中年期の食事習慣と将来の日常生活活動(ADL)変化— NIPPON DATA80 研究結果

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
研究協力者	寶澤 篤	東北大学大学院社会医学講座公衆衛生学分野 助教
研究協力者	Tanvir C. Turin	滋賀医科大学社会医学講座公衆衛生学部門 特別研究員
研究協力者	高嶋 直敬	滋賀医科大学社会医学講座公衆衛生学部門 特任助教
研究分担者	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	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
研究分担者	岡山 明	財団法人結核予防会第一健康相談所 所長
研究分担者	三浦 克之	滋賀医科大学社会医学講座公衆衛生学部門 准教授
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

先進工業諸国においては医療等の健康管理が進歩し、人口の高齢化が進んでいる。2005年には日本の65歳以上の高齢者人口比率は世界最高となった。日本の平均寿命と健康寿命は世界最長であるが、その差は約7年で、多くの高齢者が長期に亘る要介護状態を経験していることになる。日常生活活動(ADL)に影響を与える数ある環境因子の中で食事要因は多くの人々が改善可能であるため重要である。本研究では中年期の食事習慣と将来の日常生活活動(ADL)変化を検討し、介護予防の指針に寄与することを目的とした。

方法

1980年に47-60歳で循環器基礎調査を受診し、19年の追跡の後1999年にADL調査を受け脳卒中と心筋梗塞の既往の無い2,316人(男性1,042人、女性1,274人)を対象とした。1980年の追跡開始時には検診、食事摂取を含む生活習慣調査、および採血を行った。肉、鶏卵、および魚の摂取頻度と19年後のADLについて多変量ロジスティック解析を行った。肉、鶏卵、魚の摂取頻度は中央値で2群に分けた。ADLはKatzらの食事、着衣、入浴、用便、室内歩行の基本的5項目が全て可能ならADL障害なし、1項目でも介助を要する場合ADL障害ありとした[1]。調整因子として年齢、BMI、喫煙、飲酒、高血圧、糖尿病を基本変数として(モデル1)、モデル2ではさらに血清アルブミン、総コレステロール値を加え、モデル3ではモデル2に職種(専門職か否か)、住居地(都市か否か)を加えた。食事因子のADLに及ぼす影響に男女によって差があるか否かの交互作用を検討した。

結果

19年間に427人が死亡し、75人がADLに障害を来した。生存者1,889人の中で、肉摂取頻度が多い群でADL障害発生が少なかった。鶏卵、魚摂取頻度とADL障害発生との間に関連はなかった。食品摂取がADL障害発生に及ぼす影響に性別の交互作用はなかった。またいずれの食品摂取頻度も総死亡との間に関連はなく、また総死亡またはADL障害のいずれかの発生に対しても関連がなかった。

考察

動脈硬化促進因子と想定された肉食にADL障害発生予防効果があり、動脈硬化抑制因子

と想定された魚およびコレステロール含量が多い鶏卵の摂食頻度と ADL 障害発生に関連が見られなかったのは予想外の結果であった。

牛肉には飽和脂肪酸が多いので一般的に動脈硬化促進因子と考えられるが、前向き研究で牛肉摂取が心血管疾患に及ぼす影響について検討したものはない。事実地中海食に関する研究でも肉摂取因子は心血管疾患に対して何ら影響を及ぼしていなかった[2]。逆に Sauvaget らは広島・長崎コホート研究の結果、動物性食品摂取は脳出血と脳梗塞を低下させたと報告している[3]。また Geleijnse らの Rotterdam 研究では肉、鶏卵、およびチーズに含まれる食餌性メナキノンは冠動脈疾患リスクを低下させることを示している[4]。最近わが国での動物性タンパク・脂肪の摂取は増加しているものの、訪米と比べてまだ比較的低量である。かなり大量の牛肉摂取には予後に対して悪影響があるとしても、低摂取量の範囲内ではやや多い牛肉摂取量には好効果がある可能性がある。

別に考慮すべきものとして社会経済状態がある。社会経済状態が悪いと心血管発症・死亡を増加させる。本研究では肉摂取が多いことと専門職および都市在住との間に関連があった。また都市在住は ADL 障害発生と負の関連があった。しかしロジスティック解析において専門職および都市在住を調整因子に入れても肉摂取が ADL 障害発生を予防する効果は有意に存続した。

本研究では追跡開始時に ADL 調査を行わなかった。しかし検診受診者は歩行来所し、脳卒中既往者を除外しているため当初の ADL 障害者は存在しなかったと仮定できる。また社会経済状態に関する他の因子も調査すべきであった。

肉摂取が多いと将来の ADL 障害発生を抑制する可能性がある。

1. Katz S, et al. Progress in development of the index of ADL. Gerontologist 1970; 10: 20-30.
2. Trichopoulou A, et al. Adherence to a Mediterranean diet and survival in a Greek population. N Engl J Med. 2003; 348: 2599-2608.
3. Sauvaget C, et al. Intake of animal products and stroke mortality in the Hiroshima/Nagasaki Life Span Study. Int J Epidemiol. 2003; 32: 536-43.
4. Geleijnse JM, et al. Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease: the Rotterdam Study. J Nutr. 2004; 134: 3100-5.

表　1,889 人の生存者における肉食摂取と 19 年後の ADL 障害の関係－NIPPON DATA80, 1980-99.

	肉食 <1/2 日	肉食≥1/2 日	P
N　(人)	775	1,114	
ADL 障害　(人)	41	34	
オッズ比			
モデル 1	1	0.61 (0.38-0.97)	0.04
モデル 2	1	0.62 (0.38-0.99)	0.05
モデル 3	1	0.61 (0.38-0.99)	0.04

Dietary Habits in Middle Age and Future Changes in Activities of Daily Living--NIPPON DATA80.

Yasuyuki Nakamura, MD,[1,2] Atsushi Hozawa, MD,[2,3] Tanvir Chowdhury Turin, MD,[2] Naoyuki Takashima, MD,[2] Tomonori Okamura, MD,[4] Takehito Hayakawa, PhD,[5] Yoshikuni Kita, PhD,[2] Akira Okayama, MD,[6] Katsuyuki Miura, MD,[2] and Hirotsugu Ueshima, MD,[2] for the NIPPON DATA80 Research Group[7]

[1] Cardiovascular Epidemiology, Kyoto Women's University, Kyoto, Japan
[2] Department of Health Science, Shiga University of Medical Science, Otsu, Japan
[3] Department of Public Health and Forensic Medicine, Tohoku University School of Medicine, Sendai, Japan.
[4] Department of Preventive Cardiology, National Cardiovascular Center, Osaka, Japan
[5] Department of Hygiene and Preventive Medicine, Fukushima Medical University, Fukushima, Japan
[6] Japan Anti-Tuberculosis Association, Tokyo, Japan.

