Table 3. Odds Ratio of Low Ankle Brachial Index Associated with Cardiovascular Disease Risk Factors

	Odds ratio	95% CI	p
Age (5 years)	1.23	0.91–1.67	0.18
Sex (male=1)	1.77	0.74–4.23	0.20
Current smoker	3.10	1.16–8.32	0.02
Ex-smoker	1.51	0.62–3.71	0.50
Alcohol consumption (23 g/day)	1.01	0.79–1.29	0.97
Body mass index (kg/m^2)	0.89	0.80–0.99	0.03
Hypertension	4.29	1.60–11.50	<0.01
Diabetes	3.73	1.82–7.66	<0.01
Hypercholesterolemia	1.10	0.56–2.14	0.79
Low HDL cholesterol	3.39	1.69–6.81	<0.01
Use of statin drugs	3.51	1.71–7.19	<0.01
History of cardiovascular diseases	1.74	0.89–3.40	0.10
CRP			
−0.9 mg/l	1.00		
1–2.9 mg/l	2.20	1.10–4.41	0.03
3– mg/l	2.06	0.90–4.75	0.09
p for trend			0.03
CRP log-transformed (continuous)	2.15	1.21–3.82	<0.01

CI, confidence interval. Hypertension: home systolic blood pressure (BP) was at least 135 mmHg and/or home diastolic BP was at least 85 mmHg, or they were using antihypertensive agents. Diabetes: non-fasting blood glucose level was at least 200 mg/dl, or if they currently used antidiabetic medication. Hypercholesterolemia: level of total cholesterol was at least 220 mg/dl, or they currently used non-statin lipid-lowering agents. Low HDL cholesterol: level of high density lipoprotein cholesterol below 40 mg/dl.

ate CRP group and the highest CRP group had a two-fold higher OR. The *p*-value for the trend across CRP groups was statistically significant ($p=0.03$). Furthermore, when we repeated the regression by treating the log-transformed CRP value as a continuous variable, a positive trend between log-transformed CRP and low ABI was also observed ($p<0.01$).

The following relationships between other cardiovascular disease risk factors and low ABI were found (Table 3). Current smoking, low HDL cholesterol, and history of hypertension, diabetes and statin use were related significantly to low ABI. Lower BMI as a continuous variable was significantly related to low ABI. A history of cardiovascular diseases tended to be related to lower ABI, although the relationship was only marginally significant. Age, sex, alcohol consumption and history of hypercholesterolemia were not significantly related to low ABI.

When we excluded the subjects who were statin users, a significant positive relationship between log-transformed CRP and low ABI remained ($p<0.01$).

Association of OR of Low ABI with a Combination of Cardiovascular Disease Risk Factors and CRP

Table 4 shows that the OR of low ABI was associated with the combination of a number of cardiovascular disease risk factors and CRP. In this analysis, according to the results of Table 3, we treated hypertension, diabetes, current smoking and low HDL cholesterol as dichotomous cardiovascular disease risk factors. We also treated the subjects with a CRP level higher than 1.0 mg/l as high-CRP subjects, because both CRP groups above 1.0 mg/l showed a similar association with low ABI.

Irrespective of the number of cardiovascular disease risk factors, a higher CRP level was related to a higher risk of low ABI (*p* for interaction=0.70). Even among the subjects without high CRP levels, the clustering of cardiovascular disease risk factors was related to low ABI. In a multiple logistic regression that included as covariates sex, age, BMI, statin use, and history of cardiovascular disease, the OR for low ABI, compared to 0–1 risk factors, was 5.79 (95% confidence interval [CI]: 2.99–11.20) for 2 risk factors and 17.45 (95% CI: 6.78–49.91) for 3 or more risk factors; the OR for CRP>1.0 mg/l was independently 2.10 (95% CI: 1.13–3.88) compared to the lower CRP values.

Discussion

In this study, we have demonstrated that, in Japan, CRP is related to low ABI independently of other cardiovascular disease atherosclerosis risk factors, and also reconfirmed the impact of the clustering of traditional cardiovascular disease risk factors on low ABI among the Japanese population.

