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　（滋賀医科大学生活習慣病予防センター　特任教授）
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　准教授）
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）

目的

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。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

減塩に注意した日本食が寿命に及ぼす影響を 19 年間追跡した NIPPON DATA80 を用いて検討した。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。健康日本食スコアのもとになる構成要因を以下のように設定した：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。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

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、脳卒中死が有意に約 20%減少し、癌死と心筋梗塞死も低下する傾向にあった(表)。

結論

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。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。

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.

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A Japanese diet and 19-year mortality: National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980

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] and for National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980 Research Group

[1]*Cardiovascular Epidemiology, Kyoto Women's University, 35 Imakumano Kitahiyoshi-cho, Higashiyama-ku, Kyoto 605-8501, Japan*
[2]*Department of Health Science, Shiga University of Medical Science, Otsu City, Shiga, Japan*
[3]*Department of Hygiene and Preventive Medicine, Fukushima Medical University, Fukushima, Japan*
[4]*Department of Epidemiology and Biostatistics, University of Virginia School of Medicine, Charlottesville, VA, USA*
[5]*Department of Preventive Cardiology, National Cardiovascular Center, Suita City, Japan*

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Few studies have examined the association between Japanese diet and mortality outcomes. We analysed the relationship between a healthy Japanese diet and all-cause and cause-specific mortality using the database from the National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980. 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 seven components from FFQ. 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 9086 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 scores 3 and 4–7 were 0·92 (95 % CI 0·83, 1·04) and 0·78 (95 % CI 0·70, 0·88) for all-cause mortality (trend $P<0·0001$), and 0·91 (95 % CI 0·75, 1·10) and 0·80 (95 % CI 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.

Dietary pattern: Japanese diet: Cohort studies: Mortality

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 soup, and side dishes made from fish, meat, vegetable, tofu and the like, designed to add flavour to the staple food. These are typically flavoured with dashi stock, made with katsuobushi (dried skipjack tuna flakes), miso and soya 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 SFA and a high intake of PUFA, especially from fish. Long-term benefits include lower mortality from CHD 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 emphasise 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 those 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 analysed 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].

Abbreviation: BP, blood pressure.

* **Corresponding author:** Yasuyuki Nakamura, fax +81 75 531 2162, email nakamury@kyoto-wu.ac.jp

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Methods

Participants

The participants in this cohort were those in the 1980 National Survey on Circulatory Disorders[8]. A total of 10 546 community-based participants aged 30 years and above 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, the participants were followed up to 1999 (National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980, 1980–99). The overall population aged 30 years and above in the participating health districts was 13 771. The participation rate was 76·6 % (10 546 of 13 771) before exclusion for reasons mentioned later.

We reviewed the residence records of all the study participants for their vital status. In the 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 ninth International Classification of Disease for the National Vital Statistics until the end of 1994 and according to the tenth International Classification of Disease from the beginning of 1995. Deaths were confirmed in each district by computer matching of data from the National 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 National Vital Statistics records. The final sample comprised 9086 participants (4018 men and 5068 women). There were no significant differences between participants who were lost to follow-up and those who were included in the present 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 the present 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 centres. Baseline blood pressures (BP) 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 systolic BP ≥ 140 mmHg, diastolic BP ≥ 90 mmHg, or when a participant was receiving medications for the treatment of high BP. 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 that asked about the typical daily consumption of thirty-one food items, as shown in Appendix. Egg consumption was coded as ≥ 2 eggs/d, about 1 egg/d, about 1 egg/2 d, about 1–2 eggs/week and less than once per week. Fish, meat and tsukemono (preserved roots or leaves of seasonal vegetables, e.g. cucumbers and aubergine, which are consumed with rice at the end of a meal) intake was coded separately as ≥ 2 times/d, about 1 time/d, about 1 time/2 d, about 1–2 times/week and less than once per week. The participants were also asked whether they frequently consumed soup with noodles, whether they used low-salt soya sauce and what their preferred type of diet was (Japanese, Western or mixed; Q19 in Appendix). They were enquired 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 analysed in a sequential auto-analyser (SMA12/60, Technicon, Tarrytown, NY, 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[11]. Serum concentrations of glucose were measured by the cupric-neocuproine method[12]. Diabetes was determined by medical history or defined as a serum glucose concentration ≥ 2000 mg/l.