[7]Members of the NIPPON DATA80 Research Group are listed in the Appendix of reference 10.

Address correspondence and reprints to:
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

Abbreviates Title: Meat Intake and Activities of Daily Living

ABSTRACT

Background: Almost no studies have investigated the relationship between food intake measured at middle-age and future disability.

Objective: To examine the association of meat, fish and egg intake with risk of subsequent mortality and/or future decline in activities of daily living (ADL) among the elderly.

Methods: The cohort consisted of 2,316 Japanese individuals aged 47-60 at the baseline who were randomly selected throughout Japan and followed up for 19 years from 1980.

Results: Those who ate meat ≥ once every two days were younger, there were more men, daily drinkers, professional workers, and urban residents compared to those who ate meat < once every two days. Over 19 years of follow-up, 75 participants became dependent due to impaired ADL. A higher intake of meat was associated with a statistically significant decrease in impaired ADL occurrence (odds ratio=0.61, 95% confidence intervals: 0.38-0.99, P=0.04). Fish and egg intake were not associated with any difference in impaired ADL occurrence. None of the three foods were associated with any changes in mortality.

Conclusion: A higher intake of meat may prevent impaired ADL occurrence, although this was not associated with a lower mortality.

Key Words: Meat, fish, egg, activities of daily living, mortality, a cohort study

INTRODUCTION

The elderly population is increasing in developed countries and, improvements in health care have led to an increase in life expectancy. In 2005, Japan had the highest proportion of those aged 65 and older in the world [1]. Although both life expectancy and healthy life expectancy in Japan are among longest in the world, the difference in the two expectancies is about 7 years [2], indicating people in Japan suffer from the activity of daily living (ADL) reduction for a long time before death. Among many environmental factors that may influence ADL in the elderly, the role played by food is important. However, almost no studies have investigated the relationship between food intake measured at middle-age and future disability.

The objective of this prospective study was to clarify the relationship between food intake and impaired ADL surveyed at 19 years after a baseline survey among a Japanese general population aged 47-59 years. Previous studies on food intake and all-cause and cause-specific mortality led us to hypothesize that food that is known to promote atherosclerosis, such as eggs or meat, would have a negative influence on future ADL, and food that is known to prevent atherosclerosis, such as fish, would have a beneficial influence on future ADL [3-9].

METHODS

Subjects and follow-up

The dataset of the cohort study of the National Survey on Circulatory Disorders comprising the National Integrated

Project for Prospective Observation of Non-communicable Disease and Its Trends in the Aged (NIPPON DATA) was used. A baseline survey was performed in 1980 (NIPPON DATA80) (10-13). We analyzed the 19-year follow-up data from NIPPON DATA80 in this study.

The study population comprised 3,227 participants (1,413 men and 1,814 women, aged 47 to 59) from 300 randomly selected districts in 1980. The baseline surveys were carried out at local public health centers and all participants had to be capable of reaching the examination center without assistance. The participation rate was about 77%. We excluded 286 participants who had a history of coronary heart disease or stroke (n = 39), were missing information in the baseline survey (n = 54), or were lost to follow-up (n = 193) due to an incomplete residential address at the baseline. Thus, 2,941 were eligible for follow-up. Among them, 427 died and information about ADL was gathered from 2,514 survivors by physicians and public health nurses at public health centers in 1999. Consequently, 75% (1,889) of the survivors completed the information. No potential differences between responders and non-responders in terms of baseline age, gender, BP values, use of antihypertensive medication, body mass index (BMI), smoking status or serum albumin concentration were observed. Participants were asked about five basic ADL items (feeding, dressing, bathing, toileting, and transfer: walking indoors) modified from Katz, et al. [14] and whether each of these could be accomplished without help, with partial help or with full help. This survey was conducted through telephone interviews (10.5%), face-to-face interviews at home (80.0%), and other methods (9.5%). In this study, we basically analyzed participants who completed the ADL information alone (N=1,889), and together with participants who died before the ADL survey (N=2,316). The Institutional Review Board of Shiga University of Medical Science (NO.12-18, 2000) approved the study.

Biochemical and baseline examinations

Baseline BP was measured by trained observers using a standard mercury sphygmomanometer on the right arm of seated participants after at least 5 minutes of rest. Hypertension was defined as a systolic blood pressure ≥ 140 mmHg, a diastolic blood pressure ≥90 mmHg, or when a participant was receiving medication for high blood pressure. BMI was calculated as weight (kg) divided by height^2 (m).

A lifestyle survey was also carried out using a self-administered questionnaire which included the daily consumption of meat, eggs and fish. Egg consumption was coded as ≥2 eggs per day, about 1 egg per day, about 1 egg every 2 days, about 1 to 2 eggs per week, and less than one egg per week. Fish, and meat intake were coded separately as ≥2 times per day, about 1 time per day, about 1 time every 2 days, about 1 to 2 times per week, and less than once per week. 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). Serum concentrations of glucose were measured by the cupric-neocuproline method [15]. Diabetes was determined by medical history or defined as a serum glucose concentration ≥200 mg/dl.

Statistical analysis

SAS version 9.1 for Windows (SAS Institute, Cary, NC) was used. Because the number of participants was not large, participants were classified into the two groups according to meat consumption as < once every 2 days and ≥ once every 2 days, and fish and egg consumption as < once per day and ≥ once per day around the median of these consumption categories. The chi-square test was used to compare dichotomous variables and the Student's *t*-test was used to compare means between two groups according to food consumption. The relationship between food intake categories and impaired ADL or impaired ADL together with all-cause mortality was calculated using multiple adjusted logistic regression models, taking a lower food consumption group as a reference. Age-sex-adjusted and multivariate-adjusted odds ratios were calculated. For multivariate analyses, we adjusted for age, BMI, and cigarette smoking (never and former smokers, current smokers < 20 cigarettes/day, current smokers 20 to 40 cigarettes/day, and current smokers ≥ 41 cigarettes/day), alcohol drinking (never, past, non-daily, and daily), hypertension and diabetes (Model 1). Model 1 was also adjusted for serum albumin and total cholesterol concentrations (Model 2). Model 2 was further adjusted for job type (professional or not) and urban residence (yes, no) (Model 3). Interactions between sex and the effect of food intake on impaired ADL or impaired ADL together with all-cause mortality were examined.

RESULTS

The baseline characteristics and outcomes of 1,413 male and 1,814 female study participants in each meat, fish and egg consumption category are shown in Table 1. In male participants who ate meat ≥ once every two days, there were more professional workers compared to those who ate meat < once every two days. In men who ate fish ≥ once per day, there were more daily drinkers and hypertension, and fewer professional workers than in men who ate fish < once per day. In men who ate eggs ≥ once per day, the mean BMI was smaller than in those who ate eggs < once per day. In women who ate meat ≥ once every two days, there were more younger participants, more smokers and more professional workers compared to those

who ate meat < once every two days. In women who ate eggs≥ once per day, the mean total cholesterol concentration was higher than those who ate eggs < once per day. No differences in crude outcomes (incidence of death, stroke, CHD, or leg fracture) were noted between the two groups in each of the three food intake categories. The baseline characteristics and outcomes of the 1,889 survived participants were basically as in Table 1.

