Original Article

Fish and meat intakes and prevalence of anemia among the Japanese elderly

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Background and Objectives: Information about an association between animal food intakes and risk of anemia is still limited. This study aimed to investigate the association between fish and meat intake and anemia risk in the Japanese elderly. **Methods and Study Design:** A nationally representative sample of 6,469 aged 65 years and over was obtained from pooled data of annual National Health and Nutritional Survey in Japan during 2002–2011. Anemia was defined as hemoglobin concentrations <13.0 g/dL in males and <12.0 g/dL in females. Logistic regression analysis, with the lowest intake tertile as the reference, was applied to estimate anemia risk for each nutrient and food group. **Results:** After adjustment for putative confounding factors, males in the highest tertile of animal protein intake had significantly lower risk of anemia than those in the lowest tertile (odds ratio (OR): 0.77; 95% confidence interval (CI): 0.63, 0.95; *p* for trend=0.017). These associations were not seen in females (OR: 0.72, 95% CI: 0.49, 1.06; *p* for trend=0.100). Multivariate analyses revealed that anemia risk (OR: 0.80; 95% CI: 0.65, 0.97; *p* for trend =0.002) was lower for males in the highest tertile of fish intake than in the lowest tertile; this effect was also observed for females (OR: 0.64; 95% CI: 0.45, 0.92; *p* for trend =0.014). In both sexes, the highest tertile of meat intake was not associated with lower anemia risk in the multivariate-adjusted models. **Conclusions:** The current cross-sectional study in Japanese elderly males suggests that higher animal protein, specifically the high protein content of fish may be associated with a lower prevalence of anemia.

Key Words: anemia, elderly, fish, meat, Japanese

INTRODUCTION

The elderly population is increasing worldwide in numbers and proportions, especially in developed countries. In Japan, the elderly, defined as individuals aged ≥65 years, is the most rapidly growing segment of the population, which is estimated to quadruple to 21 million by 2050. Collaterally, there has been a noticeable increase in the proportion of elderly individuals carrying one or more primary diseases.

Anemia is a common health problem in older populations and the prevalence of anemia is reported to increase with advancing age. In the US, the prevalence of anemia increases with advancing age,[1,2] and are reported to be much higher among older nursing home residents than among community-dwelling elderly.[3] In Japan, the only one study reported that the prevalence of anemia increased with age.[4] However, this study was not conducted in a nationally representative sample and limited the highest age category to ≤80 years. Recently, we clarified that the prevalence of anemia in community dwelling elderly aged ≥65 were about 20%, which is higher than in developed countries.[5]

Some studies have reported that anemia as one of the factors responsible for health decline among the elderly, such as the increased risk in all-cause mortality,[6-9] decline in cognitive function, dementia,[10] increased fracture risk[11] and frailty[12,13] As for “mild anemia”, only a few studies have reported the risks of mortality[14,15] in addition to cognitive, functional, mood, and quality of life outcomes.[16]

In addition, anemia is not considered a natural consequence of the aging process. Anemia in the elderly may be the result of underlying chronic conditions and nutritional deficiencies of key nutrients, such as iron, folate, and vitamin B-12. Nearly one-thirds of elderly anemia cases are due to nutrient deficiencies, according to the National Health and Nutrition Examination Survey (NHANES).[1] Iron, vitamin B-12 or folate deficiencies are common in the elderly population[1,17] and are associated with prolonged insufficient intakes of folate, vitamin B-12, and iron.[18] Animal products, particularly fish and meat, are excellent sources of vitamin B-12[19] and iron (heme iron). Furthermore, previous work has reported that malnutrition resulting from reduced intake of protein is one of the risk factors for anemia.[20] From the National Health and Nutritional Survey in Japan (NHNS),[21] daily

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vitamin B-12 intake from fish is higher than that from meat, and both fish and meat are sources of iron. Among the elderly population, only 2 studies have demonstrated associations between meat consumption and risk of anemia.[18,22] In order to promote a balanced diet in the elderly to prevent nutritional anemia, we need to identify the intakes of foods that are related to anemia risk. However, food sources of animal products may differ between Western and Asian populations, and fish consumption is much higher in Japan than in the United States (US).[23] Furthermore, the Japanese elderly aged ≥70 years tend to consume more fish but less meat.[21] However, there have been no previous studies that examined the association between fish intake and risk of anemia.

