# Recommendations for Fish Intake by Postmenopausal Japanese

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**Abstract**

In Japan, postmenopausal women have higher plasma levels of lipids than premenopausal women. Elevated plasma levels of lipids are risk factors for coronary events. As fish intake in Japan is high, the intake of marine-derived n-3 fatty acids may be associated with a reduced risk of coronary events. Ninety-one postmenopausal women（average age 64.7 ± 0.7, range: 51-83 years old）, who underwent a physical examination between April 2007 and March 2008 in the Yokohama district of Japan, were recruited in the present study. Weekly frequency of fish intake was evaluated by questionnaire simultaneously with a medical examination of body features and plasma levels of lipids and hemoglobin A1c. Informed consent was obtained from each subject for the use of the data obtained. The present study was approved by our ethics committee. Body mass index and waist circumference were well correlated with a high coefficient（r=0.869）. Plasma triglyceride, and total and low density lipoprotein-cholesterol levels were reduced in subjects who ate fish more than 7 times a week（45.1 %）with a slight elevation in high density lipoprotein-cholesterol levels, compared with those who had fish less than 6 times a week, i.e. 0 to 6 times a week（54.9 %）. The threshold of waist circumference for obesity in these postmenopausal women was calculated as 90.0 cm. Fish intake lowered triglyceride, total cholesterol and low density lipoprotein-cholesterol levels, and slightly raised high density lipoprotein-cholesterol levels.

**Key words** —— postmenopausal women, high plasma levels of lipids, fish intake

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## Introduction

General adiposity and/or abdominal adiposity are associated with a risk of death, and measurements of waist circumference（WC）in addition to the body-mass index（BMI: weight in kilograms divided by the square of height in meters）are useful for defining adiposity[1)]. BMI and particularly WC are both strongly linked to cardiovascular disease（CVD）and especially to diabetes mellitus（DM）[2)]. In prospective studies with 900,000 adults in western Europe and North America, mortality was lowest in people with a BMI of 22.5 to 25.0 kg/m$^2$. Excess mortality above and below this range was due mainly to CVD and smoking-related diseases, respectively[3)]. An 18-year prospective study with 9,087 middle-aged Japanese found metabolic syndrome to be a major determinant of ischemic CVD among men and women[4)]. In Japan, postmenopausal women had higher total choles-terol（TCh）and triglyceride（TG）levels than premenopausal women, resulting in reduced metabolism of steroids after menopause[5)], and in 176 Caucasian Canadians, women had stiffer arteries than men resulting in an increase in coronary heart disease（CHD）risk[6)].

Elevated levels of TG in plasma are also often, but not always, a risk factor for atherosclerotic CHD. Japan has the lowest rate of CHD among developed countries[7]. As fish intake in Japan is the highest in the world, additional supplementation or intake of marine-derived n-3 fatty acids may be associated with a reduced risk of nonfatal coronary events[8–11]. The n-3 fatty acids are polyunsaturated fatty acids found in the oils of fish and other seafoods that, when consumed, lower TG levels and reduce the risk of cardiovascular events[12]. High intakes of fish or eicosapentaenoic acid (EPA) plus docosahexaenoic acid (DHA) tended to be protective against CHD in women, but not men[13]. Among older adults, consumption of tuna or other broiled or baked fish, but not fried fish, was associated with a lower incidence of CHD[14]. Obesity has been playing a more important role in the high prevalence of hypertension in Japan[15]. The intake of n-3 fatty acids was related inversely to blood pressure[16].

As previously reported[17], in postmenopausal Japanese women, a daily walking for more than one hour significantly reduced serum levels of TCh, but not TG. Thus, in the present study, the effect of fish intake was investigated in terms of body features and plasma levels of lipids and hemoglobin A1c in postmenopausal women who underwent a medical examination between April 2007 and March 2008 in the Yokohama district of Japan.

## Materials and Methods

Ninety-one postmenopausal Japanese (average age 64.7 ± 0.7, range: 51-83 years old), who underwent a physical examination between April 2007 and March 2008 in the Yokohama district of Japan, were recruited in the present case-control study.

Past history, present condition, body height and weight, waist circumference and blood pressure were recorded as part of a physical check-up and routine blood testing was performed. Weekly frequencies of the intake of vegetables, beans, dairy products and fish including oily fish were evaluated by questionnaire conducted simultaneously with the medical examination. In terms of nutrition, the subjects were divided into those who ate vegetables, beans, dairy products and fish less than 6 times (0 to 6 times) a week, and those who did so more than 7 times a week (mostly everyday). Informed consent was obtained from each subject for the use of the data obtained. The present study was approved by our ethics committee.