Statistical analysis and components of the Reduced-Salt Japanese Diet Score

Statistical Analysis Systems statistical software package version 9.1 for Windows (SAS Institute, Cary, NC, USA) 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 seven components from the nutritional survey to measure a healthy reduced-salt Japanese diet. The components included egg intake ≤ 2 eggs/week, fish intake once or more often in 2 d, meat intake ≤ 2 times/week, tsukemono intake once or more often per day, infrequent intake of soup with noodles, use of low-salt soya sauce and occasional drinking. The afore-mentioned cut-off values were determined based on the 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 soya sauce were used as markers of salt restriction. Because data on the 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 1 and 0 otherwise. Thus, the total score ranged from 0 to 7, with 0 being least healthy and 7 being most healthy. The participants were divided into approximate tertiles of dietary scores (0–2, 3 and 4–7 scores). To obtain trend P, the Mantel–Haenszel χ^2 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 ANOVA 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 -, sex- 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/d, current smokers 20–40 cigarettes/d and current smokers ≥41 cigarettes/d) 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 afore-mentioned 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 years, 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 (years), men (%), BMI (kg/m^2), current smokers (%), systolic BP (mmHg), diastolic BP (mmHg), on hypertension drugs (%), diabetes (%), serum total cholesterol (mg/l), albumin (mg/l), uric acid (mg/l) and creatinine (mg/l). After matching, adjusted survival curves were estimated separately for those 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 χ^2 test to determine whether 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 soya sauce) were more prevalent among those who preferred a Western diet. Small differences, but a significant trend in the Reduced-Salt Japanese Diet Score, were observed (trend $P<0{\cdot}0001$).

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 of 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 Diet Score increased as the score increased.

Table 1. Baseline characteristics according to preferred food type – National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980, 1980–99*

(Mean values and standard deviations)

	Japanese		Mixture		Western		
	Mean	SD	Mean	SD	Mean	SD	Trend *P*
Number at risk	6505		1977		403		
Age (years)	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 (/week)	4·0	2·8	4·0	2·7	4·0	2·7	0·42
Fish (times/week)	4·8	3·4	4·3	2·9	4·3	3·0	<0·0001
Meat (times/week)	3·5	2·7	4·3	3·0	4·7	3·3	<0·0001
Tsukemono (times/week)	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 soya 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 *P*s, the Mantel–Haenszel χ^2 statistical test was used for nominal variables, and the ANOVA for continuous variables.

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Table 2. Baseline characteristics according to tertiles of the Reduced-Salt Japanese Diet Score among 4018 men and 5068 women – National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980, 1980–99*

(Mean values and standard deviations)

	Score 0–2		Score 3		Score 4–7		
	Mean	SD	Mean	SD	Mean	SD	Trend *P*
No. at risk (total = 9086)	2719		3113		3254		
Age (years)	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/l)	1890	330	1890	340	1880	340	0·33
Egg ≤2 eggs/week (%)	10·1		29·5		60·3		<0·0001
Fish once or more often in 2 d (%)	26·2		35·0		38·8		<0·0001
Meat ≤2 times/week (%)	12·7		30·5		56·8		<0·0001
Tsukemono once or more often 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 soya sauce (%)	6·5		23·0		70·6		<0·0001
Occasional drinking (%)	8·8		30·4		60·8		<0·0001

No., number; TCH, serum total cholesterol concentration.

*We defined a healthy Japanese diet based on seven components: egg intake ≤2 eggs/week, fish intake once or more often in 2 d, meat intake ≤2 times/week, tsukemono (preserved roots or leaves of seasonal vegetables) intake once or more often per day, infrequent intake of soup with noodles, use of low-salt soya sauce and occasional drinking. If a dietary component was part of a typical daily diet, it was scored as 1 and 0 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 *P*s, the Mantel–Haenszel χ^2 statistical test was used for nominal variables, and the ANOVA for continuous variables.

All-cause and cause-specific mortality according to Reduced-Salt Japanese Diet Score

During the 19 years of follow-up, there were 1823 deaths. In this group, 654 were from CVD, 299 from stroke, 131 acute myocardial infarction, 551 cancer and 119 non-cardiovascular, non-cancer inflammatory diseases[17]. Table 3 shows the total person-years, numbers of cases, hazard ratios and 95 % CI 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-cause mortality, CVD and 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 mortality, CVD 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 CVD and stroke mortality, probably because of the relatively smaller number of such events at low-age strata.

Components of Reduced-Salt Japanese Diet Score and all-cause mortality

The percentage 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 percentage of male participants who observed a healthy reduced-salt Japanese dietary component 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 or more often 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 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. By contrast, a significant difference between the matched survival curves remained as shown in Fig. 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 with the higher score group), P<0·0001).