This study aimed to evaluate the association between animal food intakes and risk of anemia by using data from a very large-scale, population-based, cross-sectional study in Japan.

METHODS

Data source

We used dataset from NHNS, 2002 to 2011, which were conducted by the Ministry of Health, Labour and Welfare, Japan. The NHNS is an annual nationwide survey that covers approximately 5000 households in randomly selected census units defined by the Ministry of Health, Labour, and Welfare. It provides the largest available nationally representative sample with which to monitor dietary intakes, lifestyle factors, and selected biological indicators of Japanese people, including anthropometric measurements. The present study was approved by the Ministry of Health, Labour and Welfare, Japan.

Subjects

A total of 100,061 individuals aged ≥1 year participated in the NHNS from 2002 to 2011, and among these, 25,286 subjects aged ≥65 (range: 65–106 years) were selected for analyses in the present study. As most countries apply a retirement age of 65 years as the cutoff age for an "elderly" or "older person",[24] we also chose 65 years as the cutoff in the present study. Moreover, we excluded 18,817 subjects who had not participated in the dietary survey (n=1,448), lacked height or weight measurements (n=3,815), lacked blood hemoglobin data (n=4,667), used of Fe supplements (n=124), or did not complete the lifestyle questionnaire (n=8,763). The data from the remaining 6,469 subjects were selected for analyses in the present study.

Ethics statement

National Health and Nutrition Survey, conducted by the Ministry of Health, Labour and Welfare, Japan, have stringent protocols and procedures that ensure confidentiality and protect individual participants from being identified. The present analysis was based on secondary analysis of observational survey data. Under the Statistics Act,[25] the Ministry of Health, Labour and Welfare anonymized all individual-level data before providing the authors with the datasets for this study. No ethical review was sought based on the Ethical Guidelines for Medical and Health Research Involving Human Subjects,[26] because this present study used only information that had already been anonymized.

Lifestyle characteristics and anthropometry

The subjects reported their smoking history. "Current smokers" were those who had smoked ≥100 cigarettes in their lifetime or those who had smoked for >6 months and were also currently smoking. "Past smokers" were those who had smoked ≥100 cigarettes in their lifetime or for >6 months but were not currently smoking. The rest were defined as "never smokers." Current exercise habits were categorized into "unable to exercise because of illness", "unable to exercise because of other reasons", and "exercising regularly." Regular exercise was defined as "exercising usually for >30 min at a time on >2 days/wk." Body mass index (BMI) (kg/m^2) was calculated as body weight (kg) divided by the square of body height (m). Weight status was defined according to WHO recommendations:[27] underweight (BMI: <18.5 kg/m^2), normal weight (BMI: ≥18.5 to <25 kg/m^2), overweight (BMI: ≥25 to <30 kg/m^2), and obese (BMI: ≥30 kg/m^2). In addition, current medication status for arrhythmia and diabetes mellitus were obtained.

Dietary intakes

A weighed one-day household dietary record, with the approximate proportions by which family members share each dish was used to estimate the nutrient and food intake.[21] The nutrient intake for each family member was estimated according to the Standard Tables of Food Composition in Japan, Fifth Revised and Enlarged Edition.[28] Energy and macronutrient intake estimated using this method highly correlated to the intake estimated using individualized diet records (Pearson's correlation coefficients; r=0.89–0.91).[29] Further details regarding the methods used can be found elsewhere.[21] In the present study, energy plus 9 nutrients (carbohydrate/ total fat/ total protein/ animal protein/ plant protein/ iron/ vitamin B-12/ folate/ vitamin C) and 7 food groups (rice, bread and noodles/ vegetables/ fruits/ fish/ meat/ egg/ dairy products) were used. We included 13 food items for fish (mackerel, sardine/ salmon, trout/ sea bream, flatfish/ tuna, marlin, swordfish/ other raw fish/ shellfish/ squid, octopus/ prawn, shrimp, crab/ salted, semidried, fully dried seafood products/ canned fish products/ tsukudani/ fish paste products/ fish ham and sausage) and 9 food items for meat (beef/ pork/ ham, sausage/ other animal meat/ chicken/ poultry/ organ meat/ whale meat/ insects, frogs, and turtles). The daily intakes of fish and meat, as the total intake, were calculated as the sum of these 13 and 9 food items, respectively. Moreover, the use of iron supplements and fortified iron was evaluated.

