ± 1 | <0.001 |
| Triglyceride (mg/d*l*) | 89 ± 6 | 104 ± 5 | 129 ± 8* | <0.001 | 111 ± 4 | <0.001 |
| Glucose (mg/d*l*) | 94 ± 2 | 96 ± 1 | 101 ± 2* | 0.003 | 97 ± 1 | NS |
| Insulin (mU/m*l*) | 6.5 ± 0.8 | 5.5 ± 0.4 | 5.5 ± 0.3 | NS | 5.6 ± 0.3 | <0.001 |
| HOMA-IR | 1.50 ± 0.19 | 1.34 ± 0.11 | 1.41 ± 0.11 | NS | 1.40 ± 0.07 | <0.001 |
| Koreans | | | | | | |
| Height (cm) | 167.0 ± 0.7 | 163.9 ± 0.6* | 161.3 ± 0.8* | <0.001 | 164.3 ± 0.4* | |
| Weight (kg) | 66.1 ± 1.0 | 64.4 ± 0.7 | 64.7 ± 1.0 | NS | 65.1 ± 0.5* | |
| BMI (kg/m$^2$) | 23.6 ± 0.3 | 23.9 ± 0.2 | 24.8 ± 0.3* | 0.001 | 24.0 ± 0.1* | |
| Systolic BP (mmHg) | 116 ± 1 | 116 ± 1 | 121 ± 1* | 0.001 | 117 ± 1* | |
| Diastolic BP (mmHg) | 77 ± 1 | 77 ± 1 | 80 ± 1* | 0.002 | 78 ± 1* | |
| Total cholesterol (mg/d*l*) | 192 ± 3 | 194 ± 2 | 206 ± 3* | 0.001 | 196 ± 2* | |
| LDL-cholesterol (mg/d*l*) | 132 ± 3 | 135 ± 3 | 149 ± 3* | <0.001 | 137 ± 2* | |
| HDL-cholesterol (mg/d*l*) | 51 ± 1 | 49 ± 1 | 48 ± 1 | 0.025 | 49 ± 1* | |
| Triglyceride (mg/d*l*) | 123 ± 6 | 130 ± 6 | 128 ± 7 | NS | 127 ± 4* | |
| Glucose (mg/d*l*) | 94 ± 1 | 97 ± 2 | 99 ± 2 | 0.039 | 96 ± 1 | |
| Insulin (mU/m*l*) | 7.7 ± 0.7 | 5.7 ± 0.3* | 5.6 ± 0.3* | 0.010 | 6.4 ± 0.3* | |
| HOMA-IR | 1.90 ± 0.22 | 1.43 ± 0.10 | 1.41 ± 0.10 | NS | 1.56 ± 0.05* | |
| Mongolians | | | | | | |
| Height (cm) | 159.5 ± 0.1 | 162.2 ± 0.8 | 161.6 ± 1.1 | NS | 161.1 ± 0.5 | |
| Weight (kg) | 63.8 ± 1.4 | 69.2 ± 1.3* | 69.9 ± 1.9* | 0.016 | 67.5 ± 0.9* | |
| BMI (kg/m$^2$) | 25.1 ± 0.5 | 26.2 ± 0.4 | 26.7 ± 0.6 | NS | 25.9 ± 0.3* | |
| Systolic BP (mmHg) | 116 ± 2 | 121 ± 1 | 130 ± 4* | 0.001 | 121 ± 1 | |
| Diastolic BP (mmHg) | 84 ± 2 | 85 ± 1 | 90 ± 2 | 0.027 | 86 ± 1* | |
| Total cholesterol (mg/d*l*) | 172 ± 4 | 182 ± 3 | 191 ± 6* | 0.003 | 180 ± 2* | |
| LDL-cholesterol (mg/d*l*) | 99 ± 4 | 108 ± 3 | 118 ± 6* | 0.002 | 107 ± 2* | |
| HDL-cholesterol (mg/d*l*) | 54 ± 1 | 53 ± 1 | 52 ± 2 | NS | 53 ± 1* | |
| Triglyceride (mg/d*l*) | 91 ± 6 | 110 ± 9 | 107 ± 10 | NS | 103 ± 5 | |
| Glucose (mg/d*l*) | 90 ± 3 | 97 ± 3 | 100 ± 5 | NS | 95 ± 2 | |
| Insulin (mU/m*l*) | 6.7 ± 0.6 | 7.2 ± 0.4 | 8.2 ± 0.9 | NS | 7.2 ± 0.3* | |
| HOMA-IR | 1.68 ± 0.07 | 1.82 ± 0.15 | 2.16 ± 0.33* | 0.015 | 1.81 ± 0.11* | |