During 19 years of follow-up, 502 participants either died or became dependent due to impaired ADL. Table 2 shows numbers of participants at risk and impaired ADL or death cases, odds ratio (OR), and 95% confidence intervals by age and sex-adjusted, and multivariate adjusted ORs (model 1 to 3) for death or impaired ADL. Differences in any food intake were not associated with differences in composite outcome of impaired ADL and death. There were no interactions between sex and the effect of food intake on impaired ADL together with all-cause mortality.

During 19 years of follow-up, 427 participants died. Table 3 shows numbers of participants at risk and death cases, odds ratio (OR), and 95% confidence intervals by age and sex-adjusted, and multivariate adjusted ORs (model 1 to 3) for death. Differences in any food intake were not associated with differences in mortality. There were no interactions between sex and the effect of food intake on all-cause mortality.

During 19 years of follow-up, 75 participants became dependent due to impaired ADL. Associations of impaired ADL and food intake in the 1,889 surviving participants are shown in Table 4. A higher intake of meat was associated with a statistically significant decrease in the occurrence of impaired ADL in all four models. The other covariates in model 3 that had significant contributions to the outcome were age (P=0.0004), BMI (P=0.009), and urban residence (P=0.02). There were no interactions between sex and the effect of food intake on impaired ADL.

DISCUSSION

We found that a higher intake of meat during middle age was associated with a statistically significant reduction in future occurrence of impaired ADL, although it was not associated with change in composite outcome of either died or became dependent due to impaired ADL.. Intake of fish and eggs was not associated with the composite outcome or with impaired ADL outcome. These results were unexpected since eggs and meat are believed to promote atherosclerosis, and fish is known to prevent atherosclerosis. Recently, it has been shown that low to normal serum albumin and total cholesterol concentrations were associated with impaired ADL using this cohort data, as well as those of other studies [13, 16, 17]. However, in the present study, these concentrations were not different between the two groups in all three food intake categories.

Meat products are rich in saturated fatty acids that are thought to be atherogenic. In fact, a high intake of meat is classed as a component presumed to be detrimental to health in studies on dietary patterns, including in a Mediterranean diet [18, 19]. Surprisingly, however, there has been no prospective study to demonstrate the detrimental effects of meat intake on cardiovascular outcome. Actually, a higher meat intake had a neutral association with all cause mortality while a higher intake of fruits and nuts was inversely associated with all cause mortality, in a Mediterranean diet study [18]. There have been some cross-sectional studies related to associations between intake of meat and cardiovascular disease risk factors. Sadakane et al. identified three dietary patterns from a food frequency questionnaire by factor analyses. In men, the meat pattern was associated with higher total and high-density lipoprotein (HDL), and low-density lipoprotein (LDL) cholesterol; in women, it was associated with higher total and HDL cholesterol [20]. Two small studies found no effect of animal protein intake on blood pressure [21, 22]. The large scaled INTERMAP study showed dietary animal protein intake was not associated with a higher blood pressure after adjustment for height and weight, while vegetable protein was inversely related to blood pressure [23]. To date, cross-sectional studies have failed to demonstrate any detrimental effect of meat intake or animal protein on cardiovascular disease risk factors. Interestingly, several longitudinal studies have suggested a beneficial effect of meat intake on cardiovascular outcomes. Using the Hiroshima/Nagasaki Life Span Study cohort data, Sauvaget et al. showed intake of animal products had protective effects against intracerebral hemorrhage and cerebral infarction [24, 25]. Analyzing the Rotterdam Study data, Geleijnse et al. showed CHD mortality was reduced in a higher tertiles of dietary menaquinone compared to the lower tertile [26]. Since major sources of menaquinone are meat, eggs and cheese; generally considered to be unhealthy diet, the authors thought it unlikely that the observed reduction in CHD risk was due to confounding factors. A cross-sectional study in the elderly showed protein intake, especially from animal sources, was associated with a better preservation of muscle mass [27], and a follow-up study in older, community-dwelling adults demonstrated dietary protein intake was inversely associated with 3 year lean mass loss [28]. Recently, the intake of animal protein and fat in Japan has increased significantly; however, the current mean consumption of these nutrients in Japan is still low compared with Western countries [29-32]. It is possible that even if a very high meat intake is associated with negative outcomes, a higher intake in a lower range may have beneficial effects. Thus, there appears to be enough evidence to support our present finding that a higher intake of meat may prevent occurrence of impaired ADL, although it was not associated with lower mortality.

Another factor that may relate to the association between meat intake and outcomes is socioeconomic status (SES). Lower SES is associated with all-cause, as well as cardiovascular, morbidity and mortality [33-36]. In the present study, a higher intake of meat was associated with a higher prevalence of professional work and urban residence; markers of a higher SES.

Urban residence was a significant contributor to a lower risk for impaired ADL in the logistic analysis model. After adjustment for urban residence, however, a higher intake of meat remained statistically significant.

There are some limitations in this study. We did not assess the baseline ADL condition, therefore we are not sure that all impaired ADL cases were new incidents during the follow-up period. However, because the participants came on foot to baseline examinations at local public health centers and we excluded participants who had a history of stroke, we considered the effect of any lack of information on our results to be negligible. Second, we do not have information on SES, other than professional work and urban residence. Third, the time span between baseline data collection and ADL data collection is long; diets might have been changed during this time in Japan. However, according to the National Health and Nutritional Survey in Japan, the average daily intakes of meat, fish and egg by Japanese aged 50 to 59 in 1986 were 58.7, 102.3 and 40.5 g, respectively, and those by Japanese aged 60 to 69 in 1996 were 51.4, 106.7 and 36.4 g, respectively [37]. Namely, there might not have been significant changes in diets in Japan during the study period.

In conclusion, a higher intake of meat may prevent impaired ADL occurrence, although it was not associated with a lower mortality.

ACKOWLEDGEMENT

The authors thank all public health centers that cooperated with our study.

This study was supported by a Grant-in-Aid from the Ministry of Health and Welfare under the auspices of the Japanese Association for Cerebro-cardiovascular Disease Control, a Research Grant for Cardiovascular Diseases (7A-2) from the Ministry of Health, Labor and Welfare and a Health and Labor Sciences Research Grant, Japan (Comprehensive Research on Aging and Health: H11-chouju-046, H14-chouju-003, H17-chouju-012 and H19-chouju-014).