CRP is a circulating acute-phase reactant that is increased many-fold during the inflammatory response to tissue injury or infection. CRP is synthesized primarily in the liver and its release is stimulated by interleukin 6 and other proinflammatory cytokines. This protein has received substantial attention in recent years as a promising biological predictor of atherosclerotic disease (*38*). In Western countries, some prospective studies have investigated the relationship between CRP and cardiovascular diseases, including PAD (*1–14, 21, 22*).

However, no studies have investigated the relationship between CRP and PAD in Japan, and only a few studies have investigated the relationship between PAD and classical factors in a large sample (*23, 24*).

Shinozaki *et al.* reported the relationship between low ABI (ABI<1.0) and cardiovascular disease risk factors among 446 male workers (*23*). Multiple logistic regression analyses for low ABI showed that low BMI, high SBP, and current smoking were related positively to low ABI and current drinking was related negatively to low ABI.

Cui *et al.* reported the relationship between low ABI (ABI<0.9) and cardiovascular disease risk factors among 1,219 elderly men (*24*). They found that low BMI, hyperten-

Table 4.   Odds Ratio of Low ABI Associated with a Combination of Number of Cardiovascular Disease Risk Factors and CRP

Numbers of risk factors	CRP (−0.9 mg/l)			CRP (1.0 mg/l−)		
	Odds ratio	95% CI	*p*	Odds ratio	95% CI	*p*
0–1	1.00			1.91	0.74–4.92	0.18
2	5.74	2.39–13.80	<0.01	11.21	4.46–28.20	<0.01
3−	12.46	2.89–53.69	<0.01	42.40	12.72–141.17	<0.01

ABI, ankle brachial systolic blood pressure (BP) index; CRP, C reactive protein; CI, confidence interval. Risk factors: hypertension: home systolic BP was at least 135 mmHg and/or home diastolic BP was at least 85 mmHg, or they were using antihypertensive agents; diabetes: non-fasting blood glucose level was at least 200 mg/dl, or if they currently used antidiabetic medication; current smoking; low high density lipoprotein (HDL) cholesterol: level of HDL cholesterol below 40 mg/dl; adjusted for sex, age, body mass index, statin using and history of cardiovascular diseases.

sion, low HDL cholesterol, history of stroke, major electro-cardiogram abnormality, and current smoking were significantly related to low ABI.

Our results were mostly consistent with these reports, but in our study, unlike those of Shinozaki *et al.* (*23*) and Cui *et al.* (*24*), diabetes was related independently and significantly to low ABI.

Because statins affect the CRP level (*34, 35*), we treated statin use as an independent variable. In this study we also found that statin use was related to low ABI. These relationships might have been observed because the statins were used specifically to treat PAD or because the statin users were those with the highest pre-treatment serum cholesterol.

These risk factors, *i.e.*, low BMI, hypertension, low HDL cholesterol, and current smoking, have also been associated with low ABI among Western subjects (*39–41*). Therefore, in this study, we confirmed that similar correlations of low ABI and cardiovascular disease risk factors exist among Japanese subjects and subjects in Western countries.

The CRP level was related to low ABI independently of these cardiovascular disease risk factors, and the relationship also remained when we excluded the statin users.

Since Albert *et al.* reported that CRP level is related positively to risk clustering (*37*), we attempted to investigate the relationship between ABI associated with a combination of number of cardiovascular disease risk factors and CRP. The results also showed that CRP was related independently to low ABI independent of the number of traditional cardiovascular diseases. Furthermore, the results confirmed the importance of clustering traditional cardiovascular disease risk factors; even those subjects who had multiple risk factors without high CRP levels had a higher OR. Measuring CRP together with traditional cardiovascular disease risk factors may improve our ability to identify individuals with low ABI in the Japanese population.

