食塩摂取量と血圧の関連：　NIPPON DATA80 のベースライン分析

研究分担者　三浦　克之　（滋賀医科大学社会医学講座公衆衛生学部門　教授）
研究分担者　奥田　奈賀子（財団法人結核予防会第一健康相談所　医員）
研究協力者　Tanvir C. Turin（滋賀医科大学社会医学講座公衆衛生学部門　特別研究員）
研究協力者　高嶋　直敬　（滋賀医科大学社会医学講座公衆衛生学部門　特任助教）
研究分担者　中川　秀昭　（金沢医科大学健康増進予防医学　教授）
研究協力者　中村　幸志　（金沢医科大学健康増進予防医学　講師）
研究分担者　由田　克士　（国立健康・栄養研究所栄養疫学ﾌﾟﾛｸﾞﾗﾑ　ﾌﾟﾛｼﾞｪｸﾄﾘｰﾀﾞｰ）
研究分担者　岡山　明　　（財団法人結核予防会第一健康相談所　所長）
研究代表者　上島　弘嗣　（滋賀医科大学生活習慣病予防センター　特任教授）

【目的】　本邦の高血圧者は約 4000 万人にのぼり、循環器疾患の危険因子として極めて重要である。1980 年実施の第 3 次循環器疾患基礎調査受診者の追跡研究である NIPPON DATA80 は、基本的な生活習慣や検査結果と生命予後の関連を明らかにするものとして重要な研究成果をあげてきたが、食事要因については十分な栄養摂取状況の把握はできていなかった。本邦では血圧に影響する生活習慣因子として食塩過剰摂取が重要であるが、詳細な栄養調査に基づいた食塩摂取量と血圧値の関連について検討した大規模研究はほとんどない。本研究では NIPPON DATA80 対象者が同時に受検した 1980 年国民栄養調査の統合データセットを用いて、食塩摂取量と血圧の関連を検討した。

【方法】　NIPPON DATA80 と国民栄養調査統合データセットより、30 歳以上の男女 10,422 名（男性 4,585、女性 5,837 名）を対象とした。食塩摂取量ほか栄養素摂取量は、国民栄養調査結果の世帯分摂取量を、性・年齢を考慮して案分計算したものを対象者個人の摂取量とした。国民栄養調査では食品の摂取量は秤量記録法により調査された。男女別に食塩摂取量五分位を作成し、五分位における多変量調整後の平均値（年齢(歳)、BMI(kg/m^2)、飲酒習慣の有無、カリウム摂取量(mg/日)、総エネルギー摂取量(kcal/日)を調整）を共分散分析により計算し多重比較を行った。

【結果】平均食塩摂取量は、男性で 15.1g/日、女性で 13.0g/日であった。食塩摂取量の第 1 五分位の平均食塩摂取量は男性で 8.7g/日、女性で 7.6g/日、第 5 五分位では男性で 23.5g/日、女性で 20.2g/日であった。男女ともに、食塩摂取量五分位と年齢に一定の傾向を認めなかった。食塩摂取量が多い群ほど BMI は高値であり、カリウム摂取量、総摂取エネルギーは多かった。調整平均血圧は、男性では収縮期血圧（SBP）、拡張期血圧（DBP）ともに食塩摂取量が多い群ほど高くなる傾向を示したが、女性では五分位間で有意差はなかった。

SBP では調整平均値の第 1 五分位と第 5 五分位の差は、4.3mmHg であった(第 1 五分位と第 4、5 五分位の差がそれぞれ有意(ともに p<0.001))。DBP では 1.3mmHg だった(第 1 五分位と第 4、5 五分位の差がそれぞれ有意(p=0.035, p=0.047))。高血圧既往有りのものと降圧剤内服中の者を除いた解析でも結果は同様の傾向にあった。

【結論】NIPPON DATA80 国民栄養調査統合データセットにおいて、追跡対象者のベースライン時の食塩摂取量が多いほど、特に男性において収縮期血圧が高かった。我が国を代表する一般集団において、詳細な栄養調査より得た食塩摂取量と血圧値との正の関連が示された。

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Dietary Salt Intake and Blood Pressure in a Representative Japanese Population: Baseline Analyses of NIPPON DATA80

Katsuyuki Miura[1], Nagako Okuda[1], Tanvir Chowdhury Turin[1], Naoyuki Takashima[1], Hideaki Nakagawa[2], Koshi Nakamura[2], Katsushi Yoshita[3], Akira Okayama[4], and Hirotsugu Ueshima[1], for the NIPPON DATA80/90 Research Group

[1]Department of Health Science, Shiga University of Medical Science, Ohtsu, Japan
[2]Department of Epidemiology and Public Health, Kanazawa Medical University, Ishikawa, Japan
[3]Nutritional Epidemiology Program, National Institute of Health and Nutrition, Tokyo, Japan
[4]First Institute of Health Service, Japan Anti-Tuberculosis Association, Tokyo, Japan

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ABSTRACT

Background: The relationship between dietary salt intake and blood pressure (BP) has been rarely investigated in a large population of Japanese. The characteristics of nutrients intake and foods intake in Japanese people with high salt intake have also not investigated well.

Methods: Data of 10 422 participants (4585 men and 5837 women) aged 30 or older who participated in both the National Survey on Circulatory Disorders and National Nutrition Survey in Japan conducted in 1980 were used. The nutrition surveys were performed with weighing record method for three consecutive days to each household. BP and intakes of nutrients and foods were compared by the quintiles of estimated individual salt intake per day. Analyses of covariance were used to calculate multivariate-adjusted mean BP values by the quintiles.

Results: Participants with higher salt intake showed higher intakes of soy beans/legume, fruit, other vegetables, and fish/shellfish. Intakes of protein, potassium, calcium, iron, magnesium, and fiber were higher in higher quintiles of salt intake. In men, adjusted systolic BPs were higher in the higher salt intake quintiles; there was 4.3 mm Hg difference in multivariate-adjusted systolic BP between the lowest quintile (mean salt intake 8.7 g/day) and the highest quintile (mean salt intake 23.5 g/day) ($P < 0.001$). In women, adjusted mean systolic BPs were not statistically different among the quintile of salt intake.

Conclusions: A positive relationship of dietary salt intake to BP was observed, especially in men, in this large-scale representative Japanese population.

Key words: salt intake; nutrient intake; food intake; blood pressure

The causal relationship between high salt (sodium chloride) intake and high blood pressure (BP) is now established worldwide. Evidence includes results from animal studies, epidemiological studies, clinical trials, and meta-analysis of trials. A salt-reduced diet is an established method to prevent and treat hypertension, and has been recommended in several guidelines for the treatment and prevention of hypertension.[1–5]

Japan has been one of the countries with high salt intake. In 1960, Dahl reported an ecological study on the relationship between salt intake and BP in various populations in the world, and, in this report, people living in northern Japan consumed about 30 g of salt per day and had the highest prevalence of hypertension.[6] The main reason of a dramatic decrease in population-wide BP level in the past several decades in Japan is considered to be a marked decrease in salt intake in the whole Japanese population. However, the intra-population relationship between dietary salt intake and BP in Japan has been rarely investigated, mainly because high quality assessment of the amount of dietary salt intake is difficult in a large-scale epidemiological study.

The National Nutritional Survey of Japan (NNSJ) was initiated in 1946, and, recently, the survey has been conducted once every year.[7] This survey has been performed using weighing record method for three consecutive days to each household. From this survey, high quality data on dietary salt intake are available in a large-scale sample of representative Japanese from 300 randomly selected districts in Japan. The majority of the participants for NNSJ also participated in the National Survey on Circulatory Disorders conducted every 10 years. Cohort studies based on the National Survey on Circulatory Disorders in 1980 and 1990 were names as the National Integrated Project for Prospective Observation of

Address for correspondence. Dr. Katsuyuki Miura, Department of Health Science, Shiga University of Medical Science, Seta-Tsukinowa-cho, Otsu 520-2192, Japan (e-mail: miura@belle.shiga-med.ac.jp).

Non-communicable Disease and Its Trends in the Aged (NIPPON DATA80 and NIPPON DATA90).[8,9]

In the present report, we investigated the relationship of dietary salt intake to BP and to intakes of nutrients and foods in a large-scale representative Japanese using the baseline data of NIPPON DATA80, where high-quality data on dietary salt intake from NNSJ are available.

METHODS

Participants

The participants in this cohort were those in the 1980 National Survey on Circulatory Disorders.[10] A total of 10 546 community-based participants aged 30 years and over in 300 randomly selected health districts throughout Japan participated in the survey, which consisted of history-taking, physical examinations, blood tests and self-administered questionnaires on lifestyle. Overall recruited population aged 30 years and over in the 300 participating health districts was 13 771; therefore, the participation rate of the survey was 76.6%.

Baseline examination

At baseline, non-fasting blood samples were obtained. The serum was separated and centrifuged soon after blood coagulation. These samples were shipped to one labolatory (SRL, Tokyo) for blood chemistry measurements. Serum total cholesterol was measured enzymatically. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m). Baseline BP was measured by trained observers using a standard mercury sphygmomanometer on the right arm of seated participants. History of hypertension was asked whether participants were told as having hypertension by health professionals in the past. Participants were also asked whether they are treated by antihypertensive medicine at present.

