日本食と寿命

研究分担者	中村 保幸	京都女子大学家政学部生活福祉学科 教授
研究代表者	上島 弘嗣	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	岡村 智教	国立循環器病センター予防検診部 部長
研究協力者	門脇 崇	滋賀医科大学社会医学講座公衆衛生学部門 助教
研究分担者	早川 岳人	福島県立医科大学衛生学・予防医学講座 講師
研究分担者	喜多 義邦	滋賀医科大学社会医学講座公衆衛生学部門 講師
研究協力者	Robert D. Abbott	バージニア大学医学部 教授
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

はじめに

男女ともわが国は世界最長寿国であるが、元気な高齢者が多いことも事実で、健康で自立して生活できる年齢＝健康寿命もわが国が世界1位である。世界が注目するのは日本人の長寿の秘訣は何かであり、何よりも世界が注目するのは何か日本人の生活習慣、とくに食生活に長寿の秘訣があるのではないかという点である。食物摂取に関しては個々の食品間に相互関連が強いことが近年になり認識されだし、食事パターンの概念に関心が持たれて来ている[1, 2]。

さて長寿の一因と期待される日本食であるが、飽和脂肪酸摂取が少なく、不飽和脂肪酸摂取が比較的多く、また全摂取熱量に対する脂肪由来の熱量が西洋食に比べて少ないことが心筋梗塞や乳癌が少ない一因で得あると指摘されているが、食塩摂取量が多いのがわずかある欠点である。日本食パターンに関する疫学研究は少ないため、今回検討を行った。

方法

NIPPON DATA80 研究のデータベースを用いて日本食パターンと総死亡、死因別死亡について検討した。1980 年に無作為抽出した全国 300 ヵ所において 30 才以上の男女を対象として検診を行い、食事栄養調査、生活習慣調査と血液生化学検査を行った。その後 19 年間追跡した。追跡開始時にすでに脳梗塞、心筋梗塞の既往のある対象は除外した計 9,086 例（男 4,018、女 5,068）について解析した。先行研究から得た所見に塩分制限の項目を加えて、次のように健康な日本食スコアのもとになる構成要因を決定した：卵摂取≦2 個/週、魚摂取≧1 回/2 日、肉摂取≦2 回/週、漬物摂取≧1 回/日、麺類の汁を残す、減塩醤油の使用、機会飲酒の 7 項目。したがって健康日本食度について個々人に 0～7 のスコアを与えた。さらにスコアにより各群の対象人数がほぼ等しいように 3 群に分けた：スコア 0-2 群、スコア 3 群、スコア 4-7 群。各群の総死亡率、死因別死亡率について Cox 比例ハザードモデルを用いて多変量解析した。

結果

表には日本食スコアにより分けた3群死亡率の解析結果を示す。19年間の追跡期間中に総死亡が1,823、心血管死が654、脳卒中死が299、心筋梗塞が死131、癌死が511あった。スコアが高い群ほど総死亡、心血管死、脳卒中死が有意に減少し、癌死と心筋梗塞死も低下する傾向にあった。

考案

今回の結果から塩分摂取が過多にならないよう注意した健康日本食は総死亡、心血管死、脳卒中死を有意に20%以上低下させることが判明した。日本食スコアを構成する個々の要素のうち3つは有意な総死亡低下をもたらしたが、その影響は総合スコアより小さかった。各要素の境界値はこれまでの研究結果を参考にするか、ないしは中央値近傍に設定した[3, 4]。構成要素の一つ漬物摂取1日1回以上が単独で総死亡を低下させたことは予想外であった。漬物の摂取量は少なく、食塩含有量も無視できない。恐らく漬物は伝統的日本食の一指標であるため、漬物摂取と他の健康に有用な食品、例えば魚や野菜の摂取とが密接に関連している為に見られた現象と解釈するのが妥当であろう。われわれは単に食品を無関連に食べるのでは無く、例えば日本食とか地中海食といった様にパターンとして食べる。本研究は食品パターンについての重要性を提起したと考える。

参考文献

1. Trichopoulou A, et al. Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med. 2003; 348: 2599-608.
2. Knoops KT, et al. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: the HALE project. JAMA. 2004; 292: 1433-9.
3. Nakamura Y, et al. Egg consumption, serum cholesterol, and cause-specific and all-cause mortality: the National Integrated Project for Prospective Observation of Non-communicable Disease and Its Trends in the Aged, 1980 (NIPPON DATA80). Am J Clin Nutr. 2004; 80: 58-63.
4. Nakamura Y, et al. Association between fish consumption and all-cause and cause-specific mortality in Japan: NIPPON DATA80, 1980-99. Am J Med. 2005; 118: 239-45.

表　日本食スコアにより分けた 3 群の死亡率の解析結果　男 4,018 人、女 5,068 人、
——NIPPON DATA80: 1980-99——

	スコア 0-2	スコア 3	スコア 4-7	傾向 P
人年	46,790	53,772	56,495	
総死亡（計=1,823）	556	634	633	
年齢・性調整 HR	1	0.92 (0.83-1.04)	0.78 (0.70-0.88)	<0.0001
多変量調整 HR				
モデル 1	1	0.93 (0.83-1.04)	0.78 (0.69-0.87)	<0.0001
モデル 2	1	0.92 (0.83-1.04)	0.78 (0.70-0.88)	<0.0001
心血管死（小計=654）	200	220	234	
年齢・性調整 HR	1	0.90 (0.75-1.09)	0.80 (0.66-0.96)	0.017
多変量調整 HR				
モデル 1	1	0.91 (0.75-1.10)	0.79 (0.65-0.95)	0.014
モデル 2	1	0.91 (0.75-1.10)	0.80 (0.66-0.97)	0.022
脳卒中死（小計=299）	92	107	100	
年齢・性調整 HR	1	0.95 (0.72-1.26)	0.74 (0.56-0.99)	0.035
多変量調整 HR				
モデル 1	1	0.96 (0.73-1.27)	0.74 (0.56-0.98)	0.031
モデル 2	1	0.96 (0.72-1.27)	0.75 (0.56-0.99)	0.038
心筋梗塞死（小計=131）	40	42	49	
年齢・性調整 HR	1	0.83 (0.55-1.26)	0.85 (0.55-1.31)	0.39
多変量調整 HR				
モデル 1	1	0.86 (0.56-1.33)	0.82 (0.54-1.25)	0.37
モデル 2	1	0.85 (0.55-1.32)	0.84 (0.55-1.27)	0.42
癌死（小計=551）	166	190	195	
年齢・性調整 HR	1	0.86 (0.70-1.05)	0.94 (0.77-1.16)	0.14
多変量調整 HR				
モデル 1	1	0.85 (0.69-1.05)	0.95 (0.77-1.17)	0.12
モデル 2	1	0.95 (0.77-1.17)	0.95 (0.77-1.17)	0.13