Our study had some limitations. First, most of the participants were sufficiently active and healthy to participate in the survey; therefore, we have likely underestimated the prevalence of low ABI. Secondly, since this was a cross-sectional study, we cannot conclude that CRP causes PAD or that atherosclerosis leads to higher CRP. Therefore, a prospective

study should be undertaken to confirm the relationship between CRP and low ABI in the Japanese population.

In conclusion, we have demonstrated that CRP is related to low ABI. This is the first study to clarify the relationship between CRP and low ABI among Japanese elderly.

Acknowledgements

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The Relationship between Body Mass Index and a Plasma Lipid Peroxidation Biomarker in an Older, Healthy Asian Community

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PURPOSE: To examine the association between body mass index (BMI) and the plasma level of a lipid peroxidation biomarker in a large sample of elderly healthy Asian population. This cross-sectional study included 1150 community-dwelling Japanese aged 70 years or older in 2002.

METHODS: We measured the lipid peroxidation biomarker 8-iso-prostaglandin $F_{2\alpha}$ (8-iso-$PGF_{2\alpha}$) using the ELISA method. We also measured the weight and height and calculated the BMI as weight (kg)/height $(m)^2$.

RESULTS: After adjustment for potential confounders, the mean $\pm$ SE plasma 8-iso-$PGF_{2\alpha}$ level was significantly higher in subjects with higher BMI: 21.1 ± 0.8 pg/ml in those with BMI of 30.0 or more; 20.5 ± 0.3 pg/ml in those with BMI between 25.0 and 29.9; 20.0 ± 0.2 pg/ml in those with BMI between 18.5 and 24.9; and 19.0 ± 0.7 pg/ml in those with BMI of less than 18.5 (p for trend = 0.011).

CONCLUSIONS: Our results demonstrated that in the healthy Asian population, there was a modest but significant relationship between BMI and the plasma lipid peroxidation level.

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KEY WORDS: Obesity, Body Mass Index, Oxidative Stress, Isoprostanes, Asia, Aged.

INTRODUCTION

Although obesity is an established risk factor for atherosclerotic cardiovascular diseases (1–3), its pathomechanism has been unclear (4). On the other hand, there has been considerable progress in understanding the role of lipid peroxidation in the formation and progress of atherosclerosis. Recent studies have identified isoprostane compounds as a biomarker of lipid peroxidation, and examined the association between atherosclerotic cardiovascular diseases and oxidized lipids. An association between obesity and high oxidative stress has been demonstrated by two observational epidemiologic studies of large sample populations of healthy humans in the United States (5, 6). Since ethnic variability in the level of oxidative stress was suggested (6), this finding needs to be confirmed for other ethnicities such as Asians. These previous studies dealt mainly with Caucasian populations. Given the possible ethnic variability in such factors as genetic variability and nutritional status, it is necessary to determine whether obesity is a risk factor for oxidative stress among Asian populations.

The aim of the present study was to test the hypothesis that obesity is associated with increased oxidative stress in a healthy Asian population. To estimate the oxidative stress status, we used a lipid peroxidation biomarker, 8-iso-prostaglandin F_2-α (8-iso-$PGF_{2\alpha}$), because it is one of the most reliable indices for assessing oxidative stress status in vivo (7). 8-iso-$PGF_{2\alpha}$ is one of the four known classes of F_2-isoprostanes, which are lipid peroxidation products of arachidonic acid (8).

METHODS

Study Population

The Tsurugaya Project was a community-based Comprehensive Geriatric Assessment (CGA) (9, 10) of elderly Japanese individuals living in Tsurugaya district, a suburban area of Sendai City in northern Japan, between July and October 2002. At this time, there were 2730 people aged 70

years or older living in Tsurugaya. We invited all of these individuals to participate, and 1179 (43.2%) of them did so, and gave their written informed consent for analysis of the data. The subjects also responded to interviews on the questionnaire included in the CGA. The protocol of this study was approved by the Institutional Review Board of Tohoku University Graduate School of Medicine.