Nutritional survey

Detailed methods of the nutritional survey and the estimation of individual intake of nutrients and food groups were described elsewhere.[7,11] Food intake survey by weighed food records in three consecutive representative days were conducted by specially trained dietary interviewers. Dietary interviewers visited participants' houses at least once during the survey. Weekends and holydays were avoided. Nutrient intakes were calculated using Standard Tables for Food Composition in Japan, 3rd revised edition, were used for NNSJ80. Detailed nutrient intakes; e.g. fatty acid, cholesterol, etc., were calculated using representative nutrient compositions for food groups utilizing results from dietary survey in Japan conducted for an international cooperative epidemiological study.[11]

Nutrient intakes of each household member were estimated by dividing household intake data of NNSJ80 conducted in 1980 proportionally using average intakes by sex and age groups calculated for NNSJ95 conducted in 1995.[12] The average intakes in NNSJ95 were calculated by a combination method of household-based food weighing record and an approximation of proportions by which family members shared each dish or food in the household. For each person, means of the estimated individual nutrients from the three days records were used in the analyses.

Statistical analyses

The number of participants for analysis was 10 422 (4585 men and 5837 women) who had complete data. Analyses were done in men and in women separately. Characteristics and the intakes of various nutrients and food groups were compared by the quintiles of dietary salt intake (g/day). *P* for trend of mean values by the quintiles was calculated to examine a linear relationship, using the median of each quintile. Adjusted mean values of BP by the quintiles were calculated by the analysis of covariance, and multiple comparison tests were done compared with the lowest quintile of salt intake. Mean BP (systolic and diastolic) values were adjusted for age (model 1); for age, BMI (kg/m^2), current drinking, potassium intake (mg/day), and total energy intake (kcal/day) (model 2); and for age, BMI (kg/m^2), current drinking, total energy intake (kcal/day), vegetable intake (the sum of green and yellow vegetable and other vegetable) (g/day), fruit intake (g/day) and fish/shellfish intake (g/day) (model 3). The analyses were done in all participants and in participants without history of hypertension and antihypertensive treatment.

RESULTS

Characteristics by the quintiles of salt intake

Mean values or proportion of each characteristic by the quintile of dietary salt intake (g/day) are shown in Table 1 for men and in Table 2 for women. In men, the mean salt intake was 8.7 g/day in the lowest quintile, 14.3 g/day in the middle quintile and 23.5 g/day in the highest quintile. Mean age and height were not different among the quintiles, but mean weight and BMI were significantly higher in higher quintiles. Participants with higher salt intake were significantly higher in drinking rate, systolic BP (SBP), and diastolic BP (DBP). SBP in the highest quintile was 2.9 mm Hg higher than that in the lowest quintile; DBP was 1.8 mm Hg higher.

In women, the mean salt intake was 7.6 g/day in the lowest quintile, 12.2 g/day in the middle quintile and 20.2 g/day in the highest quintile, which were 1.1 to 3.3 grams lower than men. Mean age, height, weight, and BMI were higher in higher quintiles of salt intake (Table 2). Mean SBP and DBP were not different among the quintiles.

Table 1. Characteristics and the intake of nutrients and food groups according to the quintiles of salt intake in men: NIPPON DATA80

	Quintiles of salt intake (range [g/day])					*P* for trend
	<10.8	10.8–13.1	13.1–15.5	15.5–18.8	18.8≤	
Number of participants	917	917	917	917	917	
Salt intake (g/day)	8.7 (1.8)	12.0 (0.7)	14.3 (0.7)	17.0 (1.0)	23.5 (4.9)	
Age (year)	50.6 (14.9)	49.9 (13.7)	50.0 (13.3)	49.7 (12.8)	49.6 (12.0)	0.155
Height (cm)	162.3 (6.7)	162.4 (7.0)	162.5 (6.5)	162.1 (6.7)	161.6 (6.6)	0.554
Weight (kg)	58.4 (9.3)	59.1 (9.1)	59.5 (9.1)	59.7 (9.2)	59.9 (9.2)	<0.001
Body mass index (kg/m^2)	22.1 (3.0)	22.3 (2.8)	22.5 (2.9)	22.7 (2.8)	22.9 (2.8)	<0.001
Current smoking (%)	61.5	64.7	62.1	61.2	65.7	0.172[a]
Current drinking (%)	68.7	74.6	74.8	75.8	77.3	<0.001[a]
Systolic blood pressure (mm Hg)	137.1 (21.6)	137.5 (21.6)	137.6 (20.8)	139.5 (21.0)	140.0 (20.7)	0.021
Diastolic blood pressure (mm Hg)	82.6 (12.4)	83.2 (12.7)	83.0 (12.4)	84.3 (12.5)	84.4 (12.1)	0.010
Serum total cholesterol (mg/dl)	188.3 (32.3)	187.9 (32.9)	186.8 (32.7)	186.3 (32.1)	182.1 (34.4)	0.143
Blood glucose (mg/dl)	132.6 (38.9)	128.1 (34.3)	128.9 (31.1)	132.3 (44.2)	133.2 (38.6)	0.991
History of hypertension (%)	20.5	19.2	21.1	21.7	22.2	0.560[a]
Antihypertensive treatment (%)	14.3	11.0	13.5	13.4	13.8	0.351[a]
Nutrient intake						
Total energy (kcal)	2072 (438)	2263 (385)	2415 (402)	2513 (439)	2743 (557)	<0.001
Carbohydrate (%kcal)	60.3 (7.0)	60.0 (6.2)	59.4 (6.3)	59.6 (6.1)	59.4 (6.6)	0.003
Protein (%kcal)	14.4 (2.3)	14.9 (1.8)	15.1 (1.9)	15.2 (2.0)	15.7 (2.3)	<0.001
Fat (%kcal)	20.1 (5.4)	19.9 (5.0)	20.3 (5.1)	20.0 (5.0)	19.6 (5.5)	0.914
Animal protein (%kcal)	8.5 (2.9)	8.6 (2.3)	8.7 (2.2)	8.7 (2.3)	8.8 (2.6)	0.041
Vegetable protein (%kcal)	6.9 (1.0)	7.2 (0.9)	7.2 (0.9)	7.4 (0.9)	7.6 (1.0)	<0.001
Saturated fatty acids (%kcal)	5.8 (1.6)	5.7 (1.4)	5.8 (1.5)	5.6 (1.4)	5.4 (1.5)	0.006
Monounsaturated fatty acids (%kcal)	7.6 (2.0)	7.4 (1.9)	7.6 (1.9)	7.4 (1.9)	7.2 (2.1)	0.234
Polyunsaturated fatty acids (%kcal)	5.2 (1.3)	5.2 (1.3)	5.3 (1.3)	5.3 (1.4)	5.4 (1.6)	0.046
n-3 fatty acid (%kcal)	1.0 (0.3)	1.1 (0.3)	1.1 (0.3)	1.1 (0.3)	1.2 (0.4)	<0.001
Dietary cholesterol (mg/1000 kcal)	164 (68)	166 (54)	167 (53)	163 (52)	164 (54)	0.957
Potassium (mg/1000 kcal)	1168 (229)	1252 (220)	1269 (228)	1301 (227)	1381 (243)	<0.001
Calcium (mg/1000 kcal)	211 (62)	225 (58)	228 (58)	234 (58)	250 (59)	<0.001
Iron (mg/1000 kcal)	5.6 (1.0)	6.1 (1.0)	6.2 (1.0)	6.5 (1.1)	7.1 (1.2)	<0.001
Phosphorus (mg/1000 kcal)	564 (80)	575 (63)	580 (64)	586 (66)	601 (72)	<0.001
Magnesium (mg/1000 kcal)	126 (18)	134 (17)	137 (18)	141 (19)	149 (21)	<0.001
Vitamin A (IU/1000 kcal)	697 (315)	748 (316)	742 (317)	717 (313)	727 (318)	0.248
Vitamin B1 (mg/1000 kcal)	0.48 (0.17)	0.47 (0.16)	0.48 (0.17)	0.49 (0.16)	0.48 (0.15)	0.125
Vitamin B2 (mg/1000 kcal)	0.38 (0.11)	0.40 (0.10)	0.41 (0.10)	0.41 (0.10)	0.42 (0.10)	<0.001
Vitamin C (mg/1000 kcal)	43.1 (19.3)	47.1 (18.4)	47.3 (18.0)	46.2 (17.2)	47.9 (18.1)	<0.001
Fiber (g/1000 kcal)	6.9 (1.7)	7.5 (1.6)	7.6 (1.7)	7.8 (1.8)	8.3 (1.8)	<0.001
Food intake						
Cereals (g/1000 kcal)	170.3 (32.5)	163.2 (30.3)	159.0 (28.8)	156.7 (27.7)	151.6 (30.4)	<0.001
Rice (g/1000 kcal)	130.6 (36.5)	125.9 (34.5)	124.7 (35.3)	125.5 (32.2)	125.2 (34.3)	0.001
Flour (g/1000 kcal)	41.5 (29.4)	39.4 (25.5)	36.9 (23.8)	34.3 (22.9)	30.0 (21.8)	<0.001
Nuts (g/1000 kcal)	0.4 (1.5)	0.5 (1.5)	0.5 (1.4)	0.6 (1.7)	0.6 (2.4)	0.042
Potatoes (g/1000 kcal)	23.5 (18.7)	28.7 (20.4)	28.2 (18.4)	28.1 (17.8)	29.9 (20.4)	<0.001
Sugar/sweetener (g/1000 kcal)	5.1 (3.7)	5.7 (4.1)	5.7 (3.6)	6.0 (4.0)	6.1 (4.8)	<0.001
Sweet/snacks (g/1000 kcal)	5.9 (7.7)	6.1 (6.8)	6.4 (7.2)	6.8 (6.7)	6.5 (7.5)	0.005
Fats/oils (g/1000 kcal)	7.3 (4.1)	7.0 (4.2)	7.5 (4.4)	7.0 (4.2)	6.8 (4.9)	0.567
Soy beans/legume (g/1000 kcal)	29.2 (21.1)	33.8 (22.5)	34.7 (20.0)	35.7 (19.5)	40.1 (21.0)	<0.001
Fruit (g/1000 kcal)	52.5 (41.2)	59.7 (39.5)	62.1 (39.2)	60.0 (39.0)	61.0 (39.7)	<0.001
Green and yellow vegetables (g/1000 kcal)	23.1 (17.0)	24.1 (16.0)	24.4 (16.8)	23.5 (16.0)	24.0 (17.0)	0.547
Other vegetables (g/1000 kcal)	83.0 (33.5)	91.3 (36.6)	92.7 (33.6)	100.8 (38.1)	115.5 (45.7)	<0.001
Mushrooms (g/1000 kcal)	3.8 (5.2)	3.8 (5.3)	3.9 (4.9)	4.7 (5.9)	4.5 (6.0)	<0.001
Sea algae (g/1000 kcal)	1.8 (2.0)	2.3 (3.0)	2.7 (3.4)	3.0 (3.7)	3.6 (4.4)	<0.001
Condiment/beverage (g/1000 kcal)	74.8 (95.2)	77.9 (67.8)	81.0 (68.7)	85.2 (70.2)	92.5 (69.9)	0.002
Fish/shellfish (g/1000 kcal)	47.2 (24.1)	50.3 (24.3)	51.4 (24.0)	53.7 (23.6)	58.9 (29.7)	<0.001
Meat (g/1000 kcal)	31.6 (19.3)	29.7 (15.5)	30.7 (16.4)	29.5 (15.3)	26.0 (15.1)	0.026
Egg (g/1000 kcal)	17.6 (11.4)	18.0 (9.5)	17.8 (9.2)	16.4 (9.0)	16.0 (8.5)	0.008
Milk/dairy products (g/1000 kcal)	35.0 (30.3)	32.3 (24.3)	31.3 (24.5)	28.0 (21.7)	25.1 (22.3)	<0.001
Other foods (g/1000 kcal)	2.9 (9.9)	2.7 (5.9)	2.9 (7.0)	2.8 (5.6)	2.8 (5.5)	0.998