REFERENCES

1. The Statistics Bureau and the Director-General for Policy Planning (Statistical Standards). The 2005 Population Census http://www.stat.go.jp/english/data/kokusei/2005/youkei/01.htm
2. World Health Organization. Core Health Indicators. http://www.who.int/whosis/database/core/core_select_process.cfm.
3. Nakamura Y, Okamura T, Tamaki S, Kadowaki T, Hayakawa T, Kita Y, Okayama A, Ueshima H; NIPPON DATA80 Research Group. 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, Ueshima H, Okamura T, Kadowaki T, Hayakawa T, Kita Y, Tamaki S, Okayama A; NIPPON DATA80 Research Group. Association between fish consumption and all-cause and cause-specific mortality in Japan: NIPPON DATA80, 1980-99. Am J Med. 2005; 118: 239-45.
5. Nakamura Y, Ueno Y, Tamaki S, Kadowaki T, Okamura T, Kita Y, Miyamatsu N, Sekikawa A, Takamiya T, El-Saed A, Sutton-Tyrrell K, Ueshima H. Fish consumption and early atherosclerosis in middle-aged men. Metabolism. 2007; 56: 1060-4.
6. 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.
7. Daviglus ML, Stamler J, Orencia AJ, et al. Fish consumption and the 30-year risk of fatal myocardial infarction. N Engl J Med 1997; 336: 1046–53.
8. Hu FB, Bronner L, Willett WC et al. Fish and omega-3 fatty acid intake and risk of coronary heart disease in women. JAMA 2002; 287: 1815-21.
9. Iso H, Kobayashi M, Ishihara J, Sasaki S, Okada K, Kita Y, Kokubo Y, Tsugane S; JPHC Study Group. 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.
10. Okamura T, Kadowaki T, Hayakawa T, Kita Y, Okayama A, Ueshima H; Nippon Data80 Research Group. What cause of mortality can we predict by cholesterol screening in the Japanese general population? J Intern Med 2003; 253: 169-80.
11. Ueshima H, Choudhury SR, Okayama A, Hayakawa T, Kita Y, Kadowaki T, Okamura T, Minowa M, Iimura O. Cigarette smoking as a risk factor for stroke death in Japan: NIPPON DATA80. Stroke 2004; 35: 1836-1841.
12. Okamura T, Tanaka H, Miyamatsu N, Hayakawa T, Kadowaki T, Kita Y, Nakamura Y, Okayama A, Ueshima H; NIPPON DATA80 Research Group. The relationship between serum total cholesterol and all-cause or cause-specific mortality in a 17.3-year study of a Japanese cohort. Atherosclerosis 2007; 190: 216-223.
13. Okamura T, Hayakawa T, Hozawa A, Kadowaki T, Murakami Y, Kita Y, Abbott RD, Okayama A, Ueshima H; NIPPON DATA80 Research Group. Lower levels of serum albumin and total cholesterol associated with decline in activities of daily living and excess mortality in a 12-year cohort study of elderly Japanese. J Am Geriatr Soc. 2008; 56: 529-35.
14. Katz S, Downs TD, Cash HR et al. Progress in development of the index of ADL. Gerontologist 1970; 10: 20-30.

15. Bittner D, McCleary M. The cupric-phenanthroline chelate in the determination of monosaccharides in whole blood. Am J Clin Pathol 1963; 40: 423-424.
16. Schalk BW, Visser M, Bremmer MA et al. Change of serum albumin and risk of cardiovascular disease and all-cause mortality: Longitudinal Aging Study Amsterdam. Am J Epidemiol 2006; 164: 969-977.
17. Reuben DB, Ix JH, Greendale GA et al. The predictive value of combined hypoalbuminemia and hypercholesterolemia in high functioning community-dwelling older persons: MacArthur Studies of Successful Aging. J Am Geriatr Soc 1999; 47: 402-406.
18. 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.
19. Lutsey PL, Steffen LM, Stevens J.Dietary intake and the development of the metabolic syndrome: the Atherosclerosis Risk in Communities study. Circulation. 2008; 117: 754-61.
20. Sadakane A, Tsutsumi A, Gotoh T, Ishikawa S, Ojima T, Kario K, Nakamura Y, Kayaba K. Dietary patterns and levels of blood pressure and serum lipids in a Japanese population. J Epidemiol. 2008; 18: 58-67.
21. Kestin M, Rouse IL, Correll RA, Nestel PJ. Cardiovascular disease risk factors in free-living men: comparison of two prudent diets, one based on lactoovovegetarianism and the other allowing lean meat. Am J Clin Nutr. 1989; 50: 280-7.
22. Prescott SL, Jenner DA, Beilin LJ, Margetts BM, Vandongen R. A randomized controlled trial of the effect on blood pressure of dietary non-meat protein versus meat protein in normotensive omnivores. Clin Sci (Lond). 1988; 74: 665-72.
23. Elliott P, Stamler J, Dyer AR, Appel L, Dennis B, Kesteloot H, Ueshima H, Okayama A, Chan Q, Garside DB, Zhou B. Association between protein intake and blood pressure: the INTERMAP Study. Arch Intern Med. 2006; 166: 79-87.
24. Sauvaget C, Nagano J, Allen N, Grant EJ, Beral V. Intake of animal products and stroke mortality in the Hiroshima/Nagasaki Life Span Study. Int J Epidemiol. 2003; 32: 536-43.
25. Sauvaget C, Nagano J, Hayashi M, Yamada M. Animal protein, animal fat, and cholesterol intakes and risk of cerebral infarction mortality in the adult health study. Stroke. 2004; 35: 1531-7.
26. Geleijnse JM, Vermeer C, Grobbee DE, Schurgers LJ, Knapen MH, van der Meer IM, Hofman A, Witteman JC. Dietary intake of menaquinone is associated with a reduced risk of coronary heart disease: the Rotterdam Study. J Nutr. 2004; 134: 3100-5.
27. Lord C, Chaput JP, Aubertin-Leheudre M, Labonté M, Dionne IJ. Dietary animal protein intake: association with muscle mass index in older women. J Nutr Health Aging. 2007; 11: 383-7.
28. Houston DK, Nicklas BJ, Ding J, Harris TB, Tylavsky FA, Newman AB, Lee JS, Sahyoun NR, Visser M, Kritchevsky SB; Health ABC Study. Dietary protein intake is associated with lean mass change in older, community-dwelling adults: the Health, Aging, and Body Composition (Health ABC) Study. Am J Clin Nutr. 2008; 87: 150-5.
29. Iso H, Stampfer MJ, Manson JE, Rexrode K, Hu F, Hennekens CH, Colditz GA, Speizer FE, Willett WC. Prospective study of fat and protein intake and risk of intraparenchymal hemorrhage in women. Circulation. 2001; 103: 856-63.
30. Ueshima H. Changes in dietary habits, cardiovascular risk factors and mortality in Japan. Acta Cardiol. 1989; 44: 475-7.
31. Kromhout D, Menotti A, Bloemberg B, Aravanis C, Blackburn H, Buzina R, Dontas AS, Fidanza F, Giampaoli S, Jansen A, et al. Dietary saturated and trans fatty acids and cholesterol and 25-year mortality from coronary heart disease: the Seven Countries Study. Prev Med. 1995; 24: 308-15.
32. Shimamoto T, Komachi Y, Inada H, Doi M, Iso H, Sato S, Kitamura A, Iida M, Konishi M, Nakanishi N, et al. Trends for coronary heart disease and stroke and their risk factors in Japan. Circulation. 1989; 79: 503-15.
33. Dragano N, Bobak M, Wege N, Peasey A, Verde PE, Kubinova R, Weyers S, Moebus S, Möhlenkamp S, Stang A, Erbel R, Jöckel KH, Siegrist J, Pikhart H. Neighbourhood socioeconomic status and cardiovascular risk factors: a multilevel analysis of nine cities in the Czech Republic and Germany. BMC Public Health. 2007;7: 255.
34. Shishehbor MH, Litaker D, Pothier CE, Lauer MS. Association of socioeconomic status with functional capacity, heart rate recovery, and all-cause mortality. JAMA. 2006; 295: 784-92.
35. Fukuda Y, Nakamura K, Takano T. Higher mortality in areas of lower socioeconomic position measured by a single index of deprivation in Japan. Public Health. 2007; 121: 163-73.
36. Fukuda Y, Nakamura K, Takano T. Municipal socioeconomic status and mortality in Japan: sex and age differences, and trends in 1973-1998. Soc Sci Med. 2004; 59: 2435-45.
37. Outline for the Results of the National Health and Nutrition Survey Japan. http://www.nih.go.jp/eiken/chosa/kokumin_eiyou/