ハザード比（HR）と 95% 信頼区間を示す。多変量解析モデル 1:年齢、性、BMI，喫煙(生涯非喫煙、喫煙既往、現在喫煙 < 20 本/日，現在喫煙 20～40 本/日，現在喫煙≥41 本/日)により調整。モデル 2: モデル 1＋高血圧、糖尿病により調整。
BMI=body mass index.

A Japanese diet and 19-year mortality: NIPPON DATA80.

Yasuyuki Nakamura[1,2], Hirotsugu Ueshima[2], Tomonori Okamura[2], Takashi Kadowaki[2], Takehito Hayakawa[3], Yoshikuni Kita[2], Robert D Abbott[2,4], Akira Okayama[5], for NIPPON DATA80 Research Group

[1]Cardiovascular Epidemiology, Kyoto Women's University, [2]Department of Health Science, Shiga University of Medical Science, [3] Department of Hygiene & Preventive Medicine, Fukushima Medical University, [4]Department of Epidemiology and Biostatistics, University of Virginia School of Medicine, [5]Department of Preventive Cardiology, National Cardiovascular Center

Address for correspondence and reprints:
Yasuyuki Nakamura, MD, Cardiovascular Epidemiology, Kyoto Women's University
35 Imakumano Kitahiyoshi-cho, Higashiyama-ku, Kyoto 605-8501, JAPAN
FAX & Phone: +81-75-531-2162, E-mail: nakamury@kyoto-wu.ac.jp

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ABSTRACT

Few studies have examined the association between Japanese diet and mortality outcomes.

We analyzed the relationship between a healthy Japanese diet and all-cause and cause-specific mortality using the database from NIPPON DATA80. At baseline in 1980, data were collected on study participants aged ≧ 30 years from randomly selected areas in Japan. We defined a measure of a healthy reduced salt Japanese diet based on 7 components from food-frequency questionnaire. The total score ranged from 0 to 7, with 0 being least healthy and 7 being most healthy. Participants were divided into approximate tertiles of dietary scores (0-2, 3 and 4-7 scores). After excluding participants with co-morbidities, we followed 9,086 participants (44% men) for 19 years. There were 1823 all-cause and 654 cardiovascular deaths during the follow-up. With the dietary score group 0-2 serving as a reference, the Cox multivariate adjusted hazard ratios for groups with score 3 and scores 4-7 for all-cause mortality were 0.92 (95% confidence intervals: 0.83-1.04) and 0.78 (0.70-0.88) (trend P<0.0001), and 0.91 (0.75-1.10) and0.80 (0.66-0.97) for cardiovascular mortality (trend P=0.022) . Adherence to a healthy reduced salt Japanese diet was associated with an approximate 20% lower rate of all-cause and cardiovascular mortality.

Introduction

Recent interest in dietary patterns has spawned several studies of the associations between dietary patterns and longevity [1,2]. Japanese cuisine is based on combining staple foods, typically rice or noodles, with a soup, and side dishes made from fish, meat, vegetable, tofu and the like, designed to add flavor to the staple food. These are typically flavored with dashi stock, made with katsuobushi (dried skipjack tuna flakes), miso, and soy sauce and are usually low in fat and high in salt. Since Japan is an island nation, people eat much seafood. Meat-eating has been relatively rare. The beneficial aspects of the traditional Japanese diet have been attributed to its low intake of saturated fatty acids and a high intake of polyunsaturated fatty acids, especially from fish. Long-term benefits include lower mortality from coronary heart disease and from some cancers, which contribute at least in part to Japanese having the longest life expectancy in the world [3, 4]. A drawback of the Japanese diet is its high intake of salt and its association with a higher incidence and mortality from stroke and gastric cancer [5-7]. Presumably, if the Japanese diet is modified to emphasize the intake of foods that are low in salt, Japanese longevity could be increased further.

In the present study, we studied the preference for Japanese or Western diets, and from these data and data based on the previous studies, we comprehensively extracted the beneficial components of the Japanese diet and derived a healthy Reduced Salt Japanese Diet Score. We analyzed the relationship between the diet score and all-cause and cause-specific mortality using the database of the National Integrated Project for Prospective Observation of Non-communicable Diseases and Its Trends in the Aged, 1980 (NIPPON DATA80). The database includes more than 10,000 participants from randomly selected regions in Japan who were followed for 19 years [8-10].

METHODS

Participants

The participants in this cohort were participants in the 1980 National Survey on Circulatory Disorders [8]. 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 a self-administered questionnaire on lifestyle, including an essential nutritional survey by the food-frequency method. For the present study, participants were followed to 1999 (NIPPON DATA 80, 1980-99). The overall population aged 30 years and over in the participating health districts was 13,771. The participation rate was 76.6 % (10,546 of 13,771) before exclusion for reasons mentioned below.

We reviewed the residence records of all the study participants for their vital status. In cases of deaths, the causes were examined. To clarify the cause of death, we used the National Vital Statistics records. The underlying cause of death was coded according to the 9th International Classification of Disease for the National Vital Statistics until the end of 1994 and according to the 10th International Classification of Disease from the beginning of 1995. Deaths were confirmed in each district by computer-matching of data from the Vital Statistics records using the district, sex, and dates of birth and death as key codes.