Blood sample preparation

Blood chemistry analysis was performed using the SRL. Inc., (153 Komiya-cho, Hachioji, Tokyo, 192–0031 Japan).[30] Venous blood was drawn into the vacuum blood collection tube that contained EDTA and was drawn at least 4 h after the last meal, and stored at −4°C until delivered to the SRL. Blood was allowed to clot at room temperature and centrifuged at 1,500g for 10 min. Serum samples were divided into separate tubes and stored at

−4°C until delivered to the SRL. Inc. Blood hemoglobin was determined by the sodium lauryl sulfate (SLS)-hemoglobin method, and red blood cell and hematocrit were determined by the sheath flow direct current (DC) detection method. The values for mean corpuscular volume (MCV) were calculated according to the following formula: MCV (fL) = hematocrit (%) × 10/red blood cell count (millions/mm3 blood). MCV is defined a priori as microcytic if <80 fL, normocytic if between 80 and 100 fL, and macrocytic if >100 fL.

Definitions of anemia

In this study, anemia was defined according to the WHO definition as hemoglobin concentrations <13.0 g/dL in males and <12.0 g/dL in females.[31]

Statistical analysis

Analyses were separately performed for males and females. Results are expressed as means ± SD or medians with 25th and 75th percentiles. To compare the mean nutrient intake values along with the subjects' characteristics between the anemic and nonanemic groups, the Student's t-test was applied for continuous variables, and the chi-square test was applied for categorical variables. The Spearman's rank correlation coefficients were used to assess simple correlations between energy-adjusted dietary nutrient variables and energy-adjusted fish or meat intake. Because the blood hemoglobin values were normally distributed, the data are expressed as means and standard deviations. Food groups, and energy and nutrient intakes were skewed when all subjects were taken into consideration; therefore, Wilcoxon rank-sum test (Mann Whitney U test) was used to examine these variables.

To determine how iron, vitamin B-12, folate, fish or meat intakes were associated with anemia risk in the elderly subjects, we used multiple logistic analyses, with adjustment for putative confounding variables. Results were expressed as odds ratios (ORs; 95% CI) for associations between tertiles of iron, vitamin B-12, folate, fish or meat intakes and anemia risk. The first analysis was adjusted for age (continuous), and the second analysis was further adjusted for BMI (continuous), smoking status (current, past, or never) exercise habits (unable to exercise because of illness, unable to exercise because of other reasons, or exercise regularly), current medication status for diabetes (yes or no), survey year (continuous), and intake of energy (continuous). A trend association was assessed by assigning the ordinal numbers 0–2 to the 3 categories of iron, vitamin B-12, folate, fish or meat consumption. We tested interactions by introducing a multiplicative term into the main effect models. For all analyses, two-tailed p values <0.05 were considered to indicate statistical significance. All statistical analyses were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA).

RESULTS

The characteristics of the anemic and nonanemic groups are summarized in Table 1 according to sex. In both sexes, anemic subjects were slightly older and lesser tendency to be overweight or obese, lower serum albumin, higher tendency to be underweight, less likely to exercise, and more likely to be currently smoking, compared to non-anemic subjects. Microcytosis anemia was higher in the anemic subjects than in the nonanemic subjects (p<0.01). Conversely, there was no significant difference in mactocytosis anemia between the anemic and nonanemic subjects. However, the proportion was about 40%, which was higher than microcytosis anemia. Anemic males tended to consume less fish, meat, total energy, animal protein, iron, vitamin B-12, and folate compared with those consumed by the nonanemic males (p<0.05). In addition, the anemic females tended to consume less fish, meat, total energy, total protein, animal protein, iron, vitamin B-12, and folate compared with those consumed by the nonanemic females (p<0.05).