Discussion

The cut-off values for the egg, fish and drinking components were determined based on the 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 SFA in the Japanese[3,4,18,19]. Although frequent intake of tsukemono is also a character-

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Table 3. All-cause and cause-specific mortality according to Reduced-Salt Japanese Diet Score among 9089 men and women – National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980, 1980–99*
(Hazard ratios (HR) and 95% confidence intervals)

	Score 0–2	Score 3		Score 4–7		
		HR	95% CI	HR	95% CI	Trend *P*
Person-years	46790		53772		56495	
All-cause death (total = 1823)	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	0·69, 1·05	0·12
Model 2	1	0·95	0·77, 1·17	0·85	0·69, 1·05	0·13
Non-CVD, non-cancer, Inflam. death (subtotal = 119)	40		37		42	
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

AMI, acute myocardial infarction; Inflam., inflammatory disease.
*Multivariate, multivariate-adjusted Cox analysis. Model 1: adjusted for age, sex, BMI and smoking (never and ex-smokers, current smokers < 20 cigarettes/d, current smokers 20–40 cigarettes/d and current smokers ≥ 41 cigarettes/d). Model 2: adjusted for model 1 covariates plus hypertension and diabetes.

istic 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 soya bean products.

Table 4. Components of Reduced-Salt Japanese Diet Score and all-cause mortality among 9089 men and women – National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980, 1980–99*
(Hazard ratios (HR) and 95% confidence intervals)

Component	Total (%)	Men %	HR	95% CI	*P*
Egg ≤ 2 eggs/week	36·1	40·0	0·93	0·84, 1·02	0·11
Fish once or more often in 2 d	71·9	45·9	0·98	0·88, 1·08	0·67
Meat ≤ 2 times/week	38·1	40·6	0·97	0·88, 1·06	0·51
Tsukemono once or more often 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 soya 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

Total (%), percentage of total participants who had each component of Reduced-Salt Japanese Diet Score; men %, percentage of men who had each component.
*Multivariate, multivariate-adjusted Cox analysis adjusted for age, sex, BMI, hypertension, diabetes and smoking (never and ex-smokers, current smokers < 20 cigarettes/d, current smokers 20–40 cigarettes/d and > 40 cigarettes/d).

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Table 5. Variables used for propensity score matching and survival rate – National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980, 1980–99

(Mean values and standard deviations)

	Before matching					After matching				
	Score 4–7		Score 0–3			Score 4–7		Score 0–3		
	Mean	SD	Mean	SD	*P*	Mean	SD	Mean	SD	*P*
n	3254		5832			3196		3196		
Age (years)	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/l)	1880	340	1890	340	0·24	1880	340	1870	330	0·47
Albumin (mg/l)	44	03	44	03	0·66	44	03	44	03	0·91
Uric acid (mg/l)	49	13	50	13	0·07	49	13	50	13	0·76
Creatinine (mg/l)	9·3	1·7	9·4	2·0	0·02	9·3	1·7	9·3	2·1	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	

BP, blood pressure; TCH, serum total cholesterol concentration.

We merely do not eat foods, but in certain patterns[20], such as those in the Mediterranean and 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 three 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 present 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.

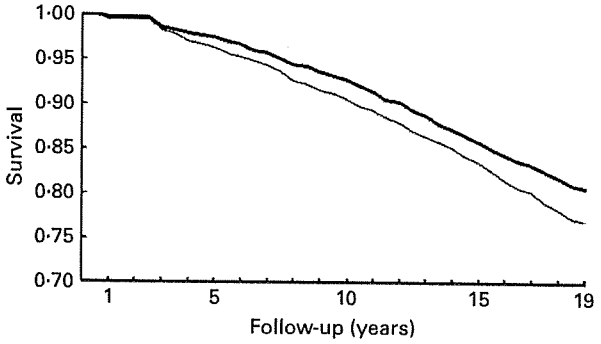

Fig. 1. Kaplan–Meier survival curve after propensity score matching. Significant differences in the average propensity score and the variables used in its calculation before matching in the two groups disappeared after matching. By contrast, a significant difference between the matched survival curves remained as shown in the figure (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). The thick line indicates survival for the participants with the Reduced-Salt Japanese Diet Score 4–7 and the thin line with the Reduced-Salt Japanese Diet Score 0–3.

Strengths and limitations of the study

The strengths of the present 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 generalisable 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 PUFA. To obtain these data, detailed food records or 24-h 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 soya bean 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 the 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 multicollinearity that exists among food item intake. Within each component of the Japanese diet, there can also be considerable heterogeneity in nutrient

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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 acute myocardial infarction as 'heart failure' is also not an issue in the present report since both outcomes are collectively categorised as CVD[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.