Participants were excluded from follow-up because of a past history of coronary disease, stroke, or significant co-morbidities such as renal insufficiency (N=539), because of missing baseline data (N=51), or because of a loss to follow-up (N=870). The latter group was excluded because of the absence of a permanent address that was required for linking to vital statistics records. The final sample comprised 9,086 participants (4,018 men and 5,068 women). There were no significant differences between participants who were lost to follow-up and those who were included in the current study in terms of several risk factor characteristics. Therefore, the potential bias regarding the 870 participants lost to follow-up is thought to be negligible. Permission to use the National Vital Statistics records was obtained from the Management and Coordination Agency, Government of Japan. Approval for this study was obtained from the Institutional Review Board of Shiga University of Medical Science for ethical issues (No. 12–18, 2000).

Biochemical and Baseline Examinations

The baseline surveys were conducted at public health centers. Baseline blood pressures were measured by trained research nurses using a standard mercury sphygmomanometer on the right arm of seated participants after at least 5 min of rest. Hypertension was defined as a systolic blood pressure (BP) ≥140 mmHg, a diastolic BP ≥90 mmHg, or when a participant was receiving medications for the treatment of high blood pressure. Height and weight were measured in stocking feet and light clothing. BMI was calculated as weight (kg) divided by the square of height (m^2).

A lifestyle survey was also carried out using a self-administered questionnaire which asked about the typical daily consumption of 31 food items as shown in Appendix. Egg consumption was coded as ≥2 eggs/day, about 1 egg/day, about 1 egg/2 days, about 1 to 2 eggs/week, and less than once/week. Fish, meat, and tsukemono (preserved roots or leaves of seasonal vegetables (e.g., cucumbers, and eggplant) that are consumed with rice at the end of a meal) intake were coded separately as ≥2 times/day, about 1 time/day, about 1 time/2 days, about 1 to 2 times/week, and less than once/week. Participants were also asked if they frequently consumed soup with noodles, whether they used low salt soy sauce, and what was their preferred type of diet (Japanese, western, or mixed, Q19 in Appendix). Participants were asked about their alcohol drinking habit (never, past, occasional, and daily drinkers). Reported information was confirmed by public health nurses through interviews with the study participants regarding food consumption, smoking, drinking habit, and present and past medical histories.

Non-fasting blood samples were drawn and centrifuged within 60 min of collection and stored at -70°C until analyses. Serum total cholesterol, albumin, uric acid and creatinine were analyzed in a sequential auto-analyzer (SMA12/60; Technicon, Tarrytown, USA) at a single laboratory (Osaka Medical Center for Health Science and Promotion). This laboratory is a member of the Cholesterol Reference Method Laboratory Network (CRMLN) [11]. Serum concentrations of glucose were measured by the cupric-neocuproline method [12]. Diabetes was determined by medical history or defined as a serum glucose concentration ≥200 mg/dl.

Statistical Analysis and Components of the Reduced Salt Japanese Diet Score

SAS version 9.1 for Windows (SAS Institute, Cary, NC) was used throughout the analyses. We examined the relationship between the type of preferred diet and the frequency of dietary components from the nutritional survey. Then, we defined 7 components from the nutritional survey to measure a healthy Reduced Salt Japanese Diet. The components included egg intake ≤ 2 eggs/week, fish intake ≥ once in 2 days, meat intake ≤ 2 times/week, tsukemono intake ≥ once per day, infrequent intake of soup with noodles, use of low salt soy products, and occasional drinking. The above cut-off values were determined based on previous studies on the intake of eggs, fish and alcohol [9, 10, 13-15]. For meat and tsukemono, a near median was used as the cut-off. Infrequent intake of soup with noodles and the use of low salt soy sauce were used as markers of salt restriction. Because data on amounts of alcohol consumed were not available, and the association between all-cause mortality and alcohol consumption is known to be J-shaped [15], we chose occasional drinking as a component of a healthy reduced salt Japanese diet. Moderate alcohol consumption was also a component of a Mediterranean diet [2]. If any single dietary component was part of a typical daily diet, it was scored as one and zero otherwise. Thus, the total score ranged from 0 to 7, with 0 being least healthy and 7 being most healthy. Participants were divided into approximate tertiles of dietary scores (0-2, 3 and 4-7 scores). To obtain trend P, the Mantel-Hansel chi-square statistical test was used to detect deviation from linearity in the association between nominal variables and the categories according to the diet score, and the analysis of variance was used to detect deviation from linearity in the association between continuous variables and the categories. To examine the association between the reduced salt Japanese diet score and all cause and cause-specific mortality, age- and sex-adjusted and multivariate-adjusted hazard ratios were calculated using a Cox proportional hazards model. For multivariate analyses, age, sex, BMI, and cigarette smoking (never and past smokers, current smokers < 20 cigarettes/day, current smokers 20 to 40 cigarettes/day, and current smokers ≥ 41 cigarettes/day) were entered as covariates for model 1. For model 2, hypertension, and diabetes were added. The dietary score group 0-2 served as a reference for comparison with the other tertiles. Sensitivity analyses were performed on the above Cox analysis by excluding those who did not report a preferred food type, by stratifying the lower and higher age groups at median age, 49.3 y, and by stratifying by sex. To examine the association between each of the components of a Reduced Salt Japanese Diet Score and all-cause mortality, adjustments were made for the covariates in model 2.

To estimate adjusted survival probabilities, we derived Kaplan-Meier survival curves after propensity score matching [16]. Variables used in the propensity score were selected from the non-dietary variables: age (y), men (%), BMI (kg/m^2), current smokers (%), systolic BP (mmHg), diastolic BP (mmHg), on hypertension drugs (%), diabetes (%), serum total cholesterol (mg/dl), albumin (mg/dl), uric acid (mg/dl), creatinine (mg/dl). After matching, adjusted survival curves were estimated separately for participants who fell in the Japanese dietary grouping that ranged from 0 to 3 and for those in grouping strata 4 and higher. Comparison of the survival curves was based on the log-rank test. We further examined survival differences by the two groups according to the diet score, with age and sex as the dependent variables in a regression model. The statistical model used was a life-table regression procedure, with a Weibull distribution assumption for failure time included. The variables used in the calculation of the propensity score were also compared by t-test and chi-square test to determine if the propensity score matching was successful in mitigating risk factor differences.