All parameters were expressed as the mean ± standard error (SEM). Statistical analyses were performed using StatView-J 4.11 of MacOSX, the unpaired t-test and a one-way analysis of variance (ANOVA). A p value of less than 0.05 was considered statistically significant.

## Results

Mean body height and weight were 152.3 ± 0.6 cm and 52.9 ± 0.9 kg, respectively (**Table 1**). Mean WC was 83.5 ± 1.0 cm. When 90.0 cm was adapted as the threshold of WC for obese females as defined by the Japanese Society of Internal Medicine in 2005[18], the proportion of abnormal subjects was 24.2 %. The average BMI value was 22.8 ± 0.3 kg/m$^2$. The percentage of subjects with a BMI of more than 25 kg/m$^2$ was 23.1 %. When the blood pressure in elderly subjects with hypertension was more than 140/90 mmHg, the frequency of higher blood pressure was 16.5 % with or without medical treatment. There was no correlation between BMI and blood pressure. BMI and WC correlated well with a coefficient of 0.869 (WC = 2.86 × BMI + 18.4) (data not shown). When the threshold of BMI for obesity was set at 25.0 kg/m$^2$, WC was 89.9 cm.

In the present study, results were evaluated according to normal limits used in the Kanagawa Welfare Federation of Agricultural Cooperatives. Hypertriglyceridemia was found in 16.5 % of subjects (**Table 2**). Hypercholesterolemia and high levels of low density lipoprotein-cholesterol (LDL-Ch) were found in 39.6 % and 30.8 % of subjects, respectively. A high hemoglobin A1c value was found in 8.8 % of subjects.

Plasma levels of TG and TCh were markedly reduced in subjects who ate fish more than 7 times a week, at least everyday (45.1 %), compared with those who had fish less than 6 times a week, i.e. 0 to 6 times a week (54.9 %) ($p < 0.01$) (**Figure 1**). Daily intake of fish slightly increased plasma levels of high density lipoprotein-

Table 1 Age, height, body weight, waist circumference, body mass index and blood pressure.

| (n=91) | Mean values | No. (%) of subjects with abnormalities |
|---|---|---|
| 1 Age (years old) | 64.7 ± 0.7 | |
| 2 Height (cm) | 152.3 ± 0.6 | |
| 3 Body weight (kg) | 52.9 ± 0.9 | |
| 4 Waist circumference (cm) | 83.5 ± 1.0 | 22 (24.2 %) |
| 5 Body mass index (BMI) ($kg/m^2$) | 22.8 ± 0.3 | 21 (23.1 %) |
| 6 Systolic pressure (mmHg) | 123.6 ± 1.7 | 15 (16.5 %) |
| 7 Diastolic pressure (mmHg) | 73.1 ± 1.0 | 2 (2.2 %) |

Data are the mean ± SEM.
Normal limits used in the present study:
1) Waist circumference: less than 90.0 cm
2) Body mass index: less than 25.0 $kg/m^2$
3) Blood pressure: less than 140/90 mmHg

Table 2 Plasma levels of lipids and hemoglobin A1c

| | Mean values | No. (%) of subjects with abnormalities |
|---|---|---|
| Triglyceride (mg/*dl*) | 106.9 ± 5.0 | 15 (16.5 %) |
| Total cholesterol (mg/*dl*) | 210.6 ± 2.8 | 36 (39.6 %) |
| High density lipoprotein-cholesterol (mg/*dl*) | 64.2 ± 1.7 | 2 (2.2 %) |
| Low density lipoprotein-cholesterol (mg/*dl*) | 126.0 ± 3.2 | 28 (30.8 %) |
| Hemoglobin A1c (%) | 5.42 ± 0.06 | 8 (8.8 %) |

Data are the mean ± SEM.
Normal limits used in the present study:
Triglyceride: 50 to149 (mg/*dl*)
Total cholesterol: 150 to 219 (mg/*dl*)
High density lipoprotein-cholesterol: 40 to 77 (mg/*dl*)
Low density lipoprotein-cholesterol: 70 to 139 (mg/*dl*)
Hemoglobin A1c: less than 5.8 (%)

cholesterol (HDL-Ch) ($p < 0.05$) and decreased LDL-Ch levels, compared with the consumption of fish less than 6 times a week. The intake of vegetables, beans and dairy products did not affect the plasma levels of lipids (data not shown). There was no correlation between fish consumption and blood pressure in the present study(data not shown).