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Appendix NIPPON DATA80 Dietary Questionnaire

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 soya bean products, such as natto (fermented soya beans) or tofu more than three 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 three times per week?	Yes	No
Q10.	Do you eat potatoes more than three 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/week	<1/week
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) Thick (2) Intermediate (3) Light

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

From Q22 to Q31, please choose one that fits best 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 soya sauce? (1) Dip it in a small dish with soya sauce (2) Pour soya sauce over tofu.		
Q28.	When you eat curry and rice, do you pour Worcestershire sauce or soya sauce over it?	Yes	No
Q29.	Are you trying to eat soups less often?	Yes	No
Q30.	Have you ever used low-salt soya sauce?	Yes	No
Q31.	Are you trying to eat tsukudani (a shellfish boiled in sweetened soya sauce), shiokara (fish guts pickled in salt), or salted salmon less often?	Yes	No

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5年間の都老研式 IADL の推移と循環器疾患危険因子のリスク集積との関連 —NIPPON DATA90—

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　准教授）
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）
研究協力者　渡邉　至　（国立循環器病センター予防検診部）
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）

Abstract

OBJECTIVES
日本人の代表集団において、65 歳以上の高齢者の循環器疾患危険因子の集積と5年間の手段的日常生活動作（IADL）の関連を明らかにする。
DESIGN
地域集団におけるコホート研究
METHODS
1990 年に全国から無作為抽出された 30 歳以上の住民を対象として循環器健診を実施した。この参加者のうち 1995 年の 65 歳以上の生存者を対象として都老研式 IADL 調査を行い、2000 年に再度同じ対象者に IADL の調査を行った。対象者数は 1995 年と 2000 年に調査ができ、調査項目をすべて回答した 1,222 名である。1990 年の循環器疾患危険因子の集積と 5 年間の IADL の変化との関連を分析した。
RESULTS
男女とも、5年間の IADL の変化量は高年齢群ほど有意に大きく低下していた。男女ともほぼすべての危険因子で、危険因子を有するほうが有さない場合に比して IADL 減少の絶対値が大きかった。ロジスティック回帰で性別、年齢、飲酒、過去の喫煙歴を調整すると、循環器疾患危険因子数と IADL の変化量は有意な負の関連を示した（p=0.029）。1995 年に身体的 ADL が自立していた者のみで解析しても、循環器疾患危険因子数と IADL 変化量の負の関連は有意であった（p=0.028）。
CONCLUSION
日本人の代表集団において、5年間の IADL 得点は循環器疾患危険因子数が増加するほど有意に低下していた。循環器疾患危険因子の集積は循環器疾患の発症や死亡に影響するだけでなく、IADL の低下にも影響していることが明らかになった。

Original Article

Relationship between 5-Year Decline in Instrumental Activity of Daily Living and Accumulation of Cardiovascular Risk Factors: NIPPON DATA90

Takehito Hayakawa[1], Tomonori Okamura[2], Akira Okayama[3], Hideyuki Kanda[1], Makoto Watanabe[2], Yoshikuni Kita[4], Katsuyuki Miura[4], and Hirotsugu Ueshima[4]

[1]Department of Hygiene and Preventive Medicine, Fukushima Medical University, Fukushima, Japan
[2]Department of Preventive Cardiology, National Cardiovascular Center, Osaka, Japan
[3]The First Institute for Health Promotion and Health Care, Japanese Anti-Tuberuculosis Association, Tokyo, Japan
[4]Department of Health Science, Shiga University of Medical Science, Shiga, Japan

Aim: To clarify the relationship between the accumulation of cardiovascular risk factors and the 5-year decline in instrumental activity of daily living (IADL) among a cohort representative of the Japanese population aged 65 years and over.
Methods: An IADL survey was performed by public health centers throughout Japan. Study subjects were elderly men and women living in districts under the jurisdiction of collaborating health centers. Subjects were invited to participate in the IADL survey assessed by the Tokyo Metropolitan Institute of Gerontology (TMIG) Index of Competence twice in 1995 and in 2000; 1222 participants were eligible for the analysis. The relationship between the number of cardiovascular risk factors, such as hypertension, hypercholesterolemia, hypertriglycemia, low serum high-density lipoprotein cholesterol, diabetes, obesity and smoking, at baseline and the 5-year difference in IADL scores was examined by linear regression analysis and logistic regression analysis.
Results: Decrease in IADL scores was larger in those with cardiovascular risk factors than in those without. The multivariable odds ratio (OR) for decreased IADL after adding one CVD risk factor was 1.16 (95% confidence interval (CI), 1.04–1.29) after adjusting for age, sex, alcohol consumption and TMIG score at baseline. Among participants who were regarded as physically independent with respect to basic ADL in the baseline survey, the odds ratio was also similar and significant.
Conclusion: Preventive interventions directed against cardiovascular risk factors, especially against their accumulation, may contribute to maintaining IADL in the Japanese elderly.