RESULTS

Baseline Characteristics and All-Cause Mortality According to Preferred Food Type

The baseline characteristics according to the preferred food type are shown in Table 1. In this Table, we excluded 201 participants with missing data on a preferred food type. Relatively few participants preferred the western food type. Participants in this group were younger, were more likely to be women, and were less often hypertensive than participants who chose the other diet types. Those who preferred a western type of diet ate meat more frequently and consumed fish and tsukemono less often than those in the other groups. The two markers of salt restriction (infrequent consumption of soup with noodles and the use of low salt soy sauce) were more prevalent among those who preferred a western diet. Small differences, but a significant trend in the reduced salt Japanese diet score was observed (trend $P < 0.0001$).

Baseline Characteristics According to Reduced Salt Japanese Diet Score

Table 2 shows the baseline characteristics according to tertiles of the Reduced Salt Japanese Diet Score. As the score increased, the mean age and BMI increased, although the latter increase was modest. The proportion that were women and the prevalence of hypertension, daily drinking, and non-smoking also increased with diet score. The prevalence of diabetes and the mean serum total cholesterol concentration were not significantly different across the groups. As expected, the percentage with each component of the reduced salt Japanese diets score increased as the score increased.

All-Cause and Cause-Specific Mortality According to Reduced Salt Japanese Diet Score

During the 19 years of follow-up, there were 1,823 deaths. Among this group, 654 were from cardiovascular disease, 299 were from stroke, 131 were from acute myocardial infarction, 551 were from cancer, and 119 were from non-cardiovascular, non-cancer inflammatory diseases [17]. Table 3 shows the total person-years, numbers of cases, hazard ratios and 95% confidence intervals for all-cause and cause-specific mortality for each category of Reduced Salt Japanese Diet Score after adjustment for age, sex and other risk factors (multivariate models 1 and 2). As the score increased, risk of death from all-causes, from cardiovascular disease, and from stroke declined significantly in all models. Mortality from acute myocardial infarction, cancer, and inflammatory diseases tended to decrease, but without statistical significance, a possible consequence of the relatively small number of such events. Similar results were observed after excluding participants with missing data on dietary preference. At high age strata and in men, similar results were observed for all-cause, cardiovascular disease and stroke mortality. However, at low age strata and in women, results were similar for all-cause mortality only. Significant differences by the groups according to the diet score were lost at low age strata and in women for cardiovascular disease and stroke mortality, probably because of the relatively small number of such events at low age strata.

Components of Reduced Salt Japanese Diet Score and All-Cause Mortality

The percent of total participants who observed a healthy component of the Reduced Salt Japanese Diet Score and the association of each component with all-cause mortality are shown in Table 4. The percent of participants who observed a healthy reduced salt Japanese dietary component who were men is also provided. Adherence to each of the healthy dietary components tended to be associated with lower mortality. Risk of death, however, was significantly lower for participants who ate tsukemono ≥ once per day, consumed soup with noodles infrequently, and drank alcohol occasionally.

Kaplan-Meier Survival Estimates after Propensity Score Matching

The results from the propensity score matching are shown in Table 5. Fifty-eight participants with the reduced salt Japanese diet score 4-7 were unmatched due to missing data (N=56) or failure to match on a propensity scores (N=2). As can be seen, significant differences in the average propensity score and the variables used in its calculation before matching in the two groups disappeared after matching. In contrast, a significant difference between the matched survival curves remained as seen in Figure 1 (P=0.0003 by log-rank test). Survival differences by the group were significant when examined further using a regression model with a Weibull distribution that included adjustment for age and sex as the dependent variables (estimate=-0.13 [the lower score group compared to the higher score group], P< 0.0001).

DISCUSSION

The cut-off values for the egg, fish and drinking components were determined based on previous studies [11, 12, 18-23]. Near median cut-off values were used for meat and tsukemono. The low intake of meat is one of the characteristic features of the traditional Japanese diet and serves as a marker of reduced intake of saturated fatty acids in the Japanese [3, 4, 18, 19]. Although frequent intake of tsukemono is also a characteristic feature of the traditional Japanese diet, it was unexpected to find that consuming tsukemono at least once a day was associated with a statistically significant lower risk of all-cause mortality. Many types of Japanese tsukemono are prepared in a traditional Japanese fashion with high reliance on salt. It may be, however, that the more healthy nutrient content of tsukemono outweighs the adverse consequences from consuming tsukemono with high sodium content. Conversely, the healthy nutritional value from eating unsalted tsukemono may be modest and offer little prognostic significance. Rather, its association with lower mortality may be through a high likelihood of being associated with a traditional Japanese diet. Those who eat tsukemono may consume meat less often and prefer foods that are commonly enjoyed with tsukemono, such as fish, vegetables, fruits and soybean products.

We eat not only foods, but we eat them in certain patterns [20], such as in the Mediterranean and the Japanese dietary patterns. Because of highly interrelated dietary exposures, dietary patterns, rather than the specific effects of nutrients or foods have gained increasing attention [1, 2]. Although one drawback of the traditional Japanese diet is a high intake of salt, reduction in salt intake by the Japanese for the last 3 decades has been considered as one of the chief explanations for the decline in not only stroke but also stomach cancer mortality in Japan [5, 6, 21, 23]. This is consistent with the finding in the current report that infrequent consumption of soups with noodles, a marker of low salt intake, was associated with a significantly lower risk of all-cause mortality by itself.

Strengths and Limitations of the study

The strengths of our study include its prospective design and the follow-up of a randomly selected sample from the general population of Japan with a high response rate (76%). Since the study includes both men and women with a broad range of ages, findings are likely to be generalizable to middle-aged and elderly Japanese men and women.