## Discussion

In 2005, the International Diabetes Federation (IDF) released a definition of metabolic syndrome[19], i.e. central (abdominal) obesity with a WC of more than 94 cm and 80 cm in men and women, respectively, plus any two of the following four factors: 1) a raised TG level, 2) a reduced HDL-Ch level, 3) hypertension, and 4) a raised fasting plasma glucose level or type 2 diabetes. Also in 2005, the Japanese Society of Internal Medicine proposed a "Definition and diagnostic standard for metabolic syndrome" [18], i.e. central abdominal adiposity with a WC of more than 85 cm and 90 cm in men and women, respectively, or an abdominal adipose area of more than 100 $cm^2$ in both genders, plus any two of the following three factors: 1) a raised TG level or reduced HDL-Ch level, 2) a raised fasting plasma glucose level, and 3) hypertension. However, it was reported that the number of metabolic syndrome components [modified criteria of "Adult Treatment Panel (ATP) III of the

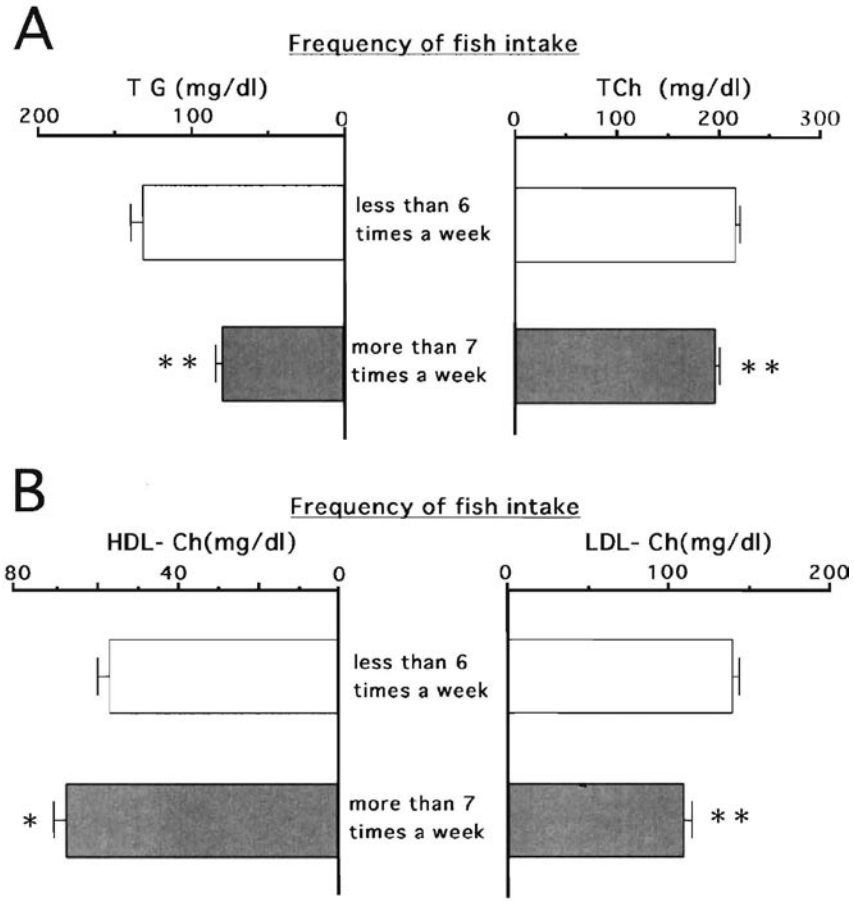


Figure 1　Weekly frequency of fish intake

A: upper figure
TG（left bars）: triglyceride（mg/dl）and TCh（right bars）: total cholesterol（mg/dl）
B: lower figure
HDL-Ch（left bars）: high density lipoprotein-cholesterol（mg/dl）and LDL-Ch（right bars）: low density lipoprotein-cholesterol（mg/dl）
Upper white bar: subjects who consume fish less than 6 times（none to 6 times）/ week.
Lower gray bar: subjects who consume fish more than 7 times/ week.
Data are the mean ± S.E.M.
**and *Significantly different from that in the subjects who consume fish less than 6 times/ week at $p < 0.01$ and 0.05, respectively.