Anemic subjects had significantly lower intake of not only animal products, but also iron, vitamin B12 and folate, as listed in Table 1 (p<0.05). Therefore, logistic analysis was initially performed to estimate the ORs of anemia risk and intake of these nutrients (Table 2). After adjustment for putative confounding factors, males in the highest tertile of total protein (odds ratio (OR): 0.77, 95% confidence interval (CI): 0.60–0.99; p for trend=0.039) and animal protein (OR: 0.77, 95% CI: 0.63–0.95; p for trend=0.017) intake had significantly lower risk of anemia than those in the lowest tertile. These associations were not seen in females (total protein; OR: 0.80, 95% CI: 0.57–1.13; p for trend=0.984, animal protein; OR: 0.72, 95% CI: 0.49–1.06; p for trend=0.100). In males, subjects in the highest tertile of folate intake were likely to be anemic compared with subjects in the lowest tertile (p for trend=0.011) after multivariate-adjustment; in contrast, iron and vitamin B-12 intakes were not associated with anemia risk. In the multivariate-adjusted analyses, iron, vitamin B-12, and folate did not reveal any significant association with anemia risk in females.

Fish and meat intake and anemia risk is also presented in Table 3. In males, higher fish intake was significantly associated with lower anemia risk after adjusting for age (p for trend=0.002); OR for anemia in tertile 3 compared with tertile 1 was 0.75 (95% CI: 0.63, 0.90). This association remained significant even after adjustment for multivariate factors (OR: 0.80, 95% CI: 0.65, 0.97, p for trend =0.002). In females, subjects in the highest tertile of fish intake had significantly lower anemia risk after adjusting for age (OR: 0.71; 95% CI: 0.51, 0.99, p for trend=0.043) and multivariate-adjusted (OR: 0.64, 95% CI: 0.45, 0.92, p for trend=0.014). In both sexes, association was not observed between meat intake and anemia risk after adjustment for multivariate factors (male; OR: 0.88, 95% CI: 0.72, 1.06, p for trend=0.169, female; OR: 1.31, 95% CI: 0.94, 1.84, p for trend=0.114). There were no significant interactions between fish intake and age, or BMI in both sexes (p>0.20).

DISCUSSION

To our knowledge, our study is the first large-scale cross-sectional study to evaluate the effects of meat and fish intake on anemia risk in a country where the dietary sources of animal products differ from those in Western countries. This study indicated that fish intake was associated with lower anemia risk, independent of dietary energy intake and major lifestyle confounders in Japanese

Table 1. The characteristics of study participants (n=6,469)

Variable	Males (n=4,898)			Females (n=1,571)		
	Anemic†	Nonanemic	*p*–value‡	Anemic†	Nonanemic	*p*–value‡
n	933	3965		324	1247	
Age, mean±SD	76.0±6.6	72.4±5.6	<0.0001	75.7±7.0	72.3±5.7	<0.0001
Body mass index, kg/m^2, %			<0.0001			<0.0001
Underweight (<18.5)	12.6	3.6		12.7	5.5	
Normal (18.5–24.9)	72.0	64.8		64.2	58.6	
Overweight (25.0–29.9)	14.5	29.7		21.9	29.5	
Obese (≥30)	0.9	1.9		1.2	6.4	
Blood hemoglobin, g/dL, mean±SD	11.8±1.0	14.6±1.0	<0.0001	11.2±0.8	13.2±0.8	<0.0001
Hematocrit, mean±SD	37.9±3.3	45.6±3.3	<0.0001	36.5±2.7	42.4±2.7	<0.0001
MCV, fL, mean±SD	98.3±8.3	98.9±5.6	0.021	98.3±6.9	98.7±4.9	0.264
Microcytosis, <80fL (%)	3.0	0.1	<0.0001	1.9	0.0	<0.0001
Macrocytosis, >100 fL (%)	40.0	39.0	0.598	39.5	36.4	0.303
Serum albumin, g/dL, mean±SD§	4.17±0.32	4.38±0.26	<0.0001	4.21±0.28	4.38±0.26	<0.0001
Current smoking, %	23.4	29.8	0.0004	8.95	19.3	0.0040
Exercise regularly, %	40.0	43.7	<0.0001	29.6	36.8	<0.0019
Food groups, g/d¶						
Fish	86.0 (41.0, 141.6)	100.0 (50.0, 159.0)	<0.0001	73.5 (30.0, 117.5)	83.5 (40.0, 131.3)	<0.0001
Meat	38.6 (0, 80.0)	49.8 (14.0, 90.3)	<0.0001	30.0 (0.0, 68.5)	30.0 (0.0, 67.0)	<0.0001
Energy and nutrients, d¶						
Total energy, kcal	1907 (1593, 2284)	2058 (1729, 2404)	<0.0001	1597 (1305, 1925)	1660 (1379, 1978)	0.104
Total protein, g	69.8 (55.6, 86.0)	75.4 (61.1, 91.1)	<0.0001	60.3 (47.0, 76.8)	63.8 (51.2, 77.1)	0.034
Animal protein, g	33.7 (22.7, 46.6)	38.3 (27.2, 50.7)	<0.0001	29.2 (20.3, 41.4)	32.2 (22.3, 42.7)	0.029
Iron, mg	8.4 (6.5, 10.71)	8.76 (6.81, 11.10)	0.002	7.51 (5.67, 10.03)	8.00 (6.06, 10.22)	0.080
Vitamin B-12, µg	5.78 (2.76, 11.00)	6.41 (3.31, 11.76)	0.001	4.63 (1.95, 9.09)	5.18 (2.47, 9.98)	0.062
Folate, µg	336 (251, 445)	352 (261, 455)	0.043	302 (235, 415)	331 (241, 423)	0.099