HOMA-IR, homeostasis model assessment-insulin resistance. Data are means ± SEMs.
One-way ANOVA for the age group or three ethnic groups was used to assess the differences in anthropometric and metabolic parameters by age group or ethnicity, and *post hoc* analyses were performed by the Bonferroni test for two independent samples, using the youngest group or the Japanese as a reference category. One-way ANOVA performed for logarithimically transformed values for triglyceride, insulin and HOMA-IR.

similar tendencies with age: a tendency for increases in EPA, DHA and n-3 PUFA, and a tendency for decreases in linoleic acid, n-6 PUFA and n-6 PUFA/n-3 PUFA. The Mongolians showed different features, such as a tendency for an increase in oleic acid, and for decreases in linoleic acid, AA, DHA and n-6 PUFA with age.

**Table 3.** Fatty acid composition (mol%) of subjects by age and ethnicity

| Ethnicity / Fatty acid composition | Age group (yr) 30–39 | 40–49 | 50–60 | *p* by age | Total | *p* by ethnicity |
|---|---|---|---|---|---|---|
| **Japanese** | | | | | | |
| Palmitic acid, $C_{16:0}$ | 24.4 ± 0.2 | 24.6 ± 0.2 | 25.5 ± 0.2* | <0.001 | 24.9 ± 0.1 | <0.001 |
| Stearic acid, $C_{18:0}$ | 7.8 ± 0.1 | 7.8 ± 0.1 | 8.0 ± 0.1 | NS | 7.8 ± 0.1 | <0.001 |
| Oleic acid, $C_{18:1}$ | 18.5 ± 0.4 | 18.6 ± 0.3 | 19.0 ± 0.3 | NS | 18.8 ± 0.2 | <0.001 |
| Linoleic acid, $C_{18:2(n\text{-}6)}$ | 33.7 ± 0.5 | 33.1 ± 0.4 | 30.2 ± 0.4* | <0.001 | 32.1 ± 0.2 | <0.001 |
| α-Linolenic acid, $C_{18:3(n\text{-}3)}$ | 0.5 ± 0.0 | 0.6 ± 0.0 | 0.6 ± 0.0 | NS | 0.6 ± 0.0 | <0.001 |
| Arachidonic acid, $C_{20:4(n\text{-}6)}$ | 6.3 ± 0.1 | 6.1 ± 0.1 | 5.7 ± 0.1* | 0.003 | 6.0 ± 0.1 | <0.001 |
| Eicosapentaenoic acid, $C_{20:5(n\text{-}3)}$ | 2.5 ± 0.2 | 2.7 ± 0.1 | 3.6 ± 0.1* | <0.001 | 3.0 ± 0.1 | <0.001 |
| Docosapentaenoic acid, $C_{22:5(n\text{-}3)}$ | 0.9 ± 0.0 | 0.9 ± 0.0 | 1.0 ± 0.0* | <0.001 | 0.9 ± 0.0 | <0.001 |