Weight and height of the subjects were measured at the baseline survey. Body mass index (BMI) was calculated as the weight (kg)/height $(m)^2$ and then classified into four categories: less than 18.5 kg/m², between 18.5 kg/m² and 24.9 kg/m², between 25.0 kg/m² and 29.9 kg/m², and 30.0 kg/m² or more. Smoking and drinking status were classified into three groups: current smokers/drinkers, past smokers/drinkers, or never smokers/drinkers. Definition for hypertension included a self-reported history of hypertension or use of oral hypotensive drugs, and that for hyperlipidemia included a casual serum total cholesterol level greater than or equal to 220 mg/dl or casual serum triglyceride level greater than or equal to 150 mg/dl, or use of hypolipidemic drugs, or a self-reported history of hyperlipidemia, and that for diabetes included a casual plasma glucose level greater than or equal to 200 mg/dl, or use of oral hypoglycemic drugs or insulin, or a self-reported history of diabetes.

Plasma 8-iso-prostaglandin $F_{2\alpha}$ Measurements

Among the 1179 subjects, plasma 8-iso-$PGF_{2\alpha}$ data were obtained from 1150 (mean age, 75.7 ± 4.8 years; men, 41.3%). For 8-iso-$PGF_{2\alpha}$ measurement, peripheral venous blood was collected in EDTA2Na (Ethylenediaminetetraacetic acid 2Na)- and EDTA4Na-coated cold polyethylene tubes containing 1 mmol indomethacin, an inhibitor of cycloxygenese, and aprotinin, an inhibitor of kellikreins, to prevent any in vitro formation of 8-iso-$PGF_{2\alpha}$. After collection, blood samples were cooled immediately at 4°C and transferred to the laboratory within 4 hours. In the laboratory, the samples were centrifuged at 3000 × g at 4°C for 10 minutes. The plasma fraction was removed and stored at −80°C for later 8-iso-$PGF_{2\alpha}$ assay. A specific enzyme immunoassay kit (Cayman Chemical, Ann Arbor, MI) (11) was used to measure the 8-iso-$PGF_{2\alpha}$ concentration in plasma samples. The assay was validated directly by gas chromatography/mass spectrometry. The antiserum used in this assay has 100% cross-reactivity with 8-iso-$PGF_{2\alpha}$, 0.2% with prostaglandin (PG) F_2-α, PGF_3-α, PGFI, and PGF_2, and 0.1% with 6-keto PGF_2-α1. The intra-assay and interassay variabilities were within 6% for both. Data obtained in this manner correlate well with those obtained using electrospray-negative ionization gas chromatography–mass spectroscopy (GC/MS) (12). The detection limit of the assay was 4 pg/ml.

Statistical Analysis

The association between plasma 8-iso-$PGF_{2\alpha}$ levels and baseline characteristics was examined and the standard error (SE) of plasma 8-iso-$PGF_{2\alpha}$ level was estimated using t test or ANOVA, as appropriate. Then plasma 8-iso-$PGF_{2\alpha}$ levels were compared with BMI categories, adjusting for potential confounders using ANCOVA and trend tests were performed by including the ordinal variable in a linear regression analysis. Since previous studies have shown that F_2-isoprostane levels might be elevated under conditions such as the use of multivitamin/vitamin C/vitamin E supplements (13, 14), non-steroidal anti-inflammatory drugs (NSAIDs) (14), smoking (5, 6, 15), hyperlipidemia (5, 16), and diabetes (5, 17), we used the following confounders as covariates in these analyses. First, we regarded the following data as covariates: sex, age (continuous variable), physical function status (being able to perform vigorous or moderate activities, being independent in activities of daily living, or being dependent in activities of daily living), consumption frequencies of soy beans products such as tohu (daily, 1–6 times per week, or less than 1 time per week) and Japanese green tea (more than 4 cups per day, 1–3 cups per day, or less than 1 cup per day), use of multivitamin/vitamin C/vitamin E supplements, use of NSAIDs, and smoking (never, former, current smoking), and alcohol drinking (never, former, current drinking). Second, we adjusted for the obesity-related comorbid conditions; hypertension, hyperlipidemia, and diabetes.