Table 1 Baseline Characteristics and Outcomes of 1,042 Male and 1,274 Female Participants in the Meat, Fish and Egg Intake Groups, NIPPON DATA80, 1980-99.

	Meat < 1/2 d	Meat ≥1/2 d	P	Fish < 1/d	Fish ≥1/d	P	Egg < 1/d	Egg ≥1/d	P
Men									
N	375	667		555	487		599	443	
Age (years)	53.2±3.6	52.9±3.5	0.27	52.9±3.5	53.1±3.5	0.52	53.1±3.5	52.9±3.5	0.51
BMI (kg/m^2)	22.4±2.9	22.7±2.7	0.15	22.5±2.9	22.7±2.7	0.14	22.7±2.8	22.4±2.9	0.048
Smoking (%)	69.9	65.4	0.13	68.5	65.3	0.28	66.9	67.0	0.97
Daily drinking (%)	49.1	52.5	0.29	47.9	55.0	0.02	51.6	50.8	0.80
Hypertension (%)	58.1	54.9	0.31	52.6	60.0	0.02	57.3	54.4	0.36
Diabetes (%)	7.7	10.2	0.19	10.6	7.8	0.12	9.9	8.6	0.48
Albumin (mg/dl)	4.4±0.3	4.4±0.2	0.48	4.4±0.3	4.4±0.2	0.47	4.4±0.3	4.4±0.3	0.95
TCH (mg/dl)	186±34	188±34	0.49	188±35	187±33	0.53	189±35	185±32	0.10
Professional work (%)	33.7	40.7	0.03	41.1	34.9	0.04	38.7	37.5	0.69
Urban residence (%)	25.3	31.0	0.05	31.2	26.5	0.10	30.4	27.1	0.25
Incidence of									
Death (%)	25.1	25.5	0.88	25.2	25.5	0.93	25.2	25.5	0.91
Stroke (%)	9.8	7.4	0.26	8.6	7.9	0.72	9.1	7.1	0.30
CHD (%)	5.1	5.0	0.94	5.2	4.8	0.81	6.0	3.7	0.16
Leg fracture (%)	1.5	2.1	0.54	1.7	2.0	0.80	2.3	1.2	0.29
Women									
N	573	701		750	524		877	397	
Age (years)	53.6±3.8	53.1±3.8	0.02	53.1±3.7	53.5±3.9	0.10	53.3±3.8	53.3±3.7	0.997
BMI (kg/m^2)	23.3±3.6	23.3±3.2	0.98	23.4±3.4	23.2±3.4	0.39	23.4±3.4	23.2±3.3	0.39
Smoking (%)	9.8	6.0	0.01	8.8	6.1	0.08	7.8	7.6	0.90
Daily drinking (%)	1.8	2.0	0.74	2.3	1.3	0.23	1.6	2.5	0.26
Hypertension (%)	51.3	46.9	0.12	49.2	48.5	0.80	50.1	46.4	0.22
Diabetes (%)	3.8	4.0	0.89	3.3	4.8	0.19	3.8	4.3	0.66
Albumin (mg/dl)	4.4±0.2	4.4±0.2	0.67	4.4±0.2	4.4±0.2	0.80	4.4±0.2	4.4±0.2	0.71
TCH (mg/dl)	196±35	199±32	0.20	197±33	198±33	0.73	196±32	201±35	0.01
Professional work (%)	15.4	22.0	0.003	17.6	21.0	0.13	18.5	20.2	0.47
Urban residence (%)	28.5	32.0	0.18	32.0	28.1	0.13	29.8	31.7	0.48

Incidence of									
Death (%)	13.8	12.0	0.34	12.3	13.6	0.50	11.9	14.9	0.14
Stroke (%)	5.0	3.6	0.28	3.2	5.6	0.05	4.7	3.0	0.20
CHD (%)	2.9	3.0	0.94	2.8	3.2	0.72	2.9	3.0	0.90
Leg fracture (%)	0.8	1.8	0.16	1.7	0.9	0.26	0.9	2.4	0.05

Data are shown in % or mean±SD. BMI=body mass index, TCH=total cholesterol concentration, CHD=coronary heart disease

Table 2 Associations of Impaired ADL or Death and Food Intake in 2,316 Participants in the Meat, Fish and Egg Intake Group, NIPPON DATA80, 1980-99.