| Docosahexaenoic acid, $C_{22:6(n\text{-}3)}$ | 5.5 ± 0.2 | 5.6 ± 0.1 | 6.4 ± 0.1* | <0.001 | 5.9 ± 0.1 | <0.001 |
| Saturated FA | 32.1 ± 0.3 | 32.4 ± 0.2 | 33.5 ± 0.3* | 0.001 | 32.8 ± 0.1 | <0.001 |
| Monounsaturated FA | 18.5 ± 0.4 | 18.6 ± 0.3 | 19.0 ± 0.3 | NS | 18.8 ± 0.2 | <0.001 |
| Polyunsaturated FA | 48.5 ± 0.6 | 48.1 ± 0.4 | 46.5 ± 0.5* | 0.005 | 47.6 ± 0.3 | <0.001 |
| n-6 PUFA (%) | 39.9 ± 0.5 | 39.2 ± 0.4 | 35.9 ± 0.4* | <0.001 | 38.1 ± 0.3 | <0.001 |
| n-3 PUFA (%) | 8.5 ± 0.3 | 8.9 ± 0.2 | 10.6 ± 0.3* | <0.001 | 9.5 ± 0.2 | <0.001 |
| n-6 PUFA /n-3 PUFA | 5.23 ± 0.22 | 4.98 ± 0.16 | 3.75 ± 0.12* | <0.001 | 4.56 ± 0.10 | <0.001 |
| USI | 162 ± 2 | 163 ± 1 | 166 ± 2 | 0.025 | 164 ± 1 | <0.001 |
| **Koreans** | | | | | | |
| Palmitic acid, $C_{16:0}$ | 23.6 ± 0.2 | 23.8 ± 0.2 | 24.2 ± 0.2 | 0.046 | 23.8 ± 0.1* | |
| Stearic acid, $C_{18:0}$ | 6.7 ± 0.1 | 6.7 ± 0.1 | 6.7 ± 0.1 | NS | 6.7 ± 0.1* | |
| Oleic acid, $C_{18:1}$ | 19.6 ± 0.3 | 19.3 ± 0.3 | 19.4 ± 0.3 | NS | 19.4 ± 0.2* | |
| Linoleic acid, $C_{18:2(n\text{-}6)}$ | 37.2 ± 0.4 | 36.0 ± 0.4 | 34.5 ± 0.5* | <0.001 | 36.0 ± 0.2* | |
| α-Linolenic acid, $C_{18:3(n\text{-}3)}$ | 0.6 ± 0.0 | 0.6 ± 0.0 | 0.6 ± 0.0 | NS | 0.6 ± 0.0 | |
| Arachidonic acid, $C_{20:4(n\text{-}6)}$ | 6.4 ± 0.1 | 6.2 ± 0.1 | 6.1 ± 0.1 | 0.042 | 6.2 ± 0.1* | |
| Eicosapentaenoic acid, $C_{20:5(n\text{-}3)}$ | 1.4 ± 0.1 | 2.0 ± 0.1* | 2.6 ± 0.0* | <0.001 | 2.0 ± 0.1* | |
| Docosapentaenoic acid, $C_{22:5(n\text{-}3)}$ | 0.5 ± 0.0 | 0.6 ± 0.0* | 0.7 ± 0.0* | <0.001 | 0.6 ± 0.0* | |
| Docosahexaenoic acid, $C_{22:6(n\text{-}3)}$ | 4.0 ± 0.1 | 4.8 ± 0.1* | 5.1 ± 0.1* | <0.001 | 4.6 ± 0.1* | |
| Saturated FA | 30.2 ± 0.2 | 30.5 ± 0.2 | 30.9 ± 0.3 | 0.040 | 30.5 ± 0.1* | |
| Monounsaturated FA | 19.6 ± 0.3 | 19.3 ± 0.3 | 19.4 ± 0.3 | NS | 19.4 ± 0.2* | |