All statistical analyses were performed using SAS software, version 8.02 (18). We used approximate variance formulae to calculate the 95% confidence intervals (CI). All the statistical tests reported here were two-sided. Differences at $p < 0.05$ were accepted as statistically significant.

RESULTS

Table 1 shows the baseline characteristics and plasma 8-iso-$PGF_{2\alpha}$ levels of the study subjects. The mean age of the subjects was 75.7 years (standard deviation [SD] 4.8), and 20.6% were aged 80 years or older. Sex and BMI were significantly associated with the plasma 8-iso-$PGF_{2\alpha}$ level ($p = 0.0158$ and 0.0173, respectively). The plasma 8-iso-$PGF_{2\alpha}$ levels were higher among past/current smokers than never smokers, although not statistically significant.

Table 2 shows the association between BMI and plasma 8-iso-$PGF_{2\alpha}$. After adjustment for sex, age, physical function status, use of multivitamin/vitamin C/vitamin E supplements, use of NSAIDs, consumption frequencies of soy beans products and Japanese green tea, smoking, and alcohol drinking, significant dose–response relationships between BMI and the plasma 8-iso-$PGF_{2\alpha}$ level were observed (Model 1: p for trend = 0.0082). Even after

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TABLE 1. Characteristics of the subjects and 8-iso-PGF$_{2\alpha}$ levels

	N	Mean	SE	p-value
		8-iso-PGF$_{2\alpha}$		
BMI				
<18.5	63	18.94	0.68	0.016
18.5–24.9	684	19.96	0.21	
25.0–29.9	354	20.46	0.29	
30.0<	49	20.98	0.77	
Sex				
Male	475	20.55	0.25	0.017
Female	675	19.79	0.21	
Age (years)				
70–74	563	20.18	0.23	0.86
75–79	350	19.80	0.29	
80+	237	20.38	0.35	
Smoking				
Current smoking	144	20.21	0.44	0.28
Past smoking	338	20.43	0.29	
Never smoking	646	19.87	0.21	
Drinking				
Current drinking	441	20.40	0.25	0.32
Past drinking	144	20.38	0.45	
Never drinking	510	19.91	0.24	
Consumption frequencies of soy beans products				
Daily	587	20.07	0.22	0.99
1–6 times per week	511	20.06	0.24	
Less than 1 time per week	34	19.92	0.92	
Consumption frequencies of Japanese green tea				
More than 4 cups per day	522	19.75	0.24	0.16
1–3 cups per day	377	20.45	0.28	
Less than 1 cup per day	231	20.11	0.35	
Use of vitamin supplement*				
Yes	155	19.87	0.43	0.56
No	995	20.14	0.17	
Use of NSAIDs†				
Yes	250	20.35	0.34	0.42
No	900	20.04	0.18	

*Multivitamin/vitamin C/vitamin E.
†Non-steroidal anti-inflammatory drug.

adjustment for obesity-related confounding factors such as hypertension, hyperlipidemia, and diabetes there was no change in the linear relationship between plasma 8-iso-PGF$_{2\alpha}$ level and BMI. The mean ± SE plasma 8-iso-PGF$_{2\alpha}$

level was significantly higher in subjects with higher BMI: 21.1 ± 0.8 pg/ml in those with BMI of 30.0 or more; 20.5 ± 0.3 pg/ml in those with BMI between 25.0 and 29.9; 20.0 ± 0.2 pg/ml in those with BMI between 18.5 and 24.9; and 19.0 ± 0.7 pg/ml in those with BMI of less than 18.5 (Model 2: p for trend = 0.011). The gender difference that was significant in the unadjusted analysis was no longer so after adjustment (data not shown).

Furthermore, stratified analyses of obesity-related co-morbid states such as hypertension, hyperlipidemia, and diabetes did not change the main findings (data not shown). The most significant linear relationship between plasma 8-iso-PGF$_{2\alpha}$ level and BMI was observed among the subjects with hyperlipidemia.