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Key words; Accumulation of cardiovascular risk factors, Instrumental activity of daily living, Cohort study, General population

Objectives

It is very important to create a society in which the elderly can live a healthy and active life for as long as possible. To minimize disability in elderly people in Japan, where the numbers of those aged 65 and older are increasing each year, we need to clarify modifiable risk factors that predict the future decline in activity of daily living (ADL)[1, 2]. ADL is often used to evaluate the disabled elderly, for example, those requiring rehabilitation or nursing home admission; however, as ADL is not suitable for screening elderly residents who are not disabled but have a potential need for home health-care services[3], another indicator is needed to evaluate the ability to live independently in the community. Instrumental activity of daily living (IADL) has been used in this manner[4]; however, most previ-

Address for correspondence: Takehito Hayakawa, Department of Hygiene and Preventive Medicine, Fukushima Medical University, 1 Hikarigaoka, Fukushima City, Fukushima 960-1295, Japan
E-mail: thayaka@fmu.ac.jp
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ous studies to clarify the determinants of IADL have been cross-sectional in design.

Cardiovascular risk factors, such as hypertension, dyslipidemia, and diabetes, are often clustered[5-7]. The presence of multiple risk factors, recently termed metabolic syndrome, has been reported to increase the risk of developing or dying from cardiovascular disease such as myocardial infarction and stroke[8, 9]. However, to our knowledge, few studies have examined the relationship between the accumulation of cardiovascular risk factors and a future decline in IADL in a community setting.

Accordingly, we attempted to followup a cohort thought to be representative of the Japanese population to evaluate the relationship between the 5-year decline in IADL and the accumulation of cardiovascular risk factors measured in the National Survey of Circulatory Disorders, 1990.

Methods

A cohort study of the participants in the 4th National Survey on Circulatory Disorders, Japan was performed in 1990, NIPPON DATA90 (National Integrated Project for Prospective Observation of Non-communicable Disease And its Trends in the Aged, 1990). The details of this cohort have been previously reported[1, 2, 5, 10-14]. A total of 8,384 community residents (3,504 men and 4,880 women, ≥30 years old) from 300 randomly selected districts participated in the survey and were followed until November 15, 2000. The overall population aged 30 years and older in all districts was 10,956, and the participation rate was 76.5%. Accordingly, these participants were thought to be representative of the Japanese population.

We performed a survey of basic ADL and IADL in 1995 (baseline) and 2000 of the elderly (≥65 years in 1995) members of this cohort. This survey was performed by the public health centers whose jurisdiction included cohort districts of NIPPON DATA90. Of 284 health centers, 245 collaborated with the present study; 1945 participants were living in districts under the jurisdiction of collaborating health centers in 1995, and 301 had died or moved to different districts by 2000. Accordingly, 1644 participants were included in the present study. Of these, 36 declined to participate, 89 could not be contacted, and 297 had missing information at 2000; therefore, 1222 subjects (492 men, 730 women) were eligible for analysis.

We used the Tokyo Metropolitan Institute of Gerontology (TMIG) Index of Competence, a widely used scale for measuring IADL with demonstrated reliability and validity[3, 15]. The first five questions (No. 1–5) inquire about instrumental independence, the subsequent four (No. 6–9) about intellectual activity, and the final four (No. 10–13) about social roles. The respondent selects either "yes" (one point) or "no" (zero points), for a maximum score of 13 points[3, 15]. Participants were also asked about five basic (physical) ADL items (Feeding, Dressing, Bathing, Toileting, and Transfer: walking indoors) and whether each of these could be accomplished without help, with partial help, or with full help. "Physical ADL decline" was defined as partial or full support needed to perform any of the five basic ADL items[1, 2].

We used home-visit interviews to assess subjects; if this was impractical, the questions were asked over the phone or the questionnaire was mailed.

Risk factors for cardiovascular disease were defined as the following seven items in 1990: hypertension (systolic blood pressure, SBP ≥140 mmHg and/or diastolic blood pressure, DBP ≥90 mmHg), diabetes (casual blood glucose ≥200 mg/dL and/or HbA1c ≥6.0), hypercholesterolemia (total cholesterol, TCH ≥240 mg/dL), low serum high-density lipoprotein (HDL) cholesterol (HDLC <40 mg/dL), high serum triglyceride (TG) (TG >150 mg/dL), obesity (BMI ≥25 kg/m^2), and current smoking.

We examined whether the difference in IADL scores differs depending on the presence or absence of each risk factor. A *t*-test or one-way analysis of variance was conducted for continuous variables and a chi-square test for proportions, and linear regression analysis to evaluate the relationship between the number of risk factors and the 5-year difference in IADL scores. The individual 5-year difference in IADL scores was calculated by subtracting the score in 1995 from that in 2000. We also performed logistic regression analysis to evaluate the relationship between the number of risk factors and IADL decline. In logistic regression analysis, we defined IADL decline as a 2-point decline in the TMIG score between 1995 and 2000, as a previous study reported that a difference of ±1 point in the TMIG score was within the error range[16]. In both regression analyses, we adjusted for age, sex and alcohol consumption as confounding factors (Model 1). Further adjustment of the TMIG score at baseline (in 1995) was also performed (Model 2). A p value of <0.05 was considered significant.