| Polyunsaturated FA | 50.1 ± 0.4 | 50.2 ± 0.4 | 59.7 ± 0.5 | NS | 50.0 ± 0.3* | |
| n-6 PUFA (%) | 43.6 ± 0.4 | 42.1 ± 0.4* | 40.6 ± 0.5* | <0.001 | 42.3 ± 0.3* | |
| n-3 PUFA (%) | 6.5 ± 0.1 | 8.1 ± 0.2* | 9.1 ± 0.3* | <0.001 | 7.8 ± 0.2* | |
| n-6 PUFA /n-3 PUFA | 7.20 ± 0.18 | 5.65 ± 0.14* | 4.92 ± 0.17* | <0.001 | 5.99 ± 0.10* | |
| USI | 155 ± 1 | 160 ± 1* | 162 ± 1* | <0.001 | 159 ± 1* | |
| **Mongolians** | | | | | | |
| Palmitic acid, $C_{16:0}$ | 23.9 ± 0.3 | 24.5 ± 0.2 | 25.0 ± 0.4 | 0.031 | 24.4 ± 0.2* | |
| Stearic acid, $C_{18:0}$ | 8.3 ± 0.1 | 8.1 ± 0.1 | 8.3 ± 0.2 | NS | 8.2 ± 0.1* | |
| Oleic acid, $C_{18:1}$ | 20.7 ± 0.3 | 22.1 ± 0.3* | 23.2 ± 0.5* | <0.001 | 21.9 ± 0.2* | |
| Linoleic acid, $C_{18:2(n\text{-}6)}$ | 34.6 ± 0.5 | 33.2 ± 0.4 | 31.7 ± 0.7* | 0.001 | 33.4 ± 0.3* | |
| α-Linolenic acid, $C_{18:3(n\text{-}3)}$ | 0.7 ± 0.0 | 0.7 ± 0.0 | 0.7 ± 0.1 | NS | 0.7 ± 0.0* | |
| Arachidonic acid, $C_{20:4(n\text{-}6)}$ | 6.3 ± 0.1 | 5.9 ± 0.1 | 5.7 ± 0.2* | 0.08 | 6.0 ± 0.1 | |
| Eicosapentaenoic acid, $C_{20:5(n\text{-}3)}$ | 1.0 ± 0.1 | 1.0 ± 0.1 | 1.1 ± 0.1 | NS | 1.0 ± 0.0* | |
| Docosapentaenoic acid, $C_{22:5(n\text{-}3)}$ | 1.1 ± 0.0 | 1.1 ± 0.0 | 1.2 ± 0.0 | NS | 1.1 ± 0.0* | |
| Docosahexaenoic acid, $C_{22:6(n\text{-}3)}$ | 3.5 ± 0.1 | 3.2 ± 0.1* | 3.2 ± 0.1* | 0.014 | 3.3 ± 0.1* | |
| Saturated FA | 32.2 ± 0.3 | 32.6 ± 0.2 | 3.3 ± 0.4 | 0.042 | 32.6 ± 0.2 | |
| Monounsaturated FA | 20.7 ± 0.3 | 22.1 ± 0.3* | 23.2 ± 0.5* | <0.001 | 21.9 ± 0.2* | |
| Polyunsaturated FA | 46.0 ± 0.6 | 44.1 ± 0.5* | 42.3 ± 0.8* | 0.001 | 44.4 ± 0.3* | |
| n-6 PUFA (%) | 40.8 ± 0.5 | 39.1 ± 0.4* | 37.3 ± 0.8* | 0.001 | 39.4 ± 0.3* | |
| n-3 PUFA (%) | 5.1 ± 0.1 | 5.0 ± 0.1 | 5.0 ± 0.1 | NS | 5.0 ± 0.1* | |
| n-6 PUFA /n-3 PUFA | 8.08 ± 0.15 | 7.99 ± 0.12 | 7.56 ± 0.19 | 0.031 | 7.94 ± 0.08* | |
| USI | 148 ± 1 | 144 ± 1* | 142 ± 2* | 0.002 | 145 ± 1* | |