DISCUSSION

In this population of elderly Japanese individuals, we observed a modest but significant dose–response relationship between a higher BMI and a higher plasma 8-iso-PGF$_{2\alpha}$ level, after adjustment for a variety of potential confounders. To our knowledge, this is the first study to examine the association between BMI and oxidative stress in an Asian population.

The present study has a number of strengths. First, our sample size was large enough (N = 1150) to detect a positive, negative or null association. Second, we adjusted for a variety of possible confounders that would affect the 8-iso-PGF$_{2\alpha}$ level or BMI: age, sex, use of vitamin A/vitamin C/vitamin E supplements, use of NSAIDs, consumption frequencies of soy beans products and Japanese green tea, smoking, drinking, and physical function. Furthermore, even when we stratified the subjects according to the complications of diabetes, hypercholesterolemia, and hypertension, the finding of a positive association between obesity and the 8-iso-PGF$_{2\alpha}$ level was unchanged.

The present results indicated that the 8-iso-PGF$_{2\alpha}$ level was significantly associated with a higher BMI. Our results are consistent with previous studies of a USA population (5, 6) and a small intervention study of obesity (19) in the USA. Keaney et al. examined 2828 subjects aged 33 to 88 years from the Framingham Heart Study and measured

TABLE 2. The relationship between 8-iso-PGF$_{2\alpha}$ and body mass index

8-isoprostane (± SE)	BMI [weight (kg)/height (m)^2]				
	<18.5	18.5–25.0	25.0–30.0	>30.0	p for trend
Model 1	19.04 ± 0.69	19.94 ± 0.21	20.56 ± 0.29	21.16 ± 0.77	0.0082
Model 2	19.01 ± 0.70	19.95 ± 0.21	20.54 ± 0.29	21.14 ± 0.77	0.011

Model 1: Adjusted for sex, age, multivitamin/vitamin C/vitamin E supplement use, non-steroidal anti-inflammatory drug use, physical functioning status, smoking status (current-smoking, ex-smoking, and never smoking), drinking status (current-drinking, ex-drinking, and never drinking), consumption frequencies of soy bean products (daily, 1–6 times per week, or less than 1 time per week), and consumption frequencies of Japanese green tea (more than 4 cups per day, 1–3 cups per day, or less than 1 cup per day).
Model 2: Adjusted for variables above and history of hypertension, diabetes mellitus, and hyperlipidemia.

urinary creatinine-indexed 8-epi-PGF$_{2\alpha}$ as a marker of systemic oxidative stress (5). Block et al. measured urinary plasma 8-epi-PGF$_{2\alpha}$ among 298 subjects aged 19 to 78 years (6). Those two studies of healthy populations indicated that BMI was associated with a higher plasma level of 8-epi-PGF$_{2\alpha}$. Davi et al. conducted an intervention study of obese women aged 24 to 63 years and demonstrated the possibility that successful weight loss may be adequate for minimizing oxidative stress in obese subjects with a BMI of 28 or more (19). Our study confirmed the positive association between BMI and plasma 8-epi-PGF$_{2\alpha}$ in this Asian population, which is largely different from Caucasian in terms of genetic background and nutritional intake. The role of lipid peroxidation in the formation and progress of atherosclerosis has been well understood. The present results support the hypothesis that oxidative stress is one of the mechanisms responsible for atherosclerosis in obesity.

Several hypotheses for the association between oxidative stress and obesity have been proposed. Obesity is associated with insulin resistance and several mechanisms have been suggested to explain the association between oxidative stress and insulin resistance (5). For example, insulin itself promotes hydrogen peroxide formation in human fat cells (20). Nutritional intake is also suggested to explain the association between obesity and oxidative stress. Glucose intake increases more reactive oxygen species generation from leukocytes in obese subjects than in normal subjects (21). The results of the present study support these basic researches.

Previous studies have suggested a relationship between isoprostanes level and smoking (5, 6, 15). In this study, we confirmed the relationship between the plasma 8-iso-PGF$_{2\alpha}$ level and smoking, although not statistically significant.