The Statistical Package for the Social Sciences (SPSS Japan Inc. version 14.0J, Tokyo, Japan) was used for analyses.

The present study was approved by the Institutional Review Board of Shiga University of Medical Science (No. 12-18, 2000).

Table 1. Mean scores of instrumental activities of daily living (IADL) assessed by the Tokyo Metropolitan Institute of Gerontology (TMIG) Index of Competence

	N	1995		2000		Mean IADL	*p* value*
		Mean	SD	Mean	SD		
Men							
65-69	204	12.0	1.9	11.4	2.9	−0.412	
70-74	164	11.9	1.8	10.7	3.3	−1.134	
75-79	81	11.8	2.0	9.4	3.9	−2.222	<0.001
80-84	37	10.7	3.3	7.9	3.8	−2.568	
85+	6	7.6	2.6	3.2	1.9	−3.167	
Women							
65-69	290	12.2	1.6	11.6	2.2	−0.476	
70-74	208	11.9	2.0	10.8	3.1	−1.154	
75-79	142	11.2	2.2	9.4	3.6	−1.634	<0.001
80-84	69	9.8	3.0	6.8	3.8	−2.855	
85+	21	7.4	3.9	4.4	3.6	−3.143	

Maximum score is 13.
Mean IADL was calculated by substracting the score in 1995 from than in 2000.
*Comparison between age groups by chi-square test.

Results

The mean age of subjects in 1995 was 71.9 (standard deviation, SD=5.0) years for men and 72.8 (SD=5.7) years for women. The difference in IADL scores rated by the TMIG Index of Competence is shown by sex and age group in **Table 1**. Between the two surveys, mean IADL scores decreased significantly in the older age groups in both men and women. The absolute value of decrease in the IADL scores was also large in the older age groups in both men and women. In men aged 65 to 69, the decrease in the IADL score was 0.412 points, while in those aged 85 years and older, it was 3.167. In women aged 65 to 69, the decrease in IADL score was 0.476 points, while in those aged 85 and older it was 3.143.

Participants were classified into "risk status categories" according to the number of cardiovascular risk factors (obesity, hypertension, hypercholesterolemia, diabetes, low serum HDLC, high serum TG, and current smoking). **Table 2** shows the means and prevalence of each risk factor. There was no difference in mean age between the risk status categories. Hypertension was the most prevalent risk factor in all categories except for the 4+ risk factor category in women. In the 4+ risk factor category, obesity was observed in 63.4% of men and 80.0% of women. In this category, diabetes was also detected in 66.2% of men and 79.5% of women. The mean decreases in IADL scores according to the number of CVD risk factors (0, 1, 2, 3, 4) were -0.90, -1.03, -1.05, -1.67 and -1.25, respectively.

Table 3 shows the difference in IADL scores between 1995 and 2000, focusing on the presence/absence of cardiovascular risk factors. The decrease in IADL scores was larger in both men and women with any cardiovascular risk factors (with the exception of hypercholesterolemia and high serum TG) than in those without. In this comparison, however, no significant difference was observed other than for low serum HDLC in women.

Table 4 shows the relationship between the 5-year difference in IADL scores and the number of cardiovascular risk factors at the baseline survey. As the number of cardiovascular risk factors increased, IADL scores decreased significantly. Among subjects who were regarded as independent with respect to basic (physical) ADL in the first IADL survey in 1995, IADL scores also decreased significantly as the number of cardiovascular risk factors increased.

The multivariable odds ratio (OR) for decreased IADL after adding one CVD risk factors in model 1 was 1.15 (95% confidence interval (CI), 1.04-1.28). When we performed further adjustment for the TMIG score at baseline (Model 2), the odds ratio was almost the same (OR, 1.16; 95%CI, 1.04-1.29). Among participants who were regarded as physically independent with respect to basic ADL in the baseline survey, the odds ratio was also similar and significant.