	Meat < 1/2 d	Meat ≥1/2 d	P	Fish < 1/d	Fish ≥1/d	P	Egg < 1/d	Egg ≥1/d	P
N	948	1,368		1,305	1,011		1,476	840	
Case with impaired ADL or death	214	288		271	231		306	196	
Odds ratio									
Age-sex adjusted	1	0.89 (0.72-1.09)	0.25	1	1.06 (0.86-1.30)	0.58	1	1.09 (0.88-1.34)	0.44
Model 1	1	0.91 (0.74-1.12)	0.35	1	1.09 (0.89-1.34)	0.40	1	1.10 (0.89-1.36)	0.40
Model 2	1	0.91 (0.74-1.12)	0.38	1	1.10 (0.89-1.35)	0.39	1	1.10 (0.89-1.36)	0.39
Model 3	1	0.91 (0.73-1.12)	0.36	1	1.08 (0.87-1.33)	0.50	1	1.09 (0.88-1.35)	0.43

Over 19 years of follow-up, 502 participants either died or became dependent due to impaired ADL. Numbers of participants at risk and impaired ADL or death cases, odds ratio (OR), and 95% confidence intervals by age and sex-adjusted, and multivariate adjusted (model 1 to 3) ORs for death or impaired ADL, are shown. Model 1 included age, sex, smoking (never and former smokers, current smokers < 20 cigarettes/day, current smokers 20 to 40 cigarettes/day, and current smokers ≥ 41 cigarettes/day), alcohol drinking (never, past, non-daily, and daily), hypertension, diabetes, and BMI. Model 2 included model 1 variables + serum albumin and total cholesterol concentration. Model 3 included model 2 variables + job type (professional or not), urban residence.

Table 3 Associations of Death and Food Intake in 2,316 Participants in the Meat, Fish and Egg Intake Group, NIPPON DATA80, 1980-99.

	Meat < 1/2 d	Meat ≥1/2 d	P	Fish < 1/d	Fish ≥1/d	P	Egg < 1/d	Egg ≥1/d	P
N	948	1,368		1,305	1,011		1,476	840	
Case with death	173	254	0.87	232	195	0.79	255	172	0.26
Odds ratio	1	0.98 (0.79-1.22)	0.98	1	1.03 (0.83-1.28)	0.57	1	1.14 (0.91-1.42)	0.26
Age-sex adjusted	1	1.00 (0.80-1.25)	0.96	1	1.07 (0.86-1.33)	0.55	1	1.14 (0.91-1.43)	0.26
Model 1	1	1.00 (0.80-1.26)	0.99	1	1.07 (0.86-1.33)	0.65	1	1.14 (0.91-1.43)	0.29
Model 2	1	1.00 (0.80-1.25)		1	1.06 (0.84-1.32)		1	1.13 (0.90-1.42)	
Model 3									

Over 19 years of follow-up, 427 participants died. Numbers of participants at risk and death cases, odds ratio (OR), and 95% confidence intervals by age and sex-adjusted, and multivariate adjusted (model 1 to 3) ORs for death, are shown. Model 1 included age, sex, smoking (never and former smokers, current smokers < 20 cigarettes/day, current smokers 20 to 40 cigarettes/day, and current smokers ≥ 41 cigarettes/day), alcohol drinking (never, past, non-daily, and daily), hypertension, diabetes, and BMI. Model 2 included model 1 variables + serum albumin and total cholesterol concentration. Model 3 included model 2 variables + job type (professional or not), urban residence.

Table 4 Associations of Impaired ADL and Food Intake in 1,889 Survived Participants in the Meat, Fish and Egg Intake Group, NIPPON DATA80, 1980-99.

	Meat < 1/2 d	Meat ≥1/2 d	P	Fish < 1/d	Fish ≥1/d	P	Egg < 1/d	Egg ≥1/d	P
N	775	1,114		1,073	816		1,221	668	
Case with impaired ADL	41	34		39	36		51	24	
Odds ratio									
Age-sex adjusted	1	0.58 (0.36-0.93)	0.02	1	1.19 (0.75-1.89)	0.47	1	0.86 (0.52-1.42)	0.55
Model 1	1	0.61 (0.38-0.97)	0.04	1	1.25 (0.78-2.01)	0.35	1	0.89 (0.54-1.48)	0.66
Model 2	1	0.62 (0.38-0.99)	0.05	1	1.23 (0.77-1.97)	0.39	1	0.90 (0.54-1.49)	0.67
Model 3	1	0.61 (0.38-0.99)	0.04	1	1.25 (0.76-1.95)	0.42	1	0.90 (0.54-1.49)	0.68

Over 19 years of follow-up, 75 participants became dependent due to impaired ADL. Numbers of participants at risk and cases with impaired ADL, odds ratio (OR), and 95% confidence intervals by age and sex-adjusted, and multivariate adjusted (model 1 to 3) ORs for impaired ADL are shown. Model 1 included age, sex, smoking (never and former smokers, current smokers < 20 cigarettes/day, current smokers 20 to 40 cigarettes/day, and current smokers ≥ 41 cigarettes/day), alcohol drinking (never, past, non-daily, and daily), hypertension, diabetes, and BMI. Model 2 included model 1 variables + serum albumin and total cholesterol concentration. Model 3 included model 2 variables + job type (professional or not), and urban residence. In the meat intake analysis, the covariates in model 3 that had significant contributions to the outcome were age (P=0.0004), BMI (P=0.009), and urban residence (P=0.02).

5年間の手段的ADL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 講師
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　神田 秀幸　福島県立医科大学衛生学・予防医学講座 講師
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 准教授

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（A population-based cohort study）

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男性492名、女性730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=0.034）。

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。

Relationship between five-year decline in instrumental activity of daily living and accumulation of cardiovascular risk factors: NIPPON DATA90

Takehito Hayakawa, Msc, PhD, [1] Tomonori Okamura, MD, [2] Hirotsugu Ueshima, MD, [3] Akira Okayama, MD, [4] Hideyuki Kanda, MD, [1] Makoto Watanabe, MD, [2] Yoshikuni Kita, PhD, [3] and Katsuyuki Miura, MD, [3] for the NIPPON DATA90 Research Group

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

Corresponding Author:
Takehito Hayakawa, Msc, PhD
Department of Hygiene and Preventive Medicine, Fukushima Medical University
1 Hikarigaoka, Fukushima City, Fukushima 960-1295, Japan.
Phone: +81-24-547-1174,
Fax: +81-24-547-1174

Abstract

OBJECTIVES
To clarify the relationship between accumulation of cardiovascular risk factors and five-year decline in instrumental activity of daily living (IADL) among a cohort representative of the Japanese population aged 65 years and over.
DESIGN
A population-based cohort study
METHODS
A cardiovascular risk survey of 8,384 men and women aged 30 years or older and randomly selected throughout Japan was performed in the 4th National Survey on Circulatory Disorders. Of these, elderly participants (aged 65 years and older) were invited to the first IADL survey assessed by the Tokyo Metropolitan Institute of Gerontology (TMIG) Index of Competence in 1995. The second IADL survey was performed in 2000. Participants in both surveys were eligible for the present study. The relationship between the number of cardiovascular risk factors at baseline and the five-year difference in IADL scores was examined by linear regression analysis.
RESULTS
Decrease in IADL scores was larger in those with cardiovascular risk factors than in those without. As the number of cardiovascular risk factors increased, IADL scores decreased significantly ($p=0.029$).
CONCLUSION
Preventive interventions directed against cardiovascular risk factors, especially against their accumulation, may contribute to maintaining IADL in the Japanese elderly.