As in any long-term follow-up study, however, there are several weaknesses. First, we surveyed essential nutritional components by the food-frequency method once at the baseline. As a result, we have no data on total caloric intake or total dietary intake of cholesterol or saturated and polyunsaturated fatty acids. To obtain these data, detailed food records or 24-hour recalls are needed. However, these methods are impractical and seldom used as the primary method for estimating usual intake in large-scale epidemiological studies. A second limitation is that the items used for the food-frequency method were not large in number, and has not been validated. We do not have data to what extent these foods contribute to the average energy intake of the studied participants. We also do not have frequency data on tofu, other soybean products, and vegetables and fruits. A high intake of these foods may also be characteristic features of the traditional Japanese diet. Several studies indicate that these foods have beneficial effects on some cause-specific mortality [24, 25]. In addition, although the use of near median values as cut- points for the consumption of meat and tsukemono appears arbitrary, they were chosen in accordance with their use in previous studies of the Mediterranean diet [2]. Unfortunately, while the intake of tsukemono, infrequent consumption of soup with noodles, and occasional drinking appeared to have the strongest association with a reduced risk of mortality, we cannot be certain that the other components of the Japanese diet are less important. As in any observational study, it is difficult to identify specific dietary effects due to multicolinearity that exists among food item intake. Within each component of the Japanese diet, there can also be considerable heterogeneity in nutrient content. In addition, overlap between components often occurs with the sharing of common ingredients or in how they are prepared and served. To better identify the effects of specific nutrients on mortality would require a controlled clinical trial. It may also be that dietary factors need to be considered in combination for an effect on longevity to be observed. An additional limitation is that we used mortality data as end points, which may lead to the misclassification of the cause of deaths. However, it has been reported that the death-certificate diagnosis for stroke and cancer in Japan is quite accurate [26]. Possible misclassification of AMI as "heart failure" is also not an issue in the current report since both outcomes are collectively categorized as cardiovascular disease [27].

Conclusions: Adherence to a healthy Japanese diet was associated with an approximate 20% lower rate of all-cause and cardiovascular mortality. While Japanese are exceptionally long-lived, placing greater emphasis on the intake of foods that are low in salt could increase longevity in Japan further.

We all have no conflicts of interest to disclose.

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CONTRIBUTION OF EACH AUTHOR

Nakamura Y participated in designing and conducting the study, analyzing and interpreting the data, and writing and preparing the manuscript. Ueshima H was the principal investigator and participated in designing and conducting the study and analyzing and interpreting the data. Okamura T, Abbott RD and Okayama A participated in conducting the study and analyzing and interpreting the data. Kadowaki T, and Kita Y participated in managing and interpreting the data. Hayakawa T participated in managing the data and conducting the study.

REFERENCES

1. Huijbregts P, Feskens E, Rasanen L, Fidanza F, Nissinen A, Menotti A, Kromhout D. Dietary pattern and 20 year mortality in elderly men in Finland, Italy, and The Netherlands: longitudinal cohort study. BMJ. 1997; 315: 13-17.

2. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med. 2003; 348: 2599-2608.

3. Robertson TL, Kato H, Gordon T, et al. Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California. Coronary heart disease risk factors in Japan and Hawaii. Am J Cardiol. 1977; 39: 244-249.

4. Carroll KK. Experimental evidence of dietary factors and hormone-dependent cancers. Cancer Res. 1975 ;35(11 Pt. 2):3374-3383.

5. Ueshima H, Zhang XH, Choudhury SR. Epidemiology of hypertension in China and Japan. J Hum Hypertens. 2000 -;14(10-11):765-769.

6. Kubo M, Kiyohara Y, Kato I, Tanizaki Y, Arima H, Tanaka K, Nakamura H, Okubo K, Iida M. Trends in the incidence, mortality, and survival rate of cardiovascular disease in a Japanese community: the Hisayama study. Stroke. 2003; 34: 2349-2354.

7. Nagata C, Takatsuka N, Shimizu N, Shimizu H. Sodium intake and risk of death from stroke in Japanese men and women. Stroke. 2004 Jul;35(7):1543-1547.

8. Okamura T, Kadowaki T, Hayakawa T, Kita Y, Okayama A, Ueshima H. What cause of mortality can we predict by cholesterol screening in the Japanese general population? J Intern Med 2003; 253: 169-180.

9. Nakamura Y, Okamura T, Tamaki S, Kadowaki T, Hayakawa T, Kita Y, Okayama A, Ueshima H. Egg consumption, serum cholesterol, and cause-specific and all-cause mortality: the National Integrated Project for Prospective Observation of Non-communicable Disease and Its Trends in the Aged, 1980 (NIPPON DATA80). Am J Clin Nutr. 2004; 80: 58-63.

10. Nakamura Y, Ueshima H, Okamura T, Kadowaki T, Hayakawa T, Kita Y, Tamaki S, Okayama A. Association between fish consumption and all-cause and cause-specific mortality in Japan: NIPPON DATA80, 1980-99. Am J Med. 2005; 118: 239-245.

11. Nakamura M, Sato S, Shimamoto T. Improvement in Japanese clinical laboratory measurements of total cholesterol and HDL-cholesterol by the US cholesterol reference method laboratory network. J Atheroscler Thromb 2003; 10: 145-153.

12. Kromhout D, Bosschieter EB, de Lezenne Coulander C. The inverse relation between fish consumption and 20-year mortality from coronary heart disease. N Engl J Med 1985; 312: 1205-1209.

13. Daviglus ML, Stamler J, Orencia AJ, Dyer AR, Liu K, Greenland P, Walsh MK, Morris D, Shekelle RB. Fish consumption and the 30-year risk of fatal myocardial infarction. N Engl J Med 1997; 336: 1046–1053.

14. Iso H, Kobayashi M, Ishihara J, Sasaki S, Okada K, Kita Y, Kokubo Y, Tsugane S. Intake of fish and n3 fatty acids and risk of coronary heart disease among Japanese: the Japan Public Health Center-Based (JPHC) Study Cohort I. Circulation. 2006; 113: 195-202.