Although the TMIG score indicated a broader

Table 2. Means and prevalences of baseline characteristics stratified by the number of risk factors at the baseline survey, NIPPON DATA90

	Number of risk factors					*p* value
	None	One	Two	Three	Four or more	
Men						
Number of participants (%)	48 (10.1)	134 (28.1)	144 (30.2)	86 (18.0)	65 (13.6)	
Age (years)	72.6±6.0	72.9±5.4	71.5±4.7	71.5±4.4	71.3±4.7	0.093
Body mass index >25 (%)	0.0	4.2	12.8	27.5	63.4	<0.001
Smoking habit						
Ex-smoker (%)	60.4	53.7	20.8	25.6	26.2	<0.001
Current smoker (%)	0.0	23.1	66.0	58.1	64.6	
Drinking habit						
Ex-drinker (%)	10.4	7.5	8.3	10.5	16.9	0.285
Daily drinker (%)	45.8	56.7	56.9	44.2	46.2	
Hypertension (%)	0.0	56.0	75.7	72.1	89.2	<0.001
Hypercholesterolemia (%)	0.0	2.2	6.3	17.4	43.1	<0.001
Low HDL (%)	0.0	6.0	18.1	47.7	75.4	<0.001
High TG (%)	0.0	7.5	16.0	69.8	83.1	<0.001
Diabetes (%)	0.0	4.5	13.2	27.9	66.2	<0.001
Women						
Number of participants (%)	80 (11.9)	207 (30.7)	193 (28.6)	121 (18.0)	73 (10.8)	
Age (yr)	72.0±5.7	72.3±5.6	72.7±5.6	73.2±5.8	73.2±5.1	0.465
Body mass index >25 (%)	0.0	10.7	31.1	49.2	80.0	<0.001
Smoking habit						
Ex-smoker (%)	2.5	1.4	1.6	4.1	2.7	<0.001
Current smoker (%)	0.0	3.4	4.7	8.3	21.9	
Drinking habit						
Ex-drinker (%)	0.0	0.0	0.0	0.8	4.1	0.008
Daily drinker (%)	5.0	1.9	4.1	3.3	4.1	
Hypertension (%)	0.0	59.9	76.7	83.5	91.8	<0.001
Hypercholesterolemia (%)	0.0	10.6	32.1	44.6	49.3	<0.001
Low HDL (%)	0.0	5.8	12.4	38.0	60.3	<0.001
High TG (%)	0.0	8.2	38.3	66.9	94.5	<0.001
Diabetes (%)	0.0	11.1	31.6	47.9	79.5	<0.001

HDL, high density lipoprotein. TG, triglyceride.
The number of risk factors was the sum of the following seven items: hypertension, diabetes, hypercholesterolemia, low serum HDL cholestrol, high serum TG, obesity, and current smoking.

range of activity in daily life for the elderly than the narrowly defined IADL, the above results were substantially similar when we only used the subscale of IADL in the TMIG score.

Discussion

The present study found a significant inverse relationship between the number of cardiovascular risk factors and the decrease in IADL scores during a 5-year period in this representative sample of elderly Japanese people. Even though the effect of each individual risk factor did not reach statistical significance, the accumulation of cardiovascular risks resulted in a significant decrease in IADL scores. These results suggest that appropriate management of the cardiovascular risk factors might prevent a decline in IADL in elderly residents.

Okamura *et al.* reported that elderly residents with systolic hypertension (≥160 mmHg) in two communities located in Akita and Kochi Prefectures showed a 3.41 times higher odds ratio for having low IADL scores than those with normal blood pressure[17]; however, they surveyed the TMIG Index of Compe-

Table 3. Decrease in IADL scores from 1995 to 2000 by the presence/absence of risk factors, NIPPON DATA90

Age (years)	Men 71.9 (±5.0)			Women 72.8 (±5.7)		
	N	mean ΔIADL	*p* value	N	mean ΔIADL	*p* value
BMI						
BMI <25	400	−1.11	0.545	513	−1.11	0.211
BMI ≥25	92	−1.32		217	−1.40	
Smoking						
Non-smoker	92	−0.87		664	−1.16	
Ex-smoker	173	−1.43	0.268	19	−2.47	0.142
Current smoker	227	−1.04		47	−1.26	
Hypertension						
SBP <140 and DBP <90	180	−1.09	0.768	258	−1.11	0.544
SBP ≥140 or DBP ≥90	312	−1.18		472	−1.24	
Hypercholesterolemia						
TCH <240	422	−1.17	0.890	500	−1.14	0.804
TCH ≥240	55	−1.11		174	−1.21	
HDL						
HDL ≥40	353	−1.10	0.483	548	−1.03	0.016
HDL <40	124	−1.32		126	−1.71	
TG						
TG <150	330	−1.24	0.410	433	−1.09	0.396
TG ≥150	147	−0.99		241	−1.29	
Diabetes						
Glucose <200 and HbA1c <6.0	443	−1.11	0.178	633	−1.12	0.209
Glucose ≧200 or HbA1c ≧6.0	34	−1.82		41	−1.71	

IADL, instrumental activities of daily living.
HDL, high density lipoprotein. TG, triglyceride.

tence only at the end of follow-up. In the Framingham Disability Study, Pinsky *et al.* reported that hypertension, obesity, and diabetes adversely affected ADL in women after 27 years, while only hypertension adversely affected ADL in men[18]; however, IADL was not evaluated in that study. We reported the impact of serum albumin and total cholesterol (TC) on ADL in NIPPON DATA80[19]. Serum albumin was inversely associated with a composite outcome of death or impaired ADL in the group below the median of TC in both sexes; however, in that study, IADL was not evaluated and ADL was assessed only at the end of follow-up.