NHNS: the National Health and Nutritional Survey in Japan; MCV: mean corpuscular volume.

†Anemia was defined as a hemoglobin concentrations <13.0 g/dL in males and <12.0 g/dL in females.

‡Student's t-test was used for continuous variables, and Wilcoxon rank-sum test was used for nonparametric continuous variables, and chi-square test for categorical variables, comparing anemic and nonanemic group.

§Blood albumin data is from 2003 to 2011.

¶Variables that have a skewed distribution; are shown as median (25th, and 75th percentiles).

Table 2. Odds ratios (ORs, 95% CIs) of anemia according to tertile categories of protein, animal protein, iron, vitamin B-12, folate intakes

Variables	Males				Females			
	Tertile 1 (lowest)	Tertile 2	Tertile 3 (highest)	*p* for trend†	Tertile 1 (lowest)	Tertile 2	Tertile 3 (highest)	*p* for trend†
Protein								
Intake range (mg/d)	≤61.9	62.0−81.7	≥81.8		≤62.1	62.2−81.6	≥81.7	
Number of anemia cases‡/ subjects	345/1397	297/1648	291/1853		175/759	86/509	63/303	
Age-adjusted	1.00 (Reference)	0.74 (0.62, 0.89)	0.72 (0.60, 0.86)	0.0003	1.00 (Reference)	0.82 (0.58, 1.16)	1.00 (0.63, 1.58)	0.686
Multivariate-adjusted§	1.00 (Reference)	0.76 (0.62, 0.93)	0.77 (0.60, 0.99)	0.039	1.00 (Reference)	0.84 (0.62, 1.15)	0.80 (0.57, 1.13)	0.984
Animal protein								
Intake range (μg/d)	≤28.9	29.0−43.3	≥43.4		≤28.9	29.0−43.3	≥43.4	
Number of anemia cases‡/ subjects	345/1490	309/1621	279/1787		160/666	96/536	68/369	
Age-adjusted	1.00 (Reference)	0.83 (0.69, 0.99)	0.72 (0.60, 0.86)	0.0004	1.00 (Reference)	0.78 (0.58, 1.04)	0.83 (0.60, 1.15)	0.263
Multivariate-adjusted§	1.00 (Reference)	0.87 (0.72, 1.05)	0.77 (0.63, 0.95)	0.017	1.00 (Reference)	0.71 (0.52, 0.98)	0.72 (0.49, 1.06)	0.100
Iron								
Intake range (mg/d)	≤7.24	7.25−9.91	≥9.92		≤7.23	7.24−9.91	≥9.92	
Number of anemia cases†/ subjects	329/1515	300/1659	304/1724		148/641	93/498	83/432	
Age-adjusted	1.00 (Reference)	0.88 (0.74, 1.06)	0.93 (0.78, 1.11)	0.433	1.00 (Reference)	0.84 (0.62, 1.13)	0.87 (0.64, 1.19)	0.389
Multivariate-adjusted§	1.00 (Reference)	1.00 (0.82, 1.22)	1.12 (0.90, 1.39)	0.324	1.00 (Reference)	0.73 (0.53, 1.02)	0.71 (0.48, 1.06)	0.092
Vitamin B-12								
Intake range (μg/d)	≤3.87	3.88−8.98	≥8.99		≤3.86	3.87−8.97	≥8.99	
Number of anemia cases‡/ subjects	330/1525	305/1659	298/1714		144/631	99/498	81/442	
Age-adjusted	1.00 (Reference)	0.85 (0.71, 1.01)	0.84 (0.70, 1.01)	0.060	1.00 (Reference)	0.91 (0.68, 1.23)	0.85 (0.62, 1.16)	0.302
Multivariate-adjusted§	1.00 (Reference)	0.89 (0.73, 1.07)	0.92 (0.75, 1.11)	0.376	1.00 (Reference)	0.84 (0.62, 1.15)	0.80 (0.57, 1.13)	0.202
Folate								
Intake range (μg/d)	≤284	285−406	≥407		≤284	285−406	≥407	
Number of anemia cases‡/ subjects	315/1566	292/1620	326/1712		138/591	96/536	90/444	
Age-adjusted	1.00 (Reference)	0.94 (0.78, 1.12)	1.06 (0.88, 1.26)	0.553	1.00 (Reference)	0.81 (0.60, 1.09)	0.96 (0.70, 1.30)	0.778
Multivariate-adjusted§	1.00 (Reference)	1.07 (0.88, 1.30)	1.31 (1.06, 1.61)	0.011	1.00 (Reference)	0.79 (0.57, 1.09)	0.89 (0.62, 1.28)	0.522