15. Tsugane S, Fahey MT, Sasaki S, Baba S. Alcohol consumption and all-cause and cancer mortality among middle-aged Japanese men: seven-year follow-up of the JPHC study Cohort I. Japan Public Health Center. Am J Epidemiol. 1999 ; 150: 1201-1207.

16. Lori S. Parsons. Reducing Bias in a Propensity Score Matched-Pair Sample Using Greedy Matching Techniques. www2.sas.com/proceedings/sugi26/p214-26.pdf

17. Jacobs DR Jr, Andersen LF, Blomhoff R. Whole-grain consumption is associated with a reduced risk of noncardiovascular, noncancer death attributed to inflammatory diseases in the Iowa Women's Health Study. Am J Clin Nutr. 2007; 85: 1606-1614.

18. Ueshima H, Iida M, Shimamoto T, Konishi M, Tanigaki M, Doi M, Nakanishi N, Takayama Y, Ozawa H, Komachi Y. Dietary intake and serum total cholesterol level: their relationship to different lifestyles in several Japanese populations. Circulation. 1982; 66: 519-526.

19. Ueshima H, Okayama A, Saitoh S, Nakagawa H, Rodriguez B, Sakata K, Okuda N, Choudhury SR, Curb JD. Differences in cardiovascular disease risk factors between Japanese in Japan and Japanese-Americans in Hawaii: the INTERLIPID study. J Hum Hypertens. 2003; 17: 631-639.

20. Jacques PF, Tucker KL. Are dietary patterns useful for understanding the role of diet in chronic disease? Am J Clin Nutr. 2001; 73: 1-2.

21. Ueshima H, Tatara K, Asakura S. Declining mortality from ischemic heart disease and changes in coronary risk factors in Japan, 1956-1980. Am J Epidemiol. 1987; 125: 62-72.

22. Tokui N, Yoshimura T, Fujino Y, Mizoue T, Hoshiyama Y, Yatsuya H, Sakata K, Kondo T, Kikuchi S, Toyoshima H, Hayakawa N, Kubo T, Tamakoshi A. Dietary habits and stomach cancer risk in the JACC Study. J Epidemiol. 2005;15 (Suppl 2): S98-S108.

23. Tsugane S, Sasazuki S, Kobayashi M, Sasaki S. Salt and salted food intake and subsequent risk of gastric cancer among middle-aged Japanese men and women. Br J Cancer. 2004; 90: 128-134.

24. Sauvaget C, Nagano J, Allen N, Kodama K. Vegetable and fruit intake and stroke mortality in the Hiroshima/Nagasaki Life Span Study. Stroke. 2003; 34: 2355-2360.

25. Yamamoto S, Sobue T, Kobayashi M, Sasaki S, Tsugane S. Soy, isoflavones, and breast cancer risk in Japan. J Natl Cancer Inst. 2003; 95: 906-913.

26. Ron E, Carter R, Jablon S, Mabuchi K. Agreement between death certificate and autopsy diagnoses among atomic bomb survivors. Epidemiology 1994; 5: 48-56.

27. Saito I, Folsom AR, Aono H, Ozawa H, Ikebe T, Yamashita T. Comparison of fatal coronary heart disease occurrence based on population surveys in Japan and the USA. Int J Epidemiol 2000; 29: 837-844.

Table 1 Baseline Characteristics According to Preferred Food Type --NIPPON DATA80, 1980-99

	Japanese		Mixture		Western		Trend P
	Mean	SD	Mean	SD	Mean	SD	
Number at risk	6,505		1,977		403		
Age (y)	52.2	13.0	45.9	12.4	44.7	12.2	<0.0001
Men (%)	48.4		33.7		32.5		<0.0001
BMI (kg/m^2)	22.8	3.2	22.5	3.0	22.4	3.1	0.003
Hypertension (%)	47.8		36.2		31.8		<0.0001
Diabetes (%)	5.8		3.6		4.5		0.0002
Daily drinkers (%)	20.6		23.2		24.3		<0.0001
Current smokers (%)	35.8		25.7		23.1		<0.0001
Egg (/wk)	4.0	2.8	4.0	2.7	4.0	2.7	0.42
Fish (times/wk)	4.8	3.4	4.3	2.9	4.3	3.0	<0.0001
Meat (times/wk)	3.5	2.7	4.3	3.0	4.7	3.3	<0.0001
Tsukemono (times/wk)	9.6	5.0	8.3	5.2	6.6	5.0	<0.0001
Infrequent consumption of soup with noodles (%)	51.0		55.2		62.5		<0.0001
Use of low salt soy sauce (%)	16.7		17.3		18.4		<0.0001
Reduced Salt Japanese Diet Score	3.2	1.1	3.0	1.1	3.0	1.1	<0.0001

We excluded 201 participants in this Table who did not choose their preferred food type. To obtain trend Ps, the Mantel-Haenszel chi-square statistical test was used for nominal variables, and the analysis of variance for continuous variables. BMI=body mass index,

Table 2 Baseline Characteristics According to Tertiles of the Reduced Salt Japanese Diet Score among 4,018 men and 5,068 women --NIPPON DATA80, 1980-99

	Score 0-2		Score 3		Score 4-7		Trend P
	Mean	SD	Mean	SD	Mean	SD	
No at risk (total=9,086)	2,719		3,113		3,254		
Age (y)	49.1	13.5	50.7	13.1	51.7	13.0	<0.0001
Men (%)	49.3		43.6		40.5		<0.0001
BMI (kg/m^2)	22.6	3.0	22.7	3.2	22.8	3.2	0.003
Hypertension (%)	41.9		45.0		47.0		<0.0001
Diabetes (%)	4.6		5.6		5.4		0.18
Daily drinkers (%)	6.3		18.8		36.1		<0.0001
Current smokers (%)	35.4		32.2		31.5		<0.0001
TCH (mg/dl)	189	33	189	34	188	34	0.33
Egg ≤ 2 eggs/wk (%)	10.1		29.5		60.3		<0.0001
Fish ≥ once in 2 days (%)	26.2		35.0		38.8		<0.0001
Meat ≤ 2 times /wk (%)	12.7		30.5		56.8		<0.0001
Tsukemono ≥ once per day (%)	22.0		35.6		42.4		<0.0001
Infrequent consumption of soup with noodles (%)	12.3		34.4		53.3		<0.0001
Use of low salt soy sauce (%)	6.5		23.0		70.6		<0.0001
Occasional drinking (%)	8.8		30.4		60.8		<0.0001