Values are mean (standard deviation) or proportion (%).
[a]*P* values by chi-square test.

Nutrients and foods intake by the quintiles of salt intake

In men, total energy intake was significantly higher in higher quintiles of salt intake (Table 1). Intakes of protein (%kcal), potassium (mg/1000 kcal), calcium (mg/1000 kcal), iron (mg/1000 kcal), phosphorus (mg/1000 kcal), magnesium

Table 2. Characteristics and the intake of nutrients and food groups according to the quintiles of salt intake in women: NIPPON DATA80

	Quintiles of salt intake (range [g/day])					*P* for trend
	<9.2	9.2–11.2	11.2–13.3	13.3–16.2	16.2≤	
Number of participants	1167	1168	1167	1168	1167	
Salt intake (g/day)	7.6 (1.4)	10.2 (0.6)	12.2 (0.6)	14.6 (0.8)	20.2 (4.1)	
Age (year)	50.5 (14.9)	49.4 (13.9)	49.3 (13.0)	49.4 (12.9)	51.6 (12.4)	0.043
Height (cm)	149.9 (6.3)	150.4 (6.4)	150.5 (5.9)	150.2 (6.2)	149.5 (6.1)	0.029
Weight (kg)	50.4 (8.6)	51.7 (8.4)	51.2 (7.9)	51.7 (8.2)	52.2 (8.3)	0.004
Body mass index (kg/m^2)	22.4 (3.4)	22.9 (3.5)	22.6 (3.3)	22.9 (3.3)	23.4 (3.3)	0.011
Current smoking (%)	13.0	8.8	10.1	7.8	9.3	<0.001[a]
Current drinking (%)	19.2	22.6	22.4	18.8	18.6	0.022[a]
Systolic blood pressure (mm Hg)	133.7 (23.1)	133.7 (22.8)	132.7 (21.3)	133.9 (21.3)	134.9 (21.1)	0.894
Diastolic blood pressure (mm Hg)	79.1 (12.6)	79.2 (12.3)	79.1 (12.0)	79.5 (11.4)	80.7 (12.3)	0.413
Serum total cholesterol (mg/dl)	193.3 (34.2)	192.0 (34.9)	190.4 (34.8)	191.0 (33.1)	188.7 (34.4)	0.066
Blood glucose (mg/dl)	127.6 (37.3)	128.8 (35.2)	127.7 (28.9)	129.8 (31.3)	131.9 (35.3)	0.223
History of hypertension (%)	19.7	20.9	18.0	19.9	22.2	0.177[a]
Antihypertensive treatment (%)	14.6	15.0	13.1	14.6	16.4	0.331[a]
Nutrient intake						
Total energy (kcal)	1673 (348)	1823 (314)	1934 (325)	2020 (348)	2198 (454)	<0.001
Carbohydrate (%kcal)	62.6 (7.3)	62.0 (6.5)	61.7 (6.9)	62.0 (6.4)	62.1 (6.9)	0.017
Protein (%kcal)	14.8 (2.1)	15.3 (1.9)	15.5 (1.9)	15.6 (2.1)	16.2 (2.2)	<0.001
Fat (%kcal)	21.9 (6.1)	21.9 (5.5)	22.1 (5.8)	21.7 (5.6)	21.0 (5.9)	0.782
Animal protein (%kcal)	8.7 (2.8)	8.9 (2.3)	8.9 (2.4)	8.9 (2.4)	9.0 (2.7)	0.022
Vegetable protein (%kcal)	7.2 (1.0)	7.3 (0.9)	7.4 (1.0)	7.6 (0.9)	7.9 (1.1)	<0.001
Saturated fatty acids (%kcal)	6.4 (1.8)	6.3 (1.6)	6.3 (1.7)	6.1 (1.6)	5.8 (1.6)	0.005
Monounsaturated fatty acids (%kcal)	8.2 (2.3)	8.2 (2.0)	8.3 (2.2)	8.1 (2.1)	7.8 (2.3)	0.239
Polyunsaturated fatty acids (%kcal)	5.6 (1.5)	5.7 (1.4)	5.8 (1.5)	5.8 (1.5)	5.8 (1.6)	0.006
n-3 fatty acid (%kcal)	1.1 (0.4)	1.2 (0.4)	1.2 (0.4)	1.2 (0.4)	1.3 (0.4)	<0.001
Dietary cholesterol (mg/1000 kcal)	178 (69)	180 (56)	180 (56)	178 (59)	178 (62)	0.955
Potassium (mg/1000 kcal)	1328 (266)	1398 (244)	1437 (262)	1471 (260)	1579 (294)	<0.001
Calcium (mg/1000 kcal)	253 (68)	268 (67)	275 (65)	281 (68)	302 (73)	<0.001
Iron (mg/1000 kcal)	6.2 (1.1)	6.7 (1.1)	6.9 (1.1)	7.3 (1.2)	8.0 (1.4)	<0.001
Phosphorus (mg/1000 kcal)	588 (75)	599 (68)	605 (67)	610 (71)	629 (76)	<0.001
Magnesium (mg/1000 kcal)	135 (20)	141 (19)	146 (20)	149 (21)	160 (24)	<0.001
Vitamin A (IU/1000 kcal)	838 (410)	861 (356)	866 (372)	852 (365)	867 (397)	0.335
Vitamin B1 (mg/1000 kcal)	0.59 (0.20)	0.59 (0.19)	0.61 (0.21)	0.60 (0.19)	0.59 (0.19)	0.041
Vitamin B2 (mg/1000 kcal)	0.56 (0.16)	0.56 (0.15)	0.57 (0.15)	0.56 (0.14)	0.59 (0.15)	0.046
Vitamin C (mg/1000 kcal)	57.7 (26.0)	60.4 (22.8)	62.1 (23.4)	61.3 (22.7)	65.0 (25.0)	<0.001
Fiber (g/1000 kcal)	8.4 (2.0)	8.9 (1.8)	9.2 (1.9)	9.4 (2.0)	10.1 (2.2)	<0.001
Food intake						
Cereals (g/1000 kcal)	164.0 (30.9)	157.4 (29.8)	153.5 (28.6)	151.7 (26.8)	145.8 (29.4)	<0.001
Rice (g/1000 kcal)	113.9 (35.3)	108.6 (32.8)	107.0 (32.9)	107.2 (30.6)	109.0 (32.0)	<0.001
Flour (g/1000 kcal)	49.1 (31.7)	47.2 (29.9)	45.0 (28.5)	42.7 (27.0)	35.0 (25.2)	<0.001
Nuts (g/1000 kcal)	0.7 (2.4)	0.8 (2.6)	0.8 (2.3)	0.9 (2.8)	0.9 (2.7)	0.047
Potatoes (g/1000 kcal)	30.0 (23.0)	32.9 (22.7)	33.5 (21.7)	34.5 (23.0)	36.7 (26.2)	<0.001
Sugar/sweetener (g/1000 kcal)	6.2 (4.5)	6.5 (4.7)	6.7 (4.4)	7.1 (4.7)	7.4 (5.5)	<0.001
Sweet/snacks (g/1000 kcal)	11.9 (13.5)	12.8 (12.6)	13.5 (13.4)	14.6 (13.9)	13.9 (14.8)	<0.001
Fats/oils (g/1000 kcal)	8.1 (4.6)	8.0 (4.5)	8.3 (4.8)	7.9 (4.8)	7.4 (5.1)	0.712
Soy beans/legume (g/1000 kcal)	32.3 (23.4)	35.6 (23.0)	37.0 (21.5)	38.6 (21.1)	43.3 (22.5)	<0.001
Fruit (g/1000 kcal)	85.0 (60.4)	93.5 (54.6)	101.1 (59.3)	98.4 (59.3)	102.4 (65.9)	<0.001
Green and yellow vegetables (g/1000 kcal)	30.4 (22.9)	30.2 (19.4)	30.7 (20.9)	30.6 (20.6)	31.5 (23.2)	0.713
Other vegetables (g/1000 kcal)	94.8 (39.3)	102.5 (39.8)	105.8 (40.2)	112.0 (41.7)	132.5 (50.5)	<0.001
Mushrooms (g/1000 kcal)	4.1 (5.7)	4.3 (5.9)	4.6 (5.7)	5.2 (6.4)	5.2 (6.6)	<0.001
Sea algae (g/1000 kcal)	2.1 (2.7)	2.7 (3.4)	3.1 (3.9)	3.7 (4.7)	4.3 (5.4)	<0.001
Condiment/beverage (g/1000 kcal)	31.4 (56.5)	33.7 (33.1)	35.5 (30.9)	35.5 (31.9)	39.7 (43.4)	0.008
Fish/shellfish (g/1000 kcal)	45.5 (23.4)	48.5 (23.6)	49.4 (23.3)	51.4 (23.2)	56.9 (27.7)	<0.001
Meat (g/1000 kcal)	29.3 (16.9)	28.7 (15.2)	28.9 (16.1)	27.5 (14.7)	25.1 (16.3)	0.016
Egg (g/1000 kcal)	19.2 (12.2)	19.1 (9.7)	18.7 (9.4)	17.9 (9.9)	17.0 (9.9)	0.001
Milk/dairy products (g/1000 kcal)	52.7 (41.1)	50.9 (37.5)	49.0 (35.5)	45.7 (33.6)	38.8 (34.3)	<0.001
Other foods (g/1000 kcal)	3.0 (8.2)	3.3 (7.3)	3.1 (6.6)	3.2 (6.6)	3.2 (6.3)	0.603