†On the basis of multiple logistic regression analysis, with ordinal numbers 0–2 assigned to the tertile categories of nutrient intake.
‡Anemia was defined as hemoglobin concentrations <13.0 g/dL in males and <12.0 g/dL in females.
§Adjusted for age (y, continuous), BMI (kg/m^2, continuous), and smoking status (currently smoking, past smoking, or never smokers), exercise habits (unable to exercise because of an illness, unable to exercise because of other reasons, exercise regularly), current medication status for diabetes (yes or no), survey year (y, continuous) and total energy intake (kcal/d, continuous).

Table 3. Odds ratios (ORs, 95% CIs) of anemia according to tertile categories of fish and meat intakes

Variables	Males				Females			
	Tertile 1 (lowest)	Tertile 2	Tertile 3 (highest)	p for trend†	Tertile 1 (lowest)	Tertile 2	Tertile 3 (highest)	p for trend†
Fish								
Intake range (g/d)	≤62.8	62.9−125.8	≥126.0		≤62.6	63.0−125.5	≥126.0	
Number of anemia cases‡/ subjects	344/1552	308/1601	281/1745		142/605	115/557	67/409	
Age-adjusted	1.00 (Reference)	0.85 (0.72, 1.02)	0.75 (0.63, 0.90)	0.002	1.00 (Reference)	0.89 (0.67, 1.19)	0.71 (0.51, 0.99)	0.043
Multivariate-adjusted§	1.00 (Reference)	0.87 (0.72, 1.05)	0.80 (0.65, 0.97)	0.002	1.00 (Reference)	0.82 (0.61, 1.11)	0.64 (0.45, 0.92)	0.014
Meat								
Intake range (g/d)	≤20.0	20.3−66.9	≥67.0		≤20.0	20.1−66.7	≥67.0	
Number of anemia cases‡/ subjects	337/1575	307/1562	289/1761		134/655	108/521	82/395	
Age-adjusted	1.00 (Reference)	0.95 (0.80, 1.14)	0.83 (0.69, 0.99)	0.038	1.00 (Reference)	1.14 (0.85, 1.53)	1.22 (0.88, 1.68)	0.229
Multivariate-adjusted§	1.00 (Reference)	0.94 (0.78, 1.13)	0.88 (0.72, 1.06)	0.169	1.00 (Reference)	1.15 (0.85, 1.56)	1.31 (0.94, 1.84)	0.114

†On the basis of multiple logistic regression analysis, with ordinal numbers 0–2 assigned to the tertile categories of nutrient intake.
‡Anemia was defined as hemoglobin concentrations <13.0 g/dL in males and <12.0 g/dL in females.
§Adjusted for age (y, continuous), BMI (kg/m2, continuous), and smoking status (currently smoking, past smoking, or never smokers), exercise habits (unable to exercise because of an illness, unable to exercise because of other reasons, exercise regularly), current medication status for diabetes (yes or no), survey year (y, continuous) and total energy intake (kcal/d, continuous).

elderly.