[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 year by year, we need to clarify modifiable risk factors that predict 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 to screen elderly residents who are not disabled but have potential needs 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 previous 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. However, to our knowledge, few studies have examined the relationship between the accumulation of cardiovascular risk factors and future decline in IADL in a community setting.

Accordingly, we attempted to follow-up a cohort thought to be representative of the Japanese population to evaluate the relationship between the five-year decline in IADL and 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; this study was called 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 (1,2,5-9). A total of 8384 community residents (3504 men and 4880 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 IADL in 1995 and 2000 of the surviving elderly (65 years and older) members of this cohort. Each survey was conducted in cooperation with the local public health centers, using the multidimensional 13-item index of competence developed by the Tokyo Metropolitan Institute of Gerontology (TMIG Index of Competence) (3,10).

Participants who were 60 or older in 1990 were designated as the subjects of the first IADL survey in 1995 (n=2831). Of these, 286 died before 1995 and 404 were inaccessible because the relevant public health centers were not able to cooperate with the survey. Therefore, 2141 were selected as subjects in 1995. Of these, 32 declined to participate and 40 were inaccessible; therefore, 2,069 subjects were available for this first IADL survey. They were followed up until 2000. During these five years, 120 moved and could not be contacted, 301 died, and four were lost to follow-up for unknown reasons. Accordingly, 1644 participants were eligible as subjects of the second IADL survey in 2000. Of these, 36 declined to participate, 89 could not be contacted, and 297 had missing information. Finally, a total of 1222 subjects (492 men, 730 women) were eligible for the analysis.

We used the TMIG Index of Competence, a widely used scale for measurement of IADL with demonstrated reliability and validity (3,4,12). The first five questions (No. 1-5) inquire about instrumental independence, the subsequent four (No. 6-9) about intellectual activity, and the remaining four (No. 10-13) about social role. The respondent selects either "yes" (one point) or "no" (zero points), and the maximum score is 13 points (3,12). The individual five-year difference in IADL scores was calculated by subtracting the score in 1995 from that in 2000. 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/m2), and current smoking.

We examined whether the difference in IADL scores differs depending on the presence or absence of each risk factor. We conducted a t-test or one-way analysis of variance for continuous variables and a chi-square test for proportions. We also performed a linear regression analysis to evaluate the relationship between the number of these risk factors and the five-year difference in scores of IADL rated by TMIG Index of Competence after adjusting for sex, age, and alcohol consumption. 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 the analyses.

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

[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 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 IADL scores was also large in the older age groups in both men and women. In men aged 65 to 69, the decrease in 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 factors 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.

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 five-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 ($p=0.029$). 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 ($p=0.034$).

[Discussion]

The present study found a significant inverse relationship between the number of cardiovascular risk factors and decrease in IADL scores during the five-year period in this representative sample of elderly Japanese people. Even though the effect of each individual risk factor did not reach statistical significance, 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 decline in IADL in elderly residents

Okamura et al. reported that elderly residents in two communities located in Akita and Kochi prefectures with systolic hypertension (≥ 160 mmHg) showed a 3.41-times-higher odds ratio (OR) for having low IADL scores than those with normal blood pressure (13). However, they surveyed TMIG Index of Competence 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 (14). However, IADL was not evaluated in that study. We reported the impact of serum albumin and total cholesterol (TC) on ADL in NIPPON DATA80 (15). 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 the assessment for ADL was performed 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 only elevate risk by a minor degree, the risk becomes more "powerful" when they are combined (16, 17). Metabolic syndrome is the concept of a cluster of risk factors comprising insulin resistance, increased abdominal fat, dyslipidemia, and hypertension (18). To our knowledge, the present study is the first to show the relationship between accumulation of cardiovascular risk factors and IADL of the community dwelling elderly in a cohort design.

The present study suggests that the presence of multiple risk factors might contribute to decline in IADL in the future. Cerebral infarction associated with impaired cognition but without a clinical history of stroke is common, even in older men and women (19). Bokura et al. suggested that the clustering of metabolic risk factors tended to increase the prevalence of such silent cerebral ischemic

lesions in 1,151 healthy Japanese subjects (20). Furthermore, Elias et al. indicated that risk factor profile for stroke was associated with low cognitive performance in a cross-sectional analysis of the Framingham Offspring Study (21). These findings were consistent with those of the present study.

There are several limitations to our study. First, the risk factors we selected were examined not in the initial IADL survey but in the survey conducted five years before this. 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 five 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. Second, we observed a significant decline in IADL in the ex-smoking group. Smoking has been recognized as an important risk factor for various health hazards. Because prevalence of former smoking was extremely high among the Japanese men in this study, we speculated that these elderly Japanese men were forced to give up smoking because of severe illness or aging, which itself correlated to decline in IADL. Finally, because the IADL survey was conducted only every five years, we could not pinpoint exactly when and why IADL declined during the five-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 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 future decline in IADL for the Japanese elderly, allowing them to live a healthy and active life.

[Acknowledgments]
The authors would like to thank all public health centers that cooperated with our study.
Financial disclosure: This study was supported by a Grant-in-Aid from the Ministry of Health, Labour and Welfare under the auspices of the Japanese Association for Cerebro-cardiovascular Disease Control, a Research Grant for Cardiovascular Diseases (7A-2) from the Ministry of Health, Labour and Welfare, and a Health and Labour Sciences Research Grant, Japan (Comprehensive Research on Aging and Health: H11-chouju-046, H14-chouju-003, H17-chouju-012 and H19-chouju-014).

【References】

1 Hayakawa T, Okayama A, Ueshima H, Kita Y, Choudhury SR, Tamaki J, NIPPON DATA80 Research Group. Prevalence of impaired activities of daily living and the impact of stroke and lower limb fracture in elderly persons in Japan. CVD Prevention 2000; 3: 187-194.
2 Hayakawa T, Okamura T, Ueshima H, Tanihara S, Okayama A, Kita Y, Fujita Y. The activities of daily living in a 5-year change of elderly persons in the Japanese general population. Kosei-No-Shihyo 2004;51:7-12, in Japanese.
3 Koyano W, Shibata H, Nakazato K, Haga H, Suyama Y. Measurement of competence in the elderly living at home: development of an index of competence. Jpn J Pub Health 1987;34:109-114, in Japanese with English summary.
4 Lawton MP. Assessment, integration, and environments for older people. Gerontologist. 1970;10:38-46.
5 Kadota A, Hozawa A, Okamura T, Kadowaki T, Nakmaura K, Murakami Y, Hayakawa T, Kita Y, Okayama A, Nakamura Y, Kashiwagi A, Ueshima H. Relationship between metabolic risk factor clustering and cardiovascular mortality stratified by high blood glucose and obesity: NIPPON DATA90, 1990-99. Diabetes Care 2007; 30:1533-8.
6. Ninomiya T, Kubo M, Doi Y, Yonemoto K, Tanizaki Y, Rahman M, Arima H, Tsuryuya K, Iida M, Kiyohara Y.Impact of metabolic syndrome on the development of cardiovascular disease in a general Japanese population: the Hisayama study.Stroke. 2007; 38: 2063-9.
7. Kokubo Y, Okamura T, Yoshimasa Y, Miyamoto Y, Kawanishi K, Kotani Y, Okayama A, Tomoike H. Impact of Metabolic Syndrome Components on the Incidence of Cardiovascular Disease in a General Urban Japanese Population: The Suita Study. Hypertens Res 2008; 31: 2027–35.
8. Okamura T, Hayakawa T, Kadowaki T, Kita Y, Okayama A, Ueshima H; NIPPON DATA90