Data are means ± SEMs. One-way ANOVA for three ethnic groups was used to assess the differences in fatty acid composition by age group or ethnicity, and *post hoc* analyses were performed by the Bonferroni test for two independent samples, using the youngest group or the Japanese as a reference category.

**Table 4.** Levels of metabolic parameters between tertiles of plasma n-3 PUFA

| Ethnicity | n-3 PUFA | 2.35–5.81% | 5.82–8.69% | 8.70–20.96% | *p* |
|---|---|---|---|---|---|
| Japanese | Number (Men/Women) | 46 (31/15) | 123 (55/68) | 243 (108/135) | NS |
| | Meat intake (≥ twice a day) | 29 (63.0%) | 59 (48.0%) | 82 (33.7%)* | <0.001 |
| | Fish intake (≥ three times a week) | 25 (54.3%) | 75 (61.0%) | 162 (66.7%) | NS |
| | Age | 43.8 ± 1.1 | 45.6 ± 0.6 | 48.4 ± 0.4* | <0.001 |
| | BMI (kg/m²) | 23.9 ± 0.7 | 22.8 ± 0.3 | 22.7 ± 0.2 | 0.044 |
| | Systolic BP (mmHg) | 119 ± 2 | 119 ± 1 | 123 ± 1* | NS |
| | Diastolic BP (mmHg) | 75 ± 2 | 74 ± 1 | 76 ± 1 | NS |
| | LDL-C (mg/d*l*) | 120 ± 4 | 127 ± 3 | 132 ± 2 | 0.003 |
| | HDL-C (mg/d*l*) | 50 ± 2 | 53 ± 1 | 58 ± 1* | 0.001 |
| | Triglyceride (mg/d*l*) | 150 ± 19 | 116 ± 8 | 100 ± 4* | 0.001 |
| | Glucose (mg/d*l*) | 97 ± 4 | 96 ± 2 | 99 ± 1 | NS |
| | HOMA-IR | 1.79 ± 0.36 | 1.46 ± 0.15 | 1.29 ± 0.07 | NS |
| Koreans | Number (Men/Women) | 91 (68/23) | 203 (104/99) | 124 (68/56) | 0.009 |
| | Meat intake (≥ twice a day) | 4 (4.4%) | 14 (6.9%) | 9 (7.3%) | NS |
| | Fish intake (≥ three times a week) | 23 (25.3%) | 99 (48.8%) | 79 (63.7%) | <0.001 |
| | Age | 39.4 ± 0.8 | 43.0 ± 0.6* | 48.0 ± 0.6* | <0.001 |
| | BMI (kg/m²) | 23.8 ± 0.3 | 24.0 ± 0.2 | 24.1 ± 0.2 | NS |
| | Systolic BP (mmHg) | 119 ± 2 | 117 ± 1 | 116 ± 1 | NS |
| | Diastolic BP (mmHg) | 78 ± 1 | 78 ± 1 | 78 ± 1 | NS |
| | LDL-C (mg/d*l*) | 140 ± 3 | 136 ± 3 | 136 ± 3 | NS |
| | HDL-C (mg/d*l*) | 48 ± 1 | 51 ± 1 | 49 ± 1 | NS |
| | Triglyceride (mg/d*l*) | 145 ± 11 | 122 ± 5 | 122 ± 6 | NS |
| | Glucose (mg/d*l*) | 98 ± 3 | 96 ± 1 | 97 ± 2 | NS |
| | HOMA-IR | 1.97 ± 0.21 | 1.43 ± 0.14 | 1.54 ± 0.12 | NS |
| Mongolians | Number (Men/Women) | 224 (91/133) | 28 (9/19) | 0 | NS |
| | Meat intake (≥ twice a day) | 193 (86.2%) | 25 (89.3%) | | NS |
| | Fish intake (≥ three times a week) | 0 (0.0%) | 0 (0.0%) | | NS |
| | Age | 43.4 ± 0.4 | 41.5 ± 1.2 | | NS |
| | BMI (kg/m²) | 26.0 ± 0.3 | 25.2 ± 0.7 | | NS |
| | Systolic BP (mmHg) | 122 ± 1 | 116 ± 5 | | NS |
| | Diastolic BP (mmHg) | 86 ± 1 | 84 ± 2 | | NS |
| | LDL-C (mg/d*l*) | 108 ± 2 | 98 ± 6 | | NS |
| | HDL-C (mg/d*l*) | 53 ± 1 | 55 ± 2 | | NS |
| | Triglyceride (mg/d*l*) | 107 ± 6 | 72 ± 6* | | 0.001 |
| | Glucose (mg/d*l*) | 96 ± 2 | 87 ± 2 | | NS |
| | HOMA-IR | 1.83 ± 0.12 | 1.65 ± 0.16 | | NS |

Data are means ± SEMs. The general Kendal test was used for the frequency of lifestyle by plasma n-3PUFA tertiles, and *post hoc* analyses by means of Kendal test for two dependent samples were used for the frequency in lifestyle by plasma n-3PUFA tertiles, using the lowest tertile of plasma n-3 PUFA as a reference category. One-way ANOVA with trend analysis was used to assess the differences in anthropometric and metabolic parameters by plasma n-3PUFA tertiles, and *post hoc* analyses were performed by the Bonferroni test for two independent samples, using the lowest tertile of plasma n-3 PUFA as a reference category.

*Tertiles of n-3 PUFA levels and CVD risk factors*

To investigate n-3 PUFA effects, metabolic parameters were compared between tertiles of plasma n-3 PUFA for the three ethnic groups (Table 4). The Japanese were categorized as 11.2% for the lowest tertile (2.35–5.81%), 29.9% for the intermediate (5.82–8.69%), and 59.1% for the highest tertile (8.70–20.96%). The Koreans and Mongolians, respectively, were rated as 20.8% and 88.9% for the lowest tertile, 48.6% and 11.1% for the intermediate, and 29.7% and 0.0% for the highest tertile of plasma n-3 PUFA. One-way ANOVAs showed n-3 PUFA in the Japanese to be associated with BMI, LDL-