We defined a healthy Japanese diet based on 7 components: egg intake ≤ 2 eggs/week, fish intake ≥ once in 2 days, meat intake ≤ 2 times/week, tsukemono (preserved roots or leaves of seasonal vegetables) intake ≥ once per day, infrequent intake of soup with noodles, use of low salt soy sauce, and occasional drinking. If a dietary component was part of a typical daily diet, it was scored as one and zero otherwise. Thus, the total Reduced Salt Japanese Diet Score ranged from 0 to 7, with 0 being least healthy and 7 being most healthy. To obtain trend Ps, the Mantel-Haenszel chi-square statistical test was used for nominal variables, and the analysis of variance for continuous variables.

No=number, TCH=serum total cholesterol concentration

Table 3 All-Cause and Cause-specific Mortality According to Reduced Salt Japanese Diet Score among 9,089 men and women --NIPPON DATA80, 1980-99

	Score 0-2	Score 3		Score 4-7		Trend P
		HR	95%CI	HR	95%CI	
Person-years	46,790	53,772		56,495		
All-cause death (total=1,823)	556	634		633		
Age, sex-adjusted HR	1	0.92	0.83-1.04	0.78	0.70-0.88	<0.0001
Multivariate HR						
Model 1	1	0.93	0.83, 1.04	0.78	0.69, 0.87	<0.0001
Model 2	1	0.92	0.83, 1.04	0.78	0.70, 0.88	<0.0001
CVD death (subtotal=654)	200	220		234		
Age, sex-adjusted HR	1	0.90	0.75, 1.09	0.80	0.66, 0.96	0.017
Multivariate HR						
Model 1	1	0.91	0.75, 1.10	0.79	0.65, 0.95	0.014
Model 2	1	0.91	0.75, 1.10	0.80	0.66, 0.97	0.022
Stroke death (subtotal=299)	92	107		100		
Age, sex-adjusted HR	1	0.95	0.72, 1.26	0.74	0.56, 0.99	0.035
Multivariate HR						
Model 1	1	0.96	0.73, 1.27	0.74	0.56, 0.98	0.031
Model 2	1	0.96	0.72, 1.27	0.75	0.56, 0.99	0.038
AMI death (subtotal=131)	40	42		49		
Age, sex-adjusted HR	1	0.83	0.55, 1.26	0.85	0.55, 1.31	0.39
Multivariate HR						
Model 1	1	0.86	0.56, 1.33	0.82	0.54, 1.25	0.37
Model 2	1	0.85	0.55, 1.32	0.84	0.55, 1.27	0.42

Cancer death (subtotal=551)	166		190		195	
Age, sex-adjusted HR	1	0.94	0.77, 1.16	0.86	0.70, 1.05	0.14
Multivariate HR						
Model 1	1	0.95	0.77, 1.17	0.85	069, 1.05	0.12
Model 2	1	0.95	0.77, 1.17	0.85	0.69, 1.05	0.13
NonCVD, NonCancer, Inflam.	40		37		42	
death (subtotal=119)						
Age, sex-adjusted HR	1	0.81	0.52, 1.27	0.74	0.48, 1.14	0.18
Multivariate HR						
Model 1	1	0.80	0.51, 1.25	0.74	0.48, 1.13	0.17
Model 2	1	0.80	0.51, 1.25	0.74	0.48, 1.14	0.18

Hazard ratio (HR) and 95% confidence intervals (95% CI) are shown. Multivariate= multivariate-adjusted Cox analysis. Model 1: adjusted for age, sex, BMI, and smoking (never and ex-, current smokers < 20 cigarettes/day, current smokers 20 to 40 cigarettes/day, and current smokers ≥ 41 cigarettes/day). Model 2: adjusted for Model 1 covariates plus hypertension and diabetes,

CVD=cardiovascular disease, AMI=acute myocardial infarction, BMI=body mass index, Inflam.=Inflammatory disease

Table 4 Components of Reduced Salt Japanese Diet Score and All-Cause Mortality among 9,089 men and women --NIPPON DATA80, 1980-99

Component	% of Total	Men%	HR	95%CI	P
Egg ≤ 2 eggs/wk	36.1	40.0	0.93	0.84, 1.02	0.11
Fish ≥ once in 2 days	71.9	45.9	0.98	0.88, 1.08	0.67
Meat ≤ 2 times /wk	38.1	40.6	0.97	0.88, 1.06	0.51
Tsukemono ≥ once per day	77.0	43.8	0.89	0.80, 0.998	0.045
Infrequent consumption of soup with noodles	51.3	36.3	0.88	0.80, 0.97	0.007
Use of low salt soy sauce	16.6	41.8	0.99	0.88, 1.12	0.86
Occasional drinking	21.2	55.4	0.81	0.71, 0.92	0.001

Hazard ratio (HR) and 95% confidence intervals (95% CI) are shown. Multivariate= multivariate-adjusted Cox analysis adjusted for age, sex, BMI, hypertension, diabetes, and smoking (never and ex-, current smokers < 20 cigarettes/day, current smokers 20 to 40 cigarettes/day, and > 40 cigarettes/day).

BMI=body mass index, % of Total=percent of total participants who had each component of Reduced Salt Japanese Diet Score, Men%=percent of men who had each component.