Values are mean (standard deviation) or proportion (%).
[a]*P* values by chi-square test.

(mg/1000 kcal), vitamin B2 and C (mg/1000 kcal), and fiber (g/1000 kcal) were higher in higher quintiles. Total fat intake (%kcal) was not different among the quintiles. Results for these nutrients were similar in women (Table 2).

Men with higher salt intake showed higher intakes (g/1000 kcal) of potatoes, sugar/sweetener, soy beans/

Table 3. Adjusted mean values of systolic blood pressure by the quintiles of salt intake in men and women: NIPPON DATA80

	Quintiles of salt intake (g/day)								
	Q1 (lowest)	Q2		Q3		Q4		Q5 (highest)	
	Adjusted SBP (mm Hg)	Adjusted SBP (mm Hg)	*P*	Adjusted SBP (mm Hg)	*P*	Adjusted SBP (mm Hg)	*P*	Adjusted SBP (mm Hg)	*P*
Men, all (n = 4585)									
Model 1	136.7	137.5	0.365	137.6	0.300	139.7	0.001	140.2	<0.001
Model 2	136.5	137.4	0.307	137.6	0.232	139.6	<0.001	140.8	<0.001
Model 3	136.9	137.6	0.490	137.6	0.439	139.5	0.006	140.2	0.002
Men without history of hypertension and/or antihypertensive treatment (n = 3616)									
Model 1	131.5	131.7	0.819	132.4	0.316	133.6	0.014	135.2	<0.001
Model 2	131.6	131.7	0.969	132.3	0.442	133.5	0.041	135.2	<0.001
Model 3	132.0	131.8	0.870	132.3	0.623	133.4	0.109	134.8	0.005
Women, all (n = 5837)									
Model 1	133.3	134.2	0.292	133.3	0.933	134.5	0.157	133.6	0.704
Model 2	133.9	134.1	0.815	133.5	0.625	134.4	0.523	133.3	0.466
Model 3	134.0	134.2	0.863	133.6	0.562	134.4	0.682	133.1	0.318
Women without history of hypertension and/or antihypertensive treatment (n = 4765)									
Model 1	127.6	127.5	0.847	128.5	0.220	128.8	0.113	128.7	0.126
Model 2	127.9	127.6	0.673	128.5	0.375	128.7	0.286	128.3	0.618
Model 3	128.0	127.7	0.627	128.6	0.458	128.7	0.374	128.1	0.917

Mean values are adjusted by analysis of covariance. *P* values are compared with the lowest quintile by multiple comparison.
Model 1 is adjusted for age.
Model 2 is adjusted for age (years), body mass index (kg/m^2), current drinking, potassium intake (mg/day), and total energy intake (kcal/day).
Model 3 is adjusted for age (years), body mass index (kg/m^2), current drinking, total energy intake (kcal/day), vegetable intake (the sum of green, yellow vegetable and other vegetable) (g/day), fruit intake (g/day) and fish/shellfish intake (g/day).
SBP, systolic blood pressure.

legume, fruit, other vegetables, sea algae, and fish/shellfish, and showed lower intakes (g/1000 kcal) of cereals, flour, meat, and milk/dairy products (Table 1). Results for these food groups were similar in women (Table 2).

Salt intake and BP

Table 3 shows adjusted mean values of SBP by the quintile of salt intake (g/day) in men and women. In all men, age-adjusted mean SBP tended to increase as salt intake increases (model 1). Age-adjusted SBP in the 4th and the highest quintile of salt intake were significantly higher than that in the lowest quintile; 3.0 mm Hg higher in the 4th quintile and 3.5 mm Hg higher in the highest quintile. Results were similar after adjustment of other confounders including BMI, current drinking, potassium intake, and total energy intake (model 2); adjusted SBP in the highest quintile was 4.3 mm Hg higher than that in the lowest quintile ($P < 0.001$). Results were also similar after adjustment of intakes of food groups (vegetable, fruit, and fish/shellfish) (model 3). When analyzing in men without history of hypertension and antihypertensive treatment, the above tendency was remained; multivariate-adjusted SBP in the highest quintile was 3.6 mm Hg higher than that in the lowest quintile ($P < 0.001$) (model 2).

In all women, adjusted mean values of SBP were not statistically different among the quintile of salt intake in any models (Table 3). Results were similar in women without history of hypertension; there were no significant differences in adjusted SBPs among the quintiles.

Table 4 shows adjusted mean values of DBP by the quintile of salt intake (g/day) in men and women. In all men, age-adjusted mean DBPs showed a tendency to increase as salt intake increases. Age-adjusted DBP in the highest quintile was 1.8 mm Hg higher than that in the lowest quintile ($P < 0.001$). The difference remained significant after adjustment of BMI, potassium intake, and total energy intake (1.3 mm Hg, $P = 0.047$) (model 2), although it was not significant after adjustment of intake of food groups (model 3). In men without history of hypertension, age-adjusted DBP in the highest quintile was 1.6 mm Hg higher than that in the lowest quintile ($P = 0.006$), but the difference was not significant after adjustment of confounders.

In all women and women without history of hypertension, age-adjusted DBPs showed an increasing tendency as salt intake increases (Table 4). However, there were no significant differences in multivariate-adjusted DBPs among the quintile (model 2 and model 3).