National Cholesterol Education Program（NCEP）[20)]"] was more strongly associated with the incidence of CVD than essential criteria（Japanese criteria）for abdomi-nal obesity in a general urban Japanese population[18)].

In the present study, the effect of fish intake was investigated in terms of body features and plasma levels of lipids and hemoglobin A1c for DM in healthy postmenopausal women. When the threshold for obesity in Japanese females was a WC of 90.0 cm, 24.2 % of subjects had abnormalities. BMI and WC were well correlated with a coefficient of 0.869. When the threshold for obesity was a BMI of 25 kg/m$^2$, WC was 89.9 cm. Thus, the threshold of WC for obesity in Japanese females may be around 90.0 cm, the diagnostic standard defined by the Japanese Society of Internal Medicine in 2005[18)]. There are few people in Japan who do not eat any fish. Daily intake of fish lowered the plasma levels of TG, TCh and LDL-Ch, though HDL-Ch levels in plasma were slightly elevated. Although mean values for TG, TCh, LDL-Ch and HDL-Ch were within normal limits, the subjects with high TG concentrations accounted for 16.5 %, and the subjects with high TCh and/or LDL-Ch concentrations, 30 to 40 %, of the total. However, fish consumption did not affect blood pressure in the present

study.

The American Heart Association has recommended consuming 2 fish meals (preferably oily fish) per week, which results in an intake of 400-500 mg DHA + EPA/day, though improved data are required to determine dietary intake values or ratios among EPA, DHA, and EPA + DHA[21-23]. The Japan Eicosapentaenoic acid Lipid Interventions Study, a randomized trial of 18,645 Japanese that examined the effectiveness of 1.8 g of EPA per day plus a statin in reducing CHD rates, reported that, after a follow-up of 4.5 years, the hazard ratio in the EPA versus control groups was 0.81 (95 % CI: 0.68 to 0.96) for nonfatal coronary events[10]. The Japan Public Health Center-Based Study, a 10-year prospective cohort study of 41,578 middle-aged Japanese, reported that dietary intake of marine-derived n-3 fatty acids has significant inverse associations with nonfatal coronary events[11]. As previously reported[24], plasma levels of TCh, free TCh and phospholipids were in-creased by feeding a high-fat diet in mice. However, supplementation with EPA markedly lowered plasma levels of TCh, free TCh, phospholipids and TG in mice fed a high-fat diet.

In conclusion, it was suggested that daily intake of fish lowered plasma levels of TG, TCh and LDL-Ch and slightly raised plasma HDL-Ch levels. Daily intake of fish could be recommended for postmenopausal women with high plasma levels of lipids.

## Competing interests

The authors declare that they have no competing interests.

## Authors' contributions

NEM made substantial contributions to the study's conception and the analysis of the data, carried out the medical examinations at Yokohama, and was involved in drafting the manuscript. KIK performed the statistical analysis. NAK, SUZ and KUD participated in drafting the manuscript. SAK conceived of the study, participated in its design and coordination, and helped to draft the manuscript. All authors read and approved the final draft.

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# 閉経後日本人女性への魚介類摂取のすすめ

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## 要旨

我が国の閉経後女性は閉経前女性よりも血中脂質が多く，上昇した血中脂質は循環器疾患のリスクとなる．我が国の魚介類摂取量は多く，この魚介類関連の n-3 脂肪酸摂取が循環器疾患を減少させているのかもしれない．そこで今回，横浜地域在住の 51 歳から 83 歳までの平均年齢 64.7 ± 0.7 歳の閉経後女性 91 名について健康診断を行った．身体計測，血液検査の他に食事習慣についてのアンケート調査を行った．各人からインフォームドコンセントを取り付け，今回の調査目的，調査内容は当倫理委員会にかけられた．肥満度と腹囲は強い正の相関を示した（相関係数＝ 0.869）．週 7 回以上魚介類摂取をする人（45.1 %）は，それほど摂取しない人（54.9 %）に較べて，HDL コレステロールの僅かな上昇を伴いながら，中性脂肪，総コレステロール，LDL コレステロールの下降を示していた．今回の結果からも，閉経後肥満女性の腹囲は 90 cm 以上ということになり，魚介類摂取は血中脂質を低めていた．

## キーワード

閉経後女性，高血中脂質，魚介類摂取