Our study also had some limitations. The study population aged 70 years or older might represent healthy aging resistance to oxidative stress. Most of the elderly participants were active and healthy enough to participate in the survey, and this might have led to small inter-individual differences in the study data. However, despite this limitation, we detected a modest but significant dose–response relationship among the population. We used ELISA rather than GC/MS because we had to process large numbers of samples in a timely manner. To minimize autoxidation, care was taken with plasma sample preparation and also to avoid artificial autoxidation.

Our study focusing on elderly Asian individuals demonstrated a statistically significant dose–response relationship between BMI and a lower plasma level of 8-iso-PGF$_{2\alpha}$. The impact of obesity upon the risk of atherosclerotic cardiovascular diseases (22–24) and medical care costs (25) in Asia are as large as those in Western countries. Obesity has been increasing rapidly in Asia (26, 27); the prevalence of obesity in Japanese men doubled between 1976 and 1995

(27). Thus, obesity is an urgent issue not only in Western but also in Asian countries. The present results confirm the hypothesis that oxidative stress is one of the pathomechanisms responsible for the association between obesity and atherosclerosis in Asians.

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Experimental
Gerontology

Short communication

Blood type B might imply longevity

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Abstract

The aim of the present study was to investigate the association between blood groups and life expectancy. We compared frequencies of ABO blood group in 269 centenarians (persons over 100 years) living in Tokyo and those in regionally matched controls ($n=7153$). Frequencies of blood types A, O, B, and AB in centenarians were 34.2, 28.3, 29.4, and 8.2%, respectively, while those in controls were 38.6, 30.1, 21.9, and 9.4%, respectively. Blood type B was observed more frequently in centenarians than in controls ($\chi^2=8.41$, $P=0.04$). This tendency also was true in comparison between centenarians and 118 elderly old individuals of the 7153. Approximate one-third of the centenarians were free from serious diseases such as malignancy. However, blood types were not associated with such medical records. Our findings suggest that blood type B might be associated with exceptional longevity. Responsible mechanisms need to be investigated.
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Keywords: Centenarian; Blood group; Longevity

1. Introduction

A variety of medical literature has been concerned with blood groups. However, only a small number of issues have been proven to be of clinical importance: the ABO blood type in transfusion, the Rh antigen in incompatible pregnancy, and the Duffy antigen in malarial infection. Recently, blood type O individuals have been reported to have lower plasma concentrations of von Willebrand factor (VWF), a marker of blood coagulability, than persons with other blood types (O'Donnell and Laffan, 2001). Since elevated VWF carries increased risk for ischemic heart disease, cardiovascular events might be less frequent in individuals with blood type O. In other words, associations are possible between blood groups and life expectancy. We therefore investigated frequencies of ABO blood groups in the very old, specifically centenarians.

2. Methods

Of 1206 centenarians living in Tokyo at the time of our study, 269 individuals, 202 women and 67 men, in ages from 100 to 109 years (Mean 101.2 [Std Dev 1.8]) gave informed consent and agreed to a visit for our medical examinations. We identified the ABO blood group using their blood samples and examined their medical records with respect to hypertension, cardiovascular disease, apoplexy, diabetes, femoral fracture, malignancy, and chronic lung disorder. As a regionally matched control group, we selected 7153 individuals (1673 women and 5480 men) aged 17–93 years (mean 54.8 [Std Dev 11.0]) who came to the Keio Health Consulting Center for annual medical check-ups in 2003. Of the 7153, the following

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Table 1
Comparison of blood group frequencies

	Blood type			
	A	O	B	AB
Observation				
Centenarians (n=269)	92 (34.2)	76 (28.3)	79 (29.4)	22 (8.2)
Controls (n=7153)	2759 (38.6)	2153 (30.1)	1570 (21.9)	671 (9.4)
Old controls (n=740)	288 (38.9)	219 (29.6)	159 (21.5)	74 (10.0)
Elderly old controls (n= 118)	48 (40.7)	34 (28.8)	27 (22.9)	9 (7.6)
Expectation				
General population[a]	109 (38.7)	83 (29.3)	63 (22.2)	28 (10.0)
Tokyo area[b]	108 (38.3)	83 (29.1)	63 (22.4)	29 (10.2)