When the energy density of salt intake (g/1000 kcal) was used instead of the absolute amount of salt intake (g/day) for the above analyses, results were similar.

DISCUSSION

In the present report, we investigated the relationship of dietary salt intake to BP in a large-scale representative Japanese, in whom high-quality data on dietary salt intake from the National Nutrition Survey of Japan are available, and

Table 4. Adjusted mean values of diastolic blood pressure by the quintiles of salt intake in men and women: NIPPON DATA80

	Quintiles of salt intake (g/day)								
	Q1 (lowest)	Q2		Q3		Q4		Q5 (highest)	
	Adjusted DBP (mm Hg)	Adjusted DBP (mm Hg)	*P*	Adjusted DBP (mm Hg)	*P*	Adjusted DBP (mm Hg)	*P*	Adjusted DBP (mm Hg)	*P*
Men, all (*n* = 4585)									
Model 1	82.6	83.3	0.231	83.0	0.455	84.3	0.002	84.4	0.001
Model 2	82.9	83.4	0.421	83.0	0.931	84.2	0.035	84.2	0.047
Model 3	83.2	83.5	0.612	83	0.751	84.1	0.137	83.8	0.362
Men without history of hypertension and/or antihypertensive treatment (*n* = 3616)									
Model 1	80.2	80.5	0.616	80.4	0.760	81.6	0.012	81.8	0.006
Model 2	80.7	80.6	0.937	80.4	0.596	81.5	0.188	81.4	0.242
Model 3	80.9	80.7	0.809	80.4	0.416	81.4	0.400	81.1	0.733
Women, all (*n* = 5837)									
Model 1	79.0	79.3	0.443	79.3	0.549	79.7	0.129	80.4	0.004
Model 2	79.7	79.4	0.536	79.4	0.547	79.6	0.746	79.7	0.950
Model 3	79.7	79.4	0.526	79.4	0.525	79.6	0.699	79.6	0.799
Women without history of hypertension and/or antihypertensive treatment (*n* = 4765)									
Model 1	76.6	76.3	0.511	77.0	0.465	77.4	0.101	78.0	0.005
Model 2	77.2	76.5	0.162	77	0.768	77.3	0.818	77.3	0.781
Model 3	77.2	76.5	0.181	77	0.807	77.3	0.750	77.3	0.750

Mean values are adjusted by analysis of covariance. *P* values are compared with the lowest quintile by multiple comparison.
Model 1 is adjusted for age.
Model 2 is adjusted for age (years), body mass index (kg/m^2), current drinking, potassium intake (mg/day), and total energy intake (kcal/day).
Model 3 is adjusted for age (years), body mass index (kg/m^2), current drinking, total energy intake (kcal/day), vegetable intake (the sum of green, yellow vegetable and other vegetable) (g/day), fruit intake (g/day) and fish/shellfish intake (g/day).
DBP, diastolic blood pressure.

we found a significant independent relationship between the amount of salt intake and BP especially in men. There was 4.3 mm Hg difference in multivariate-adjusted SBP between the lowest quintile (mean salt intake 8.7 g/day) and the highest quintile (mean salt intake 23.5 g/day). This would be the first report demonstrating salt intake-BP relationship within a large Japanese population, where salt intake was assessed using weighing record method for three consecutive days in households.

A famous report by Dahl was an ecological study on the relationship between salt intake and BP in populations in various parts of the world, including Japan.[6] However, the design of this study was not standardized for both of BP measurement and the assessment of salt intake. The international INTERSALT study was conducted, using 52 populations in 32 countries, with strictly standardized BP measurement and evaluation of salt intake by 24-hour urinary sodium excretion determination.[13–15] The INTERSALT study found that urinary sodium excretion was significantly related to individual BP and to age-dependent BP elevation, after adjustment for age, gender, obesity and alcohol consumption. It was estimated that a decrease in sodium excretion by 100 mmol (equivalent to about 5.8 g salt) lowered SBP by 2.2 mm Hg, and that SBP and DBP were reduced by 10–11 mm Hg and 6 mm Hg, respectively, between 25 and 55 years of age—a period of 30 years. The measurement of 24-hour urinary sodium excretion is considered to be the gold standard to assess dietary salt intake. However, this method is usually difficult to perform in a large-scale epidemiological study. Our results assessing salt intake by 3-day weighing record method in the National Nutrition Survey were a valuable finding, and the magnitude of salt intake-SBP relation in men would be reasonable compared to the finding in the INTERSALT.

In women, we could not find a significant relationship between salt intake and BP after adjustment of confounders, even when excluding participants with history of hypertension or antihypertensive treatment. The National Survey of Circulatory Disorder in Japan showed that, in the 30 years from 1971 to 2000, mean SBP in Japanese substantially decreased both in men and women and in younger and older age groups.[16,17] As the mean BP decreased in the whole population, including the younger generations, such a phenomenon is considered to be explained by a population-wide reduced consumption of salt through the nationwide campaign in this period.[18] Our female participants in 1980 may have begun to change their dietary habit to reduce salt intake, which would cause a null relationship between salt intake and BP in this cross-sectional study design.

In the present study, we could clarify the characteristics of nutrient intake and dietary habits in Japanese people with high salt intake. For food groups, people with higher salt intake showed higher intakes of soy beans/legume, vegetables, and fish/shellfish, which means they have Japanese style dietary pattern. On the other hand, people with lower salt intake showed higher intakes of meat and milk/dairy products, which means they have relatively westernized dietary pattern. For nutrients, people with higher salt intake showed higher intakes of potassium, phosphorus, magnesium, and fiber, which would be mainly due to higher intake of vegetables. For the prevention of hypertension and cerebro-cardiovascular diseases, Japanese should reduce salt intake with keeping intakes of vegetable, fruit, soy product, and fish/shellfish high.

One of the limitations of this study is that the amount of alcohol consumption was not adjusted in multivariate-adjusted models. If participants with high salt intake tend to consume more alcohol, the salt-BP relationship would be overestimated especially in men. Another limitation is that physical activity was not considered in the models. It is possible that rural people consume more salt and are more physically active with labor; it may cause underestimation of the salt-BP relationship. A limitation of our method to estimate individual nutrient intake from dietary record in household has been described.[11]

In conclusion, a positive relationship of dietary salt intake to BP was observed, especially in men, in this large-scale representative Japanese population, in whom high-quality data on dietary salt intake from the National Nutrition Survey of Japan are available. The long-term mortality risk of cerebro-cardiovascular diseases should be investigated in relation to baseline salt intake in the NIPPON DATA cohorts.

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日本人の一般集団における蛋白質摂取量と血清アルブミンの関連- NIPPONDATA90-

研究協力者　渡邉　至　　（国立循環器病センター予防検診部）
研究協力者　東山　綾　　（国立循環器病センター予防検診部）
研究協力者　小久保　喜弘（国立循環器病センター予防検診部）
研究協力者　小野　優　　（国立循環器病センター予防検診部）
研究分担者　岡山　明　　（財団法人結核予防会第一健康相談所　所長）
研究分担者　岡村　智教　（国立循環器病センター予防検診部　部長）

目的:これまで蛋白質摂取量と血清アルブミンの関係を検討した研究は少なく、その関係は明らかではない。そこで、日本人の代表データを用いて蛋白質摂取量と血清アルブミンとの関連について検討した。

方法:平成2年国民栄養調査とNIPPONDATA90ベースラインデータである平成2年循環器疾患基礎調査との両方を受けた7715人（男3220人、女4495人）を対象に、蛋白質摂取量と血清アルブミンの関連に関して断面的に下記のような検討を行った。栄養素の摂取量と摂取密度は按分法による推定値を使用した。

1）性・年齢階級別に蛋白質摂取量（全体、動物性、植物性）および血清アルブミン、body mass index（BMI）を比較した。
2）性・年齢階級別にエネルギー摂取1000kcalあたりの蛋白質摂取量（全体、動物性、植物性）を比較した。
3）性別に血清アルブミンを3分位に区分し、年齢、BMI、血清総コレステロール、エネルギー摂取、蛋白質摂取量、エネルギー摂取1000kcalあたりの蛋白質摂取量、喫煙者の割合、飲酒者の割合などの特徴を比較した。
4）重回帰分析により血清アルブミンと動物性・植物性蛋白質摂取量（g/day）との関連を性別に検討した。血清アルブミンを目的変数とし、モデル1では蛋白質摂取量以外に年齢、モデル2ではモデル1にBMIを追加し、モデル3ではモデル2に総コレステロールを加えた。

結果：重回帰分析において動物性蛋白質摂取と血清アルブミンとの間には弱い正の関係を認めたが、植物性蛋白質摂取と血清アルブミンとの間には関係を認めなかった。性別やモデルに関係なく、年齢と血清アルブミンとの間には統計的に有意な負の関係を認め、標準化係数も他の変数に比べ非常に大きかった。モデル2でのBMIの調整は動物性・植物性蛋白質摂取量と血清アルブミンとの関係にほとんど影響を与えなかったが、モデル3での総コレステロールの調整は明らかに関係を弱める方向に働いた。

結論：今回の研究は動物性蛋白質摂取と血清アルブミンとが関連している可能性を示した。一方、植物性蛋白質摂取と血清アルブミンとの関連は示されなかった。

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Protein Intakes and Serum Albumin Levels in a Japanese General Population: NIPPON DATA90

Makoto Watanabe[1], Aya Higashiyama[1], Yoshihiro Kokubo[1], Yuu Ono[1], Akira Okayama[2], and Tomonori Okamura[1], for the NIPPON DATA80/90 Research Group

[1]Department of Preventive Cardiology, National Cardiovascular Center, Osaka, Japan
[2]The First Institute for Health Promotion and Health Care, Japan Anti-tuberculosis Association, Tokyo, Japan

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ABSTRACT

Background: It is well-known that albumin is synthesized in the liver; serum albumin is a major component of serum proteins. However, it has not been well elucidated how dietary protein intakes are associated with serum albumin levels in general populations without extreme malnutrition. We cross-sectionally investigated in the representative Japanese the association between dietary protein intake and serum albumin levels.