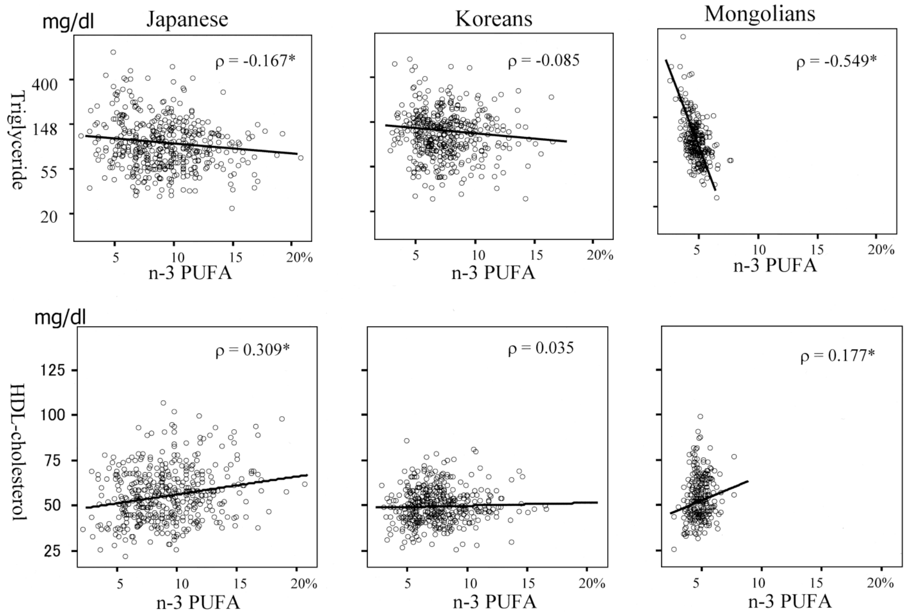


**Fig. 1.** Pearson's correlation coefficient (ρ) between n-3 PUFA and triglyceride or HDL-cholesterol by ethnicity. Values of triglyceride were transformed logarithmically. *: $p<0.05$

**Table 5.** Adjusted levels of metabolic parameters between tertiles of plasma n-3 PUFA

| | n-3 PUFA | 2.35–5.81% | 5.82–8.69% | 8.70–20.96% | *p* |
|---|---|---|---|---|---|
| Japanese | Systolic BP (mmHg) | 120 ± 3 | 119 ± 1 | 122 ± 0 | NS |
| | Diastolic BP (mmHg) | 76 ± 2 | 74 ± 1 | 75 ± 1 | NS |
| | LDL-C (mg/d*l*) | 124 ± 5 | 128 ± 3 | 130 ± 2 | NS |
| | HDL-C (mg/d*l*) | 51 ± 2 | 53 ± 1 | 58 ± 1* | <0.001 |
| | Triglyceride (mg/d*l*) | 134 ± 10 | 114 ± 5 | 96 ± 4* | <0.001 |
| | Glucose (mg/d*l*) | 98 ± 3 | 96 ± 1 | 96 ± 1 | NS |
| | HOMA-IR | 1.73 ± 0.24 | 1.50 ± 0.13 | 1.32 ± 0.10 | NS |
| Koreans | Systolic BP (mmHg) | 119 ± 2 | 118 ± 1 | 114 ± 1* | 0.031 |
| | Diastolic BP (mmHg) | 78 ± 1 | 78 ± 1 | 77 ± 1 | NS |
| | LDL-C (mg/d*l*) | 143 ± 4 | 138 ± 2 | 133 ± 3 | NS |
| | HDL-C (mg/d*l*) | 48 ± 1 | 50 ± 1 | 49 ± 1 | NS |
| | Triglyceride (mg/d*l*) | 145 ± 8 | 123 ± 5 | 122 ± 7 | NS |
| | Glucose (mg/d*l*) | 100 ± 2 | 96 ± 1 | 95 ± 2 | NS |
| | HOMA-IR | 1.78 ± 0.20 | 1.44 ± 0.12 | 1.69 ± 0.16 | NS |
| Mongolians | Systolic BP (mmHg) | 121 ± 1 | 117 ± 4 | | NS |
| | Diastolic BP (mmHg) | 85 ± 1 | 85 ± 2 | | NS |
| | LDL-C (mg/d*l*) | 108 ± 2 | 102 ± 6 | | NS |
| | HDL-C (mg/d*l*) | 53 ± 1 | 55 ± 2 | | NS |
| | Triglyceride (mg/d*l*) | 100 ± 3 | 76 ± 9* | | 0.003 |
| | Glucose (mg/d*l*) | 94 ± 2 | 89 ± 5 | | NS |
| | HOMA-IR | 1.76 ± 0.10 | 1.78 ± 0.28 | | NS |

HOMA-IR, homeostasis model assessment-insulin resistance. Data are means ± SEMs. GLM with trend analysis adjusted for gender, age, smoking, drinking, exercise habits and BMI was used to assess the differences in anthropometric and metabolic parameters by plasma n-3PUFA tertiles, *post hoc* analysis after GLM was done using a reference category of the lowest tertile of plasma n-3 PUFA.