To date, there is no information on fish consumption and anemia risk despite the fact that fish are major animal food sources among the Japanese elderly population. In the current study, the association between fish intake and anemia risk was observed. The sources of animal product intake vary among different ethnic groups. In Western countries, the major sources of animal products are meat and poultry,[32,33] whereas Asian populations, particularly the Japanese elderly, tend to consume more fish but less meat.[21] According to NHANES conducted in the US, daily intake of fish is lower (mean intake, 14.2 g/d) compared with that of red meat and poultry (mean intake, 69.9 g/d).[32] In the current study, the elderly Japanese subjects consumed approximately 2-times higher amounts of fish than of meat. Fish was the main food source of animal protein among the study subjects. Borrelli et al[34] demonstrated that in a rat model of protein energy malnutrition, anemia is not caused by iron deficiency or erythropoietin deficiency, but rather ineffective erythropoiesis, with a slow-down in protein synthesis in erythroid cells and/or a reduction in erythropoietin synthesis.

The association between animal protein intake and low risk of anemia was observed only in males in this study. Review study suggested that loss of skeletal muscle mass in elderly may lead to greater risk of anemia.[20] Loss of skeletal muscle mass with age was greater in males than in females.[35,36] These data support our results. Higher animal protein, specifically the high protein content of fish intake appeared to be related to preservation of skeletal muscle mass and was associated to a greater degree with lower risk of anemia in males than in females.

We also clarified that intake of anemia-related nutrients except for folate in male were not associated with anemia risk. Moreover, adjustment for these nutrient factors did not significantly modify our findings regarding fish/meat intake and anemia risk. An observational study reported that multiple anemia-related nutrient inadequacies are common among elderly American women, such as iron, vitamin B-12, and folate.[18] Microcytic anemia occurs in iron deficiency, and macrocytic anemia occurs in vitamin B-12 or folate deficiency. In this present study targeting the community-dwelling elderly, microcytosis and macrocytosis anemia did not differ between the anemia and nonanemia group. Fish contains significant amounts of animal protein rather than in these anemia-related nutrients. Therefore, it is possible that not vitamins but animal protein intake may be related to lower anemia risk, and animal protein intakes helpful in preventing anemia in elderly populations.

Results of previous studies, which examined the association between meat intake and risk of anemia of postmenopausal females in the US,[18] are not consistent with the present findings. A similar association between blood hemoglobin concentrations and meat consumption was observed in a study population in Brazil, where meat is consumed as a major source of animal food.[22] These studies were conducted in countries with high meat consumption, and we do not possess any data reported for studies in countries with high fish intakes such as Norway, Finland, and Korea. In the current study, meat intake was much lower compared with that in Western countries, therefore, meat intake was not significantly associated with lower anemia risk.

The strength of this study includes our large sample size, which was a population-based study. However, there were several limitations as well. First, cross-sectional studies are not designed to establish causal relations. Nutrient and food intake data may not be representative of habitual dietary intake because they do not reveal day-to-day variations that would normally occur. Second, the data accessible from the government were not the original raw data but the results of a compilation of nutrient and food items at the individual level. Therefore, we could not calculate the heme iron intakes from fish and red meat intakes and assess the relationship between anemia risk and these intakes. Third, there are four seasons in Japan, and the food consumed varies according to the season. The effect of seasonal variation is considered because the study was performed in November (Fall). Ogawa et al[37] reported seasonal variation using 3-day food records in four seasons among elderly populations. The ratio of the within-person variance (CVw%) was largest for retinol (261%), and large in vitamin C (52%), although for proteins (23%), it was small. Therefore, seasonal variations are small in protein sources of meat and fish. Fourth, for the selection of subjects in this study, participants of the NHNS were dispatched to each venue in principle because of the low number of testers for body measurements, especially for blood tests. Therefore, there is a possibility of selection bias. Finally, although we measured and adjusted for possible confounding variables, the NHNS data do not include socioeconomic status, and health factors that can affect anemia, including cancer,[38] inflammatory bowel disease,[39] and kidney disease,[1] factors which could not be ruled out in the present study.

In conclusion, in this large-scale population-based study in Japanese elderly male subjects whose fish intakes were higher compared with those of the different Western populations. Besides, the lower risk of anemia is likely explained to the intake of animal protein, specifically the high protein content of fish. Sufficient animal protein intake may have a positive effect on red blood cell formation and reduces the risk of malnutrition and anemia.

AUTHOR DISCLOSURES

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