Methods: A total of 7715 subjects (3220 men and 4495 women, aged 30 years or more) with measurement of serum albumin who participated in both the National Survey on Circulatory Disorders in 1990 and the National Nutrition Survey in 1990 were analyzed in the present analysis. Multiple-adjustments were performed with linear regression models to estimate the association between serum albumin levels and animal or vegetable protein intake adjusting for age and body mass index.

Results: The very weak positive association between animal protein and serum albumin levels was observed. On the other hand, there was no clear association observed between vegetable protein and serum albumin levels. Regardless of sex and models, age was inversely associated with serum albumin levels with statistically significance, and standardized coefficients of age were considerably larger in both sexes than other variables. Adjustment for body mass index hardly altered the coefficients of animal or vegetable protein intake, but adjustment for total cholesterol clearly attenuated the relationship between animal protein intake and serum albumin levels.

Conclusions: Present analysis indicated the possibility that animal protein intake was related with serum albumin levels, while vegetable protein intake was not related.

Key words: serum albumin; protein intake; cross-sectional study

INTRODUCTION

It is well-known that albumin is synthesized in the liver. Serum albumin is a major component of serum protein, which sustains osmotic pressure or transports many kinds of substances or hormones to organs. Serum albumin level can be lowered by decrease in synthesis (cirrhosis or some inflammatory diseases), leakage outside the body (nephrotic syndrome, severe burns or protein-losing enteropathy), or malnutrition.

Several prospective studies have reported that low albuminemia was associated with risks of mortality or cardiovascular diseases[1–7]; however, the mechanism has not been clear enough. As for serum albumin levels, there is one simple question if dietary protein intake is associated with serum albumin levels in a general population without extreme malnutrition. Solution of this question might be one of clues to solve the mechanism between serum albumin and adverse health. Accordingly, we cross-sectionally investigated in the representative Japanese the association between dietary protein intakes and serum albumin levels.

METHODS

Study subjects

The National Survey of Circulatory Disorders, Japan (NSCDJ) and the National Nutrition Survey, Japan (NNSJ) are periodically conducted for same participants (NSCDJ: every 10 years, NNSJ: every year) in the randomly sampled subjects from all the Japanese.[8,9]

In 1990, both these national surveys were conducted to the 10 956 same subjects who lived in the randomly selected 300 areas from Japan. Among them, 8926 subjects participated in the surveys (participation rate: 81%). Finally, a total of 7715

Address for correspondence. Dr. Makoto Watanabe, Department of Preventive Cardiology, National Cardiovascular Center, 5-7-1, Fujishiro-dai, Suita 565-8565, Japan (e-mail: makotow@hsp.ncvc.go.jp).

Table 1. Averages in protein intakes (total, animal, vegetable), serum albumin levels and body mass index by age groups and sex, 1990, Japan

Men		Protain intakes (g/day)			Serum albumin (g/L)	BMI (kg/m²)
Age	*n*	Total	Animal	Vegetable		
30–39	606	88.7 (18.1)	45.8 (13.4)	42.9 (8.7)	46.9 (2.5)	22.9 (3.0)
40–49	767	93.1 (18.1)	49.2 (13.8)	43.8 (8.5)	45.8 (2.7)	23.5 (2.9)
50–59	737	96.8 (20.6)	50.4 (15.5)	46.4 (9.5)	44.6 (2.5)	23.3 (2.8)
60–69	662	87.2 (18.2)	43.5 (13.4)	43.9 (9.1)	43.4 (2.7)	22.6 (3.1)
70–	448	78.1 (17.7)	38.4 (12.9)	39.8 (8.9)	42.2 (2.7)	22.0 (3.1)
P value		<0.001	<0.001	<0.001	<0.001	<0.001

Women		Protain intakes (g/day)			Serum albumin (g/L)	BMI (kg/m²)
Age	*n*	Total	Animal	Vegetable		
30–39	976	71.9 (13.0)	37.0 (9.9)	34.9 (6.3)	44.9 (2.6)	21.8 (3.0)
40–49	1097	78.2 (15.3)	41.1 (11.4)	37.1 (7.2)	44.4 (2.4)	22.8 (3.1)
50–59	967	78.1 (16.8)	39.7 (12.3)	38.5 (8.1)	44.4 (2.5)	23.4 (3.2)
60–69	847	72.6 (16.3)	35.6 (11.5)	37.1 (8.2)	43.9 (2.5)	23.4 (3.5)
70–	608	64.3 (14.2)	31.0 (10.3)	33.5 (7.1)	42.5 (2.7)	22.8 (3.4)
P value		<0.001	<0.001	<0.001	<0.001	<0.001

P values were calculated between age groups with one-way anova.
Parentheisis means standard deviation.
BMI means body mass index.

subjects (3220 men and 4495 women, aged 30 years or more) with measurement of serum albumin and nutrient intake data remained for the present analysis.

The cohort study of NSCDJ in 1990 (NSCDJ90) is referred to as NIPPON DATA 90 (the National Integrated Project for Prospective Observation of Non-communicable Disease And its Trends in the Aged). Details of NIPPON DATA 90 were previously described elsewhere.[10–12]

Data collection in NSCDJ90

Public health nurses obtained information on cigarette smoking, alcohol drinking, or medication for hypertension.[8] Blood pressure was measured using a standard mercury sphygmomanometer on the right arm of seated participants after a sufficient period of rest. Non-fasting blood samples were obtained and the serum was separated and centrifuged soon after blood coagulation. Plasma samples were also obtained in a siliconized tube containing sodium fluoride. These samples were shipped to a unique laboratory (SRL, Tokyo, Japan) for blood measurements. The serum albumin was analyzed with the bromcresol green method.

Data collection in NNSJ in 1990

Since nutrient intakes were estimated at the NNSJ in 1990 (NNSJ90) by each household with food weighing method,[9] those of each household member were estimated by proportionally dividing household intake data of NNSJ90, based on average intakes by sex and age groups calculated from NNSJ in 1995. The details of the estimation for individual nutrient intakes are described in another paper.[13] Intakes of total protein, and animal or vegetable protein were calculated as g per day and caloric densities in g/1000 kcal.

Statistical analysis

Serum albumin level was divided into three groups by its tertile to compare the characteristics. One-way analysis of variance for continuous variables and chi-square test for categorical variables were used for comparison among groups. Multiple-adjustments were performed with linear regression models to estimate association between serum albumin levels and animal or vegetable protein intake; Model 1 including age, animal and vegetable protein intake, Model 2 including variables in model 1 plus body mass index (BMI), Model 3 including variables in model 2 plus total cholesterol. In addition, as sensitivity analyses, current cigarette smoking and current alcohol drinking were added to the model 1 as dichotomized variables, and daily animal or vegetable protein intake per energy intake of 1000 kcal was entered into the model 2, instead of animal or vegetable protein intake as g per day. Adjusted coefficient of determination (adjusted R^2) was also calculated. All *P*-values were 2-tailed and the significance level was $P < 0.05$. The statistical package SPSS 12.0J for Windows (SPSS, Tokyo, Japan) performed these analyses.