C, HDL-C and TG, while n-3 PUFA was not associated with any metabolic parameters in the Koreans, and solely with TG in the Mongolians. The relationships between n-3 PUFA and TG or HDL-C are shown in Fig. 1. A significant negative correlation between n-3 PUFA and TG and a significant positive correlation between n-3 PUFA and HDL-C were observed for the Japanese and Mongolians, but not for the Koreans.

GLM multivariate analysis after adjustment for gender, age, smoking, drinking, exercise habits and BMI, which are confounding factors of CVD risk factors, showed n-3 PUFA to be associated with HDL-C and TG in the Japanese and TG in the Mongolians, while associated with systolic blood pressure in the Koreans (Table 5).

## Discussion

A major finding of the present study was the existence of a remarkable difference in plasma n-3 PUFA levels among Japanese, Korean and Mongolian workers. Plasma fatty acid composition is a reflection of the fatty acid composition of linoleic acid and n-3 PUFA in usual diet, but it does not reflect the fatty acid composition of saturated fatty acids or of monounsaturated fatty acids[22], because the metabolic conversion of other fatty acids that obscures the relationship of these fatty acids in the plasma and diet[23].

The Japanese workers had three times the EPA and two times the DHA and n-3 PUFA levels did the Mongolians, with the values for the Koreans falling between the Japanese and Mongolians. These remarkably different values of plasma n-3 PUFA, particularly EPA and DHA, in the present study, appear to reflect the differences in marine fish consumption of Japanese[13, 24], Koreans and Mongolians. Non-fish-eating vegetarians in Tanzania were reported to have significantly lower percentages of n-3 PUFA, compared to a group with a high frequency of fish intake (1.0% vs. 3.3% for EPA, 1.0% vs. 3.8% for DHA)[25]. This result is in line with our results for the remarkable differences in n-3 PUFA between the high-fish content Japanese diet and low-fish content Mongolian diet. The Japanese and Koreans showed tendencies of increase in EPA, DHA and n-3 PUFA, and a tendency for a decrease in n-6 PUFA with age. These tendencies may be a reflection of a lower frequency of fish intake and higher meat intake in the younger Japanese and Korean subjects. While the Mongolians showed no significant difference in n-3 PUFA with age, the oldest group consumed fish less frequently. The Mongolian diet appears to have $\alpha$-linolenic acid in its soybean, canola flexseed and perilla seed oils[25], which convert to EPA and DHA in small amounts, and can serve as a substitute for fish oil.

Another major finding of the present study was the remarkable difference in ethnic-specific effects of n-3 PUFA on metabolic parameters in the Japanese, Korean and Mongolian workers. Although the relationship between n-3 PUFA and TG or HDL-C was relatively constant for the Japanese and Mongolians, the magnitude of the n-3 PUFA effect depended on the ethnicity. High TG and low HDL-C often occur together, and can be described as abnormalities of the TG-HDL axis. This dyslipidemia is a fundamental characteristic of patients with metabolic syndrome, a condition strongly associated with the development of both type 2 diabetes and CVD[26]. HDL-C exerts several potentially anti-atherogenic effects including reverse cholesterol transport from peripheral cells to the liver, and n-3 PUFA has increased HDL-C in experimental and interventional investigations. Increases in HDL-C may be regulated by stimulation of apoA-I synthesis and secretion, the stimulation of ABCA1 expression, the inhibition of cholesterol ester transfer protein, and the up-regulation of scavenger receptor BI, but the molecular mechanism of n-3 PUFA is not clear[27].