Table 5 Variables Used for Propensity Score Matching and Survival Rate --NIPPON DATA80, 1980-99

	Before matching					After matching				
	Score 4-7		Score 0-3		P	Score 4-7		Score 0-3		P
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
N	3254		5832			3196		3196		
Age (y)	51.7	13.0	50.0	13.3	<0.0001	51.6	13.0	51.6	13.5	0.96
Men (%)	40.5		46.3		<0.0001	40.0		40.4		0.78
BMI (kg/m^2)	22.8	3.2	22.6	3.1	0.003	22.8	3.2	22.8	3.2	0.96
Current smokers (%)	31.5		33.7		0.008	31.4		30.0		0.48
Systolic BP (mmHg)	137.0	21.2	135.2	21.1	<0.0001	137.0	21.2	136.8	21.9	0.68
Diastolic BP (mmHg)	81.8	12.2	81.0	12.1	0.003	81.8	12.2	81.3	12.4	0.11
Hypertension Drugs (%)	10.0		6.9		<0.0001	10.0		9.5		0.58
Diabetes (%)	5.4		5.1		0.54	5.4		5.2		0.78
TCH (mg/dl)	188	34	189	34	0.24	188	34	187	33	0.47
Albumin (mg/dl)	4.4	0.3	4.4	0.3	0.66	4.4	0.3	4.4	0.3	0.91
Uric acid (mg/dl)	4.9	1.3	5.0	1.3	0.07	4.9	1.3	5.0	1.3	0.76
Creatinine (mg/dl)	0.93	0.17	0.94	0.20	0.02	0.93	0.17	0.93	0.21	0.52
Propensity score	0.64	0.05	0.65	0.05	<0.0001	0.64	0.05	0.63	0.05	0.84
(Min, Max)	0.44	0.80	0.12	0.82		0.44.	0.80	0.42	0.76	

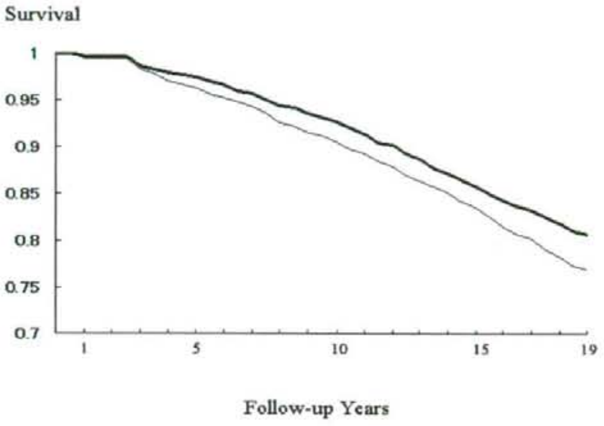
N=number, BMI=body mass index, BP=blood pressure, TCH=serum total cholesterol concentration

Figure legends

Figure 1 **Kaplan-Meier Survival Curve after Propensity Score Matching**

Significant differences in the average propensity score and the variables used in its calculation before matching in the two groups disappeared after matching. In contrast, a significant difference between the matched survival curves remained as seen in Figure 1 (P=0.0003 by log-rank test). Survival differences by the group were significant when examined further using a regression model with a Weibull distribution that included adjustment for age and sex as the dependent variables (P<0.0001). Thick line indicates survival for the participants with the Reduced Salt Japanese Diet Score 4-7, and thin line with the Reduced Salt Japanese Diet Score 0-3

Figure 1



APPENDIX NIPPON DATA80 Dietary Questionaire

Q1. Do you eat breakfast daily? Yes No

Q2. Do you daily eat green or yellow vegetables, such as carrot or spinach? Yes No

Q3. Do you daily eat fruits? Yes No

Q4. Do you daily eat salad or fresh vegetables? Yes No

Q5. Do you daily eat meat, fish or egg? Yes No

Q6. Do you daily drink milk? Yes No

Q7. Do you eat soy bean products, such as natto [fermented soybeans] or tofu more than 3 times per week? Yes No

Q8. Do you eat foods cooked with oil more than once daily? Yes No

Q9. Do you eat seaweed, such as kombu or laver more than 3 times per week? Yes No

Q10. Do you eat potatoes more than 3 times per week? Yes No

For each food listed on Q11. ～ Q16., please check the box indicating how often you eat, on average.

	≥2 /d	1/d	1/2 d	1～2 /wk	< 1/wk
Q11. Egg (how many)					
Q12. Fish (how often)					
Q13. Meat (including ham and sausage, how often)					
Q14. Noodles (how often)					
Q15. Tsukemono (how often)					
Q16. Soup (including miso soup, how often)					

Q17. Please select one food from the list that you like to eat the most:
(1) Beef (2) Pork (3) Poultry (4) Undecidable

Q18. Please select one dish from the list that you like to eat the most:
(1) Egg food (2) Meat dishes (3) Fish dishes (4) Tofu food (5) A vegetable dish

Q19. Please select one food combination from the list that you like to eat the most:
(1) Rice bowl + Sashimi + Miso soup + Tsukemono
(2) Bread + Hamburger steak + Potage soup + Salad
(3) Rice bowl + Hamburger steak + Miso soup + Salad

Q20. Which type of seasoning do you like best to eat with?
(1) Tick (2) Intermediate (3) Light

Q21. How do you eat tsukemono?
(1) As it is (2) Seasoning with soy sauce (3) Seasoning with sodium glutamate
(4) Seasoning with soy sauce plus sodium glutamate

From Q22. to Q 31, please choose one that fits best to your recent eating habit .

Q22. Do you try to eat modest amount of food? Yes No

Q23. Do you often eat processed foods, such as ham, sausage, kamaboko, or a tubular fish meat? Yes No

Q24. Are you not satisfied if you do not eat with tsukemono? Yes No

Q25. Are you not satisfied if you do not eat with a kind of soup? Yes No

Q26. Do you take soup infrequently with noodles? Yes No

Q27. When you eat tofu served cold, how do you season it with soy sauce?
(1) Dip it in a small dish with soy sauce
(2) Pour soy sauce over tofu.

Q28. When you eat curry and rice, do you pour Worcestershire sauce or soy sauce over it? Yes No

Q29. Are you trying to eat soups less often? Yes No

Q30. Have you ever used low salt soy sauce? Yes No

Q31. Are you trying to eat tsukudani [a shellfish boiled in sweetened soy sauce], shiokara [fish guts pickled in salt], or salted salmon less often? Yes No