RESULTS

Average protein intake (total, animal and vegetable), BMI, and serum albumin levels were shown by age groups and sex (Table 1). All of these variables differed significantly among age groups, and serum albumin levels decreased with age, especially more clearly in men. Regardless of sex, total, animal and vegetable protein intake is lowest in 70 years or more. BMI is higher in 40–49 years in men and in 50–69 years in women than other age groups. Prevalence of low

Table 2. Averages in protein intakes (total, animal, vegetable) per energy intake of 1000 kcal by age groups and sex, 1990, Japan

Men		Protain intakes(g/1000 kcal)		
Age	*n*	Total	Animal	Vegetable
30–39	606	37.2 (4.3)	19.3 (4.5)	18.0 (2.0)
40–49	767	38.8 (4.6)	20.5 (4.7)	18.2 (2.2)
50–59	737	39.7 (5.0)	20.6 (5.0)	19.0 (2.3)
60–69	662	38.9 (4.8)	19.4 (4.9)	19.6 (2.5)
70–	448	39.3 (5.1)	19.3 (5.4)	20.1 (2.7)
P value		<0.001	<0.001	<0.001

Women		Protain intakes(g/1000 kcal)		
Age	*n*	Total	Animal	Vegetable
30–39	976	38.3 (4.2)	19.7 (4.4)	18.6 (2.1)
40–49	1097	39.9 (4.8)	21.0 (4.8)	19.0 (2.3)
50–59	967	40.7 (5.1)	20.7 (5.2)	20.1 (2.4)
60–69	847	40.3 (5.2)	19.7 (5.2)	20.6 (2.6)
70–	608	39.9 (5.3)	19.2 (5.3)	20.8 (2.6)
P value		<0.001	<0.001	<0.001

P values were calculated between age groups with one-way anova.
Parentheisis means standard deviation.

albuminemia of 38 g/L or less were very low in both sexes; men: 2.2% ($n = 70$), women: 1.7% ($n = 77$) (table not shown).

Average protein intake (total, animal and vegetable) per energy intake of 1000 kcal were shown (Table 2). In both sexes, total protein intake per energy intake was highest in 50–59 years, and vegetable protein intake per energy intake increased with age and was highest in 70 years or more. Animal protein intake per energy intake was higher in 40–59 years than other age groups.

The characteristics by tertile of serum albumin levels were shown (Table 3). In both sexes, averages in age, total energy intake, total cholesterol, total and animal protein intakes per day, and proportion of current alcohol drinker differed significantly among categories of serum albumin levels. Animal or vegetable protein intake per energy intake of 1000 kcal also differed significantly among categories. No significant difference was observed in vegetable protein intake regardless of sex. Average BMI differed significantly only in men, and increased with serum albumin levels. In addition, average animal and vegetable protein intake were lower in low-albuminemia (albumin level of 38 g/L or less) than

Table 3. Comparison of characteristics by tertiles of serum albumin levels and sex, 1990, Japan

Men	Serum albumin (g/L)			*P*-value
	29–43	44–46	47–56	
n	1080	1231	909	
Age (years)	62.1 (12.2)	51.9 (12.0)	44.7 (10.8)	<0.001
BMI (kg/m^2)	22.3 (2.9)	23.2 (3.1)	23.4 (2.9)	<0.001
Total cholesterol (mg/dL)	188 (35)	201 (35)	209 (37)	<0.001
Total energy intake (kcal/day)	2254 (484)	2351 (465)	2372 (413)	<0.001
Protein (g/day)	87.3 (19.7)	91.0 (20.0)	91.3 (18.5)	<0.001
Animal (g/day)	44.0 (14.1)	47.0 (14.8)	47.6 (14.3)	<0.001
Vegetable (g/day)	43.4 (9.6)	43.9 (9.2)	43.7 (8.4)	0.41
Protein (g/1000 kcal)	38.9 (4.6)	38.9 (5.0)	38.6 (4.8)	0.31
Animal (g/1000 kcal)	19.6 (4.8)	20.1 (5.0)	20.1 (4.9)	0.02
Vegetable (g/1000 kcal)	19.4 (2.5)	18.8 (2.4)	18.5 (2.3)	<0.001
Current alcohol drinker (%)	53.1	58.2	63.5	<0.001
Current cigarette smoker (%)	54.0	55.2	57.4	0.30

Women	Serum albumin (g/L)			*P*-value
	31–43	44–45	46–54	
n	1768	1368	1359	
Age (years)	56.3 (14.5)	51.6 (13.3)	48.3 (12.4)	<0.001
BMI (kg/m^2)	22.8 (3.3)	22.8 (3.3)	22.8 (3.3)	0.96
Total cholesterol (mg/dL)	201 (39)	208 (38)	213 (38)	<0.001
Total energy intake (kcal/day)	1841 (383)	1868 (364)	1892 (344)	<0.001
Protein (g/day)	72.7 (16.3)	74.3 (16.2)	75.0 (15.0)	<0.001
Animal (g/day)	36.4 (11.5)	37.9 (12.0)	38.5 (11.3)	<0.001
Vegetable (g/day)	36.3 (7.9)	36.4 (7.6)	36.6 (7.1)	0.57
Protein (g/1000 kcal)	39.6 (4.9)	39.9 (4.9)	39.8 (5.0)	0.30
Animal (g/1000 kcal)	19.8 (5.0)	20.3 (5.0)	20.4 (5.0)	0.003
Vegetable (g/1000 kcal)	19.9 (2.5)	19.6 (2.6)	19.5 (2.4)	<0.001
Current alcohol drinker (%)	4.8	7.9	7.8	<0.001
Current cigarette smoker (%)	9.4	8.0	10.7	0.05

Averages are shown except for current alcohol drinker and cigarette smoker.
Parentheisis means standard deviation.
BMI means body mass index.

Table 4. Association beween serum albumin levels and protein intakes (animal, vegetable) with multiple linear regression by sex, 1990, Japan

(Dependent variables)	Men			
	Independent variables: serum albumin (g/L)			
Model 1	Coefficient	95% CI	Sandardized coefficient	*P* value
Age (10 years)	−1.18	−1.24 to −1.11	−0.52	<0.001
Animal protein (1SD, 14.5 g/day)	0.11	0.01 to 0.20	0.04	0.03
Vegetable protein (1SD, 9.2 g/day)	−0.06	−0.16 to 0.03	−0.02	0.19
	Adjusted coefficient of determination (R^2) = 0.28			
Model 2	coefficient	95% CI	Sandardized coefficient	*P* value
Age (10 years)	−1.15	−1.22 to −1.08	−0.51	<0.001
BMI (1SD, 3.0 kg/m^2)	0.34	0.25 to 0.43	0.11	<0.001
Animal protein (1SD, 14.5 g/day)	0.09	−0.01 to 0.18	0.03	0.08
Vegetable protein (1SD, 9.2 g/day)	−0.09	−0.18 to 0.00	−0.03	0.06
	Adjusted coefficient of determination (R^2) = 0.29			
Model 3	coefficient	95% CI	Sandardized coefficient	*P* value
Age (10 years)	−1.14	−1.20 to −1.07	−0.51	<0.001
BMI (1SD, 3.0 kg/m^2)	0.18	0.09 to 0.27	0.06	<0.001
Total cholesterol (1SD, 36.8 mg/dL)	0.61	0.52 to 0.70	0.20	<0.001
Animal protein (1SD, 14.5 g/day)	0.03	−0.07 to 0.12	0.01	0.55
Vegetable protein (1SD, 9.2 g/day)	−0.06	−0.15 to 0.03	−0.02	0.21
	Adjusted coefficient of determination (R^2) = 0.33			

(Dependent variables)	Women			
	Independent variables: serum albumin (g/L)			
Model 1	coefficient	95% CI	Sandardized coefficient	*P* value
Age (10 years)	−0.47	−0.52 to −0.42	−0.25	<0.001
Animal protein (1SD, 11.6 g/day)	0.10	0.02 to 0.18	0.04	0.02
Vegetable protein (1SD, 7.6 g/day)	0.03	−0.05 to 0.11	0.01	0.50
	Adjusted coefficient of determination (R^2) = 0.07			
Model 2	coefficient	95% CI	Sandardized coefficient	*P* value
Age (10 years)	−0.48	−0.54 to −0.43	−0.26	<0.001
BMI (1SD, 3.3 kg/m^2)	0.14	0.06 to 0.22	0.05	<0.001
Animal protein (1SD, 11.6 g/day)	0.09	0.01 to 0.17	0.04	0.02
Vegetable protein (1SD, 7.6 g/day)	0.02	−0.06 to 0.10	0.01	0.66
	Adjusted coefficient of determination (R^2) = 0.07			
Model 3	coefficient	95% CI	Sandardized coefficient	*P* value
Age (10 years)	−0.62	−0.68 to −0.56	−0.33	<0.001
BMI (1SD, 3.3 kg/m^2)	0.03	−0.05 to 0.10	0.01	0.44
Total cholesterol (1SD, 38.8 mg/dL)	0.65	0.58 to 0.73	0.25	<0.001
Animal protein (1SD, 11.6 g/day)	0.04	−0.04 to 0.12	0.02	0.34
Vegetable protein (1SD, 7.6 g/day)	0.03	−0.05 to 0.11	0.01	0.41
	Adjusted coefficient of determination (R^2) = 0.12			

CI means confidence interval. BMI means body mass index.

normal-albuminemia in both sexes, although difference for animal protein in women was not significant (table not shown).