The above-mentioned previous studies focused only on the relationship between the respective risk factors and ADL or IADL. As previously reported, individual risk factors, such as hypertension, dyslipidemia, and diabetes, are associated with the development of cardiovascular disease; however, even though each of these cardiovascular risk factors may elevate the risk only slightly, the risk becomes more powerful when they are combined[20, 21]. Metabolic syndrome is a cluster of risk factors comprising insulin resistance, increased abdominal fat, dyslipidemia, and hypertension[22]. To our knowledge, the present study is the first to show the relationship between the accumulation of cardiovascular risk factors and IADL in community-dwelling elderly using a cohort design.

The present study suggests that the presence of multiple risk factors might contribute to the decline in IADL in the future. Cerebral infarction associated with impaired cognition without a clinical symptom is common, even in older men and women[23]. Bokura *et al.* suggested that the clustering of metabolic risk factors tended to increase the prevalence of silent cerebral ischemic lesions in 1,151 healthy Japanese subjects[24]. Furthermore, Elias *et al.* indicated that the risk factor profile for stroke was associated with low cognitive performance in a cross-sectional analysis of the Framingham Offspring Study[25]. These findings were consistent with those of the present study.

There are several limitations to our study. First,

Table 4. Relationship between the 5-year decline in scores of instrumental activity of daily living (IADL) and the number of cardiovascular risk factors

Five- year decrease in IADL scores assessed by the TMIG Index of Competence			
Baseline risk factors	Regression coefficient (β)	95%CI	p
Total participants (n=1,222)			
Model 1	−0.149	(−0.278, −0.020)	0.029
Model 2	−0.161	(−0.285, −0.036)	0.011
Participants without physical ADL decline at baseline (n=1,155)			
Model 1	−0.146	(−0.277, −0.015)	0.028
Model 2	−0.171	(−0.297, −0.046)	0.008
Odds ratio for IADL decline* during 5-year period			
	Odds Ratio	95%CI	p
Total participants (n=1,222)			
Model 1	1.15	(1.04, 1.28)	<0.001
Model 2	1.16	(1.04, 1.29)	0.008
Participants without physical ADL decline at baseline (n=1,155)			
Model 1	1.15	(1.03, 1.28)	0.015
Model 2	1.15	(1.03, 1.29)	0.013

*The number of risk factors was the sum of the following seven items: hypertension, diabetes, hypercholesterolemia, low serum HDL cholestrol, high serum TG, obesity, and current smoking.
Model 1, include age, sex, number of risk factors, daily alcohol consumption, ex-drinker and ex-smoker;
Model 2, model 1 + TMIG at baseline (1995).
Sex was defined as Male=0 and Female=1.
Daily drinking means drinking at least 1 drink per day.
Ex-drinker means having discontinued alcohol consumption.
Ex-smoker means having discontinued smoking.

the risk factors selected were examined not in the initial IADL survey but in the survey conducted 5 years earlier. However, the accuracy of cardiovascular risk factor definition was assured because risk factors were based on medical examinations rather than on respondents' self-reports. Moreover, participants with severe disease at the time of the risk factor survey might have found it difficult to attend the first IADL survey, which was held 5 years later. This might have allowed us to avoid "reverse-causality"; in other words, participants with subclinical severe disease that was not detected by the risk factor survey were less likely to be included in the first IADL survey.

As previously reported, NIPPON DATA90 was a cohort study of a representative sample of Japanese, as participants of this cohort were randomly selected from the Japanese population; however, in the present study, as subgroup analysis of elderly participants of NIPPON DATA90, participants were limited to those living in districts under the jurisdiction of collaborating health centers, although we believe that there was no systematic bias in the regions whese public health centers did not collaborated with the present study. Non-surveyed districts were distributed uniforml throughout Japan. Furthermore, there was no difference in substantial health status between surveyed and non-surveyed districts due to the incorporation of health centers. For example, there was not significant difference in all-cause mortality between two districts during follow-up periods. Second, because the IADL survey was conducted only every 5 years, we could not pinpoint exactly when and why IADL declined during the 5-year period.

In conclusion, we found a significant relationship between the number of cardiovascular risk factors and the decrease in IADL scores among this cohort, which is thought to be representative of the Japanese population. Interventions aimed at preventing cardiovascular risk factors, especially the accumulation of such risk factors, may therefore be effective to prevent a future decline in IADL for the Japanese elderly, allowing them to live a healthy and active life.

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