Research Group: The inverse relationship between serum high-density lipoprotein cholesterol level and all-cause mortality in a 9.6-year follow-up study in the Japanese general population. Atherosclerosis 2006; 184: 143-150.
9. Nakamura K, Okamura T, Hayakawa T, Kadowaki T, Kita Y, Okayama A, Ueshima H, for the NIPPON DATA90 Research Group: Electrocardiogram screening for left high R-wave predicts cardiovascular death in a Japanese community-based population: NIPPON DATA90. Hypertens Res 2006; 29: 353-360.
10. Hozawa A, Okamura T, Kadowaki T, Murakami Y, Nakamura K, Hayakawa T, Kita Y, Nakamura Y, Okayama A, Ueshima H; The NIPPON DATA90 Research Group. Gamma-Glutamyltransferase predicts cardiovascular death among Japanese women. Atherosclerosis 2007; 194: 498-504
11. Tamakoshi K, Toyoshima H, Yatsuya H, Matsushita K, Okamura T, Hayakawa T, Okayama A, Ueshima H; NIPPON DATA90 Research Group. White blood cell count and risk of all-cause and cardiovascular mortality in nationwide sample of Japanese--results from the NIPPON DATA90. Circ J 2007; 71: 479-85
12. Koyano W, Shibata H, Nakazato K, Haga H, Suyama Y. Measurement of competence: reliability and validity of the TMIG Index of Competence; Archives of Gerontology and Geriatrics 1991; 13(2): 103-116.
13. Okamura T, Sato S, Kiyama A, Kitamura A, Nakagawa Y, Naito Y, Iida M, Iso H, Shimamoto T, Komachi Y. Follow-up study on the relationship between the findings of cardiovascular screening, and prognosis for life and the capacity of activity in the elderly (65-74 years). Kosei-No-Shihyo 1997; 44: 18-25, in Japanese.
14. Pinsky JL, Branch LG, Jette AM, Haynes SG, Feinleib M, Cornoni-Huntley JC, Bailey KR. Framingham Disability Study: relationship of disability to cardiovascular risk factors among persons free of diagnosed cardiovascular disease. Am J Epidemiol 1985 Oct;122(4):644-56.
15. Okamura T, Hayakawa T, Hozawa A, Kadowaki T, Murakami Y, Kita Y, Abbott RD, Okayama A, Ueshima H; NIPPON DATA80 Research Group. Lower levels of serum albumin and total cholesterol associated with decline in activities of daily living and excess mortality in a 12-year cohort study of elderly Japanese. J Am Geriatr Soc 2008; 56: 529-35.
16. Nakamura Y, Yamamoto T, Okamura T, Kadowaki T, Hayakawa T, Kita Y, Saitoh S, Okayama A, Ueshima H; The NIPPON DATA 80 Research Group. Combined cardiovascular risk factors and outcome: NIPPON DATA80, 1980-1994. Circ J 2006; 70: 960-4.
17. Okamura T, Nakamura K, Kanda H, Hayakawa T, Hozawa A, Murakami Y, Kadowaki T, Kita Y, Okayama A, Ueshima H; Health Promotion Research Committee, Shiga National Health Insurance Organizations. Effect of combined cardiovascular risk factors on individual and population medical expenditures: a 10-year cohort study of national health insurance in a Japanese population. Circ J 2007; 71: 807-13.
18. Malik S, Wong ND, Franklin SS, Kamath TV, L'Italien GJ, Pio JR, Williams GR. Impact of the metabolic syndrome on mortality from coronary heart disease, cardiovascular disease, and all causes in United States adults. Circulation 2004; 110: 1245-50.
19. Price TR, Manolio TA, Kronmal RA, Kittner SJ, Yue NC, Robbins J, Anton-Culver H, O'Leary DH. Silent brain infarction on magnetic resonance imaging and neurologicalabnormalities in community-dwelling older adults. The Cardiovascular Health Study. CHS Collaborative Research Group. Stroke 1997; 28: 1158-64.
20. Bokura H, Yamaguchi S, Iijima K, Nagai A, Oguro H. Metabolic syndrome is associated with silent ischemic brain lesions. Stroke 2008; 39: 1607-9.
21. Elias MF, Sullivan LM, D'Agostino RB, Elias PK, Beiser A, Au R, Seshadri S, DeCarli C, Wolf PA. Framingham stroke risk profile and lowered cognitive performance. Stroke 2004; 35: 404-9.

Appendix Questions on the multidimensional 13-item index of competence

(1) Can you use public transportation (bus or train) by yourself?	Yes. or No.
(2) Are you able to shop for daily necessities?	Yes. or No.
(3) Are you able to prepare meals by yourself?	Yes. or No.
(4) Are you able to pay bills?	Yes. or No.
(5) Can you handle your own banking?	Yes. or No.
(6) Are you able to fill out forms for your pension?	Yes. or No.
(7) Do you read newspapers?	Yes. or No.
(8) Do you read books or magazines?	Yes. or No.
(9) Are you interested in news stories or programs dealing with health?	Yes. or No.
(10) Do you visit the homes of friends?	Yes. or No.
(11) Are you sometimes called on for advice?	Yes. or No.
(12) Are you able to visit sick friends?	Yes. or No.
(13) Do you sometimes initiate conversations with young people?	Yes. or No.

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	

The maximum score is 13.
Mean ⊿IADL was calculated by substracting the score in 1995 from than in 2000.
* The comparison was made between age groups by chi-square test.

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 (yr)	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 (%)	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.

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

Age	Men 71.9 (±5.0)			Women 72.8 (±5.7)		
	N	mean ⊿IADL	P value	N	mean ⊿IADL	P value
BMI						
BMI<25	400	-1.11	0.545	513	-1.11	0.211
BMI≥25	92	-1.32		217	-1.40	
Smoking habit						
Non-smoker	92	-0.87	0.268	664	-1.16	0.142
Ex-smoker	173	-1.43		19	-2.47	
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.