The association between serum albumin levels and animal or vegetable protein intake was estimated by multiple linear regression models (Table 4). In model 1 and model 2, animal protein was positively associated with serum albumin levels, although the coefficients of animal protein were very small. On the other hand, there is no clear association observed between vegetable protein and serum albumin levels. Regardless of sex and models, age was inversely associated with serum albumin levels with statistically significance. Standardized coefficients of age were considerably larger in both sexes than other variables. BMI was positively associated with serum albumin levels in model 2, but adjustment for BMI in model 2 hardly altered the coefficients of animal or vegetable protein intake, compared to those in model 1. Adding current cigarette smoking and current alcohol drinking to model 1, or entering animal or vegetable protein intakes per 1000 kcal into the model 2, instead of animal or vegetable protein intakes, did not change the results of animal or vegetable protein intake so much. Adjustment for total cholesterol in model 3 attenuated the association between animal protein intake and serum albumin level. Any of adjusted coefficients of determination in these models were relatively small, especially in women.

DISCUSSION

In the present study, very weak positive association between animal protein and serum albumin level was observed. On the other hand, substantially strong relation between age and serum albumin level was also observed. Compared to age, associations of animal protein intake or BMI were very small, and coefficients of animal protein after adjustment for age were also considerably small. Accordingly, association between animal protein and serum albumin level might be essentially small even if it is statistically significant.

Adjustment for BMI did not change the results so much, and coefficients of BMI were also small. Although BMI was considered as one of markers of nutrition status, present results suggested BMI did not work as a strong confounding factor in the association between animal protein and serum albumin level. There are few individuals with extreme malnutrition or very low BMI in Japan recently; and the range of BMI are relatively narrow as a whole. Accordingly, BMI might not be a marker of nutrition status at least in the general population.

A few studies reported the interaction between cholesterol and albumin level in the relationship between serum albumin levels and mortality, disease incidences or activities of daily living,[14–16] although the interaction is also still controversial. In present analyses, adjustment for total cholesterol considerably attenuated the association between animal protein intake and serum albumin level, and the association of total cholesterol with albumin was strong next to age. Cholesterol is synthesized mainly in the liver as well as albumin, and both albumin and cholesterol reflects liver synthesis function. Accordingly relatively strong relation between them is reasonable. Adjustment for total cholesterol means adjusting liver synthesis function, so the attenuation of the association between animal protein intakes and serum albumin levels in model 3 might be reasonable because protein intake is also a part of albumin synthesis pathway in the liver.

The present study had several limitations. First, some prospective studies reported the possibility of existence of the threshold of low albuminemia in relation with adverse health status.[3–6,14–16] However, since prevalence of low albuminemia, such as albumin level of 38 g/L or less in the present analyses was very low, it was difficult to investigate the threshold of serum albumin levels. Second, detailed medical histories of each subject that might influence on serum albumin levels or protein intakes were unknown, such as nephrotic syndrome or liver cirrhosis. Third, the nutritional data of each household member is indirectly estimated on the basis of other reference data, so the nutritional data might not accurately reflect the individual nutrition intake. The possibility of unknown influence of this method on the present results could not be completely excluded.

In conclusion, present analysis indicated the possibility that animal protein intake was related with serum albumin levels, while vegetable protein intake was not related. Further investigation was needed to estimate the association between protein intakes and serum albumin levels, considering the above mentioned limitations.

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蛋白質摂取量と腎機能の関連
—日本人代表集団であるNIPPON DATA90における検討—

研究協力者　東山　綾　　（国立循環器病センター予防検診部）
研究協力者　渡邉　至　　（国立循環器病センター予防検診部）
研究協力者　小久保　喜弘（国立循環器病センター予防検診部）
研究協力者　小野　優　　（国立循環器病センター予防検診部）
研究分担者　岡山　明　　（財団法人結核予防会第一健康相談所　所長）
研究分担者　岡村　智教　（国立循環器病センター予防検診部　部長）

背景と目的

慢性腎臓病（CKD）の進展を予防するために、低蛋白食は有効な予防手段の一つとして考えられている。しかし、蛋白質摂取量と腎機能の関連についての見解はいまだ定まっておらず、特に比較的健常である一般住民集団においては検討されていない。日本人代表集団であるNIPPON DATA90を対象に、ベースライン調査における腎機能と、同時に行われた国民栄養基礎調査における栄養摂取状況から推定された蛋白質摂取量の関係を検討した。

方法

1990年の循環器疾患基礎調査と国民栄養基礎調査の両方を受けた30歳以上の男女7404人（男性3099人、女性4305人）を解析対象とした。蛋白質摂取量は国民栄養基礎調査のデータから按分法を用いて個人の摂取量を推定し、体重あたりの摂取量（g/kg）を算出してその4分位で対象者を男女それぞれ4群に分けた。循環器疾患基礎調査の血清クレアチニン値よりMDRD研究（the Modification of Diet in Renal Disease study）による推定式を用いて糸球体ろ過量（GFR）を算出し、GFR < 60 ml/min/1.73m² をCKDありとした。性別に4群間でGFRを共分散分析により比較し、蛋白質摂取量第1分位群に対する各群のCKDを有するオッズ比を多重ロジスティック解析により算出し比較した。

結果

蛋白質摂取量は、性、10才年齢階級により有意差があった。またCKDの有無にかかわらず、蛋白質摂取量は推奨量とされる0.8g/kg/日以下を上回っていた。男女ともに蛋白質摂取量が多くなるほど、有意にGFRは高くなる傾向があった。また女性では、蛋白質摂取量が多い群においてCKDを有するオッズ比は有意に低かった。

結論

男女ともに蛋白質摂取量が多いほどGFRは高く、特に女性においては蛋白質摂取量が多

い群で CKD を有するオッズ比が低かった。しかし、蛋白質摂取量と腎機能の関係について結論づけるには、前向き研究などの更なる研究が必要である。

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Relationships between Protein Intake and Renal Function in a Japanese General Population: NIPPON DATA90

Aya Higashiyama[1,2], Makoto Watanabe[2], Yoshihiro Kokubo[2], Yuu Ono[2], Akira Okayama[3], and Tomonori Okamura[2], for the NIPPON DATA80/90 Research Group

[1]Lifestyle-Related Disease Prevention Center, Shiga University of Medical Science, Otsu, Japan
[2]Department of Preventive Cardiology, National Cardiovascular Center, Suita, Japan
[3]The First Institute for Health Promotion and Health Care, Japan Anti-tuberculosis Association, Tokyo, Japan

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ABSTRACT

Background: It has been considered that reducing protein intake is one of important measures to delay the progression of chronic kidney disease (CKD). However, the relationship between protein intake and renal function is still uncertain, especially in relatively healthy general population.

Methods: 7404 individuals (3099 men and 4305 women) who participated in both National Survey on Circulatory Disorders and National Nutrition Survey in 1990 and were free from past history of renal diseases were included in the present study. We estimated sex-specific age- and multivariate-adjusted glomerular filtration rate (GFR) and odds ratios for the presence of CKD according to the quartiles of protein (total, animal, vegetable) intake per body weight (kg).

Results: There were significant differences in each protein intake among the age groups in both men and women. Both participants with and without CKD took more protein intake than that of each recommended level. There were positive relationships between GFR and the quartiles of each protein intake in both sexes. The odds ratios for the presence of CKD were significantly decreased in the higher quartile of protein intake in women.

Conclusions: The higher protein intake was associated with higher GFR in both sexes and low prevalence of CKD in women. However, further studies are needed to conclude the relationships between protein intake and renal function.

Key words: CKD; GFR; odds ratio; cross-sectional study; nutrition

INTRODUCTION

The hypotheses that reduction of protein intake and strict blood pressure control delays the progression of chronic kidney disease (CKD) have been tested since 1990s. Although the Modification of Diet in Renal Disease (MDRD) study did not show the statistical significance of diet intervention,[1] a recent secondary analysis of the MDRD study, with a 6-year follow up, showed that the low protein diet with tight blood pressure control may have a beneficial effect on delaying progression in CKD Stages 3 to 4.[2] However, other previous studies about the same study question did not show definitive results, either.[4–7] Furthermore, in the MDRD study, the criteria for enrollment were Cre $\geq$ 1.4 mg/dl in men and Cre $\geq$ 1.2 mg/dl in women.[1,3] Accordingly, the effect of reduced protein diet for the progression of CKD is still uncertain, especially in relatively healthy general population.

On the other hand, animal protein is considered to induce hyperfiltration,[8,9] however, other study reported that white meat or fish provide benefits.[10] In addition, whether vegetable protein is associated with decreased renal function is controversial.[11,12]

Accordingly, we cross-sectionally investigated the relationship between renal function and total, animal, and vegetable protein in a 7404 Japanese representative population, who participated in both the National Survey on Circulatory Disorders and the National Nutrition Survey in 1990.

METHODS

Study participants

The participants of the present study were 8342 community residents (3488 men and 4854 women) aged 30 and greater, who participated in both the National Survey on Circulatory Disorders, of which follow-up study is known as "*NIPPON DATA90*",[13,14] and the National Nutrition Survey in 1990. In these surveys, 300 areas were randomly selected form

Address for correspondence. Dr. Aya Higashiyama, Lifestyle-Related Disease Prevention Center, Shiga University of Medical Science, Seta-tsukinowachou, Otsu, Shiga, Ohtsu 520-2192, Japan (e-mail: ahigashi@hsp.ncvc.go.jp).