Observational and interventional studies have confirmed that fish oils containing mainly EPA and DHA have significant hypotriglyceridemic effects[6, 28, 29] by decreasing hepatic production of very low-density-lipoprotein (VLDL) TG[30]. Our results show that plasma n-3 PUFA was related to TG in the three ethnic Asian populations, after adjustment for the confounding factors. Our present results indicate n-3 PUFA remarkably affected TG levels independently in the Mongolian subjects, who also had a low fish intake. A study of a group of Caucasians, having low levels of n-3 PUFA similar to those in our Mongolian subjects, was given as little as 3 g supplement of dietary n-3 PUFA which reduced serum TG by 30%[31]. The Japanese general population has an average daily intake of 2.4–2.9 g of n-3 PUFA[13], levels similar to those reported as having therapeutic intake for Caucasians with low n-3 PUFA histories. Possible reasons for the relatively weak hypotriglyceridemic effect of n-3 PUFA in our Japanese and Korean subjects may be a reduced effect at the higher levels, and/or a diminishing effect as a result of long-term ingestion of n-3 PUFA[9, 32].

It is believed that n-3 PUFA may exert beneficial effects on many of the associated pathophysiological metabolic changes for hyperglycemia and insulin resistance[33, 34]. Any one of these changes could be a cause or consequence of defects in insulin secretion from the beta cell or peripheral insulin resistance in skeletal muscle or adipose tissue[35]. Skeletal muscle is the principal tissue responsible for insulin-stimulated glucose disposal and the major site of peripheral insulin resistance[36]. Insulin resistance has been reported to be related to lowered concentrations of PUFA in skeletal muscle phospholipid[37] and increased content of TG in skeletal muscle[38]. Changes in the fatty acid composition of skeletal muscle can affect insulin action either non-specifically through modifications in membrane fluidity, or activation of lipolytic enzyme[39], or more directly through regulation of gene expression[40, 41]. The protective effect of n-3 PUFA results from it preventing the decrease of phosphatidyl inositol 3' kinase activity, the depletion of the glucose transporter protein GLUT4 in the muscle, and the decrease of expression of GLUT4 in adipose tissue. However, in the present study favorable effects of n-3 PUFA were not observed for hyperglycemia and insulin resistance. Our results for the Koreans workers show that n-3 PUFA was associated with systolic blood pressure. These hypotensive effects of n-3 PUFA are related to beneficial effects on sodium restriction and vascular function[42].

Our methods do have some limitations. A cross-sectional approach to estimate the relationship of fatty acid composition to the metabolic parameters means that we examined no data on causality. Another limitation was the relatively small and unequal numbers of our subjects. We minimized the potential for a selection bias by a more than 95% recovery rate of participants from the workers in Japan and Korea, and by randomly choosing participants from the lists of workers in Japan and Mongolia. The mean values of n-3 PUFA for Japanese have been reported by several population-based investigations in Japan[43–45] and are in line with our results of values for n-3 PUFA in our Japanese subjects. The mean values of BMI and lipid profiles have been reported by several population-based investigations in Japan[43–45], and by national surveys in Korea[46, 47] and Mongolia[48]. The results are all in line with our results for the values of those parameters in our ethnic groups.

The remarkably different ratios of plasma n-3 PUFA in the three ethnic groups appear to reflect extended histories of significantly different frequencies of fish intake. The standard death rates from CVD in 2002 by WHO Global InfoBase Online were 44 per 100,000 population in the Japan, 112 in Korea and 194 in Mongolia[49]. The mortality rate from CVD in these three populations was related to BMI, diastolic blood pressure, insulin, HOMA-IR and plasma n-3 PUFA levels, all of which were considered in the present study. Our results indicate that n-3 PUFA was associated with HDL-C and TG in the Japanese and Mongolians, but these associations were not constant across the three Asian ethnic groups. While our investigation reveals inconstant beneficial effects of n-3 PUFA in Asian ethnic populations, the reasons are not clear. Further investigation of effects of differences in genetic background, social status and exercise should provide more insight into their roles in CVD.

*Acknowledgments*: This study was supported in part by Grants-in-Aid to A. Nogi and K. Shiwaku for Scientific Research from the Japanese Ministry of Education, Culture, Sports, Science and Technology. We gratefully acknowledge Dr. Erdembileg Anuurad, Dr. Byambaa Enkhmaa, Dr. Jung-Man Kim, Dr. In-Shik Kim, Dr. Sung-Kook Lee, Dr. Tsendsuren Oyunsuren for their cooperation with the surveys, and Ms. Yuki Fujii and Ms. Toshimi Yoneyama for their skilled assistance.

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