Data are numbers followed by percentages in parentheses. Differences between centenarians and controls and between observed and expected frequencies were investigated by χ^2-tests. Observation in centenarians was significantly different from that in controls (χ^2 [d.f.=3]=8.41, P=0.04) and from expectations (χ^2 [d.f.=3]=12.68, P=0.005 for Japan; χ^2 [d.f.=3]=11.91, P=0.007 for metropolitan Tokyo). Notably, blood type B was observed more frequently in centenarians. This predominance of blood type B, although not being statistically significant, was observed in comparison between centenarians and old controls (χ^2 [d.f.=3]=7.17, P=0.06) and between centenarians and elderly old controls (χ^2 [d.f.=3]=2.25, P=0.52).

[a] Calculated from data for 4464349 individuals in a 1978 survey throughout Japan.
[b] Calculated from data for 293688 Tokyo-area individuals among the above 4464349.

two subgroups were constituted: Old control group consisting of 740 individuals over 70 years (mean 74.8 [Std Dev 4.4]) and elderly old control group of 118 over 80 years (mean 82.8 [Std Dev 2.8]). Differences in frequencies were investigated by χ^2-tests. A P<0.05 was considered to be statistically significant.

3. Results

Frequencies of blood types A, O, B, and AB in the centenarian group were 34.2, 28.3, 29.4, and 8.2%, respectively; those in the control group were 38.6, 30.1, 21.9, and 9.4%, respectively (Table 1). Observed frequencies differed significantly between these two groups (χ^2 [d.f.=3]=8.41, P=0.04). Notably, blood type B was observed more frequently in centenarians than in controls. This predominance of blood type B, although not being statistically significant, was observed in comparison between centenarian group and old control subgroup (χ^2 [d.f.=3]=7.17, P=0.06) and between centenarian group and elderly old control subgroup (χ^2 [d.f.=3]=2.25, P= 0.52). We next compared the frequencies of ABO blood groups in the centenarians with those in a general Japanese population as calculated from a 1978 survey conducted in 4464349 individuals throughout Japan (Fujita et al., 1978). A similar result showing an increased frequency of blood type B in centenarians was obtained (χ^2 [d.f.=3]=12.68, P=0.005). This also was true when the centenarians were compared with 293688 Tokyo-area individuals among the 4464349 (χ^2 [d.f.=3]=12.02, P=0.007). The frequency distribution of blood types in the 1978 survey was almost the same as that in a 1933 survey of 121200 individuals (Furuhata, 1933) and that for 5819007 blood donors profiled in an annual report of the Japanese Red Cross (year 2000) (The Japanese Red Cross Society, 2002). Our findings

suggest that to some degree blood type B might be associated with exceptional longevity.

The following important diagnoses were recorded in centenarians: hypertension (n=78), cardiovascular disease (n=51), apoplexy (n=37), diabetes (n=9), femoral fracture (n=66), malignancy (n=24), and chronic lung disorder (n=29). Approximate one-third of the centenarians were free from these important diseases. However, blood types were not associated with such medical records (Table 2) (χ^2 [d.f.=3]=4.16, P=0.25). This finding implies that blood type B might be related to surviving serious diseases rather than escaping them.

4. Discussion

One would expect an abundance of centenarians with blood type O, since plasma concentrations of VWF, a cardiac risk factor, are lower in blood type O individuals. However, the frequency of blood type O in centenarians tended to be lower than expected. Instead, we found

Table 2
Relationship between blood groups and medical history

Blood groups	Medical history of important diseases	
	Absence	Presence
A (n=92)	32 (34.8)	60 (65.2)
O (n=76)	19 (25.0)	57 (75.2)
B (n=79)	18 (22.8)	61 (77.2)
AB (n=22)	8 (36.4)	14 (63.6)
Total (n=269)	77 (28.6)	192 (71.4)

Data are numbers followed by percentages in parentheses. Relationship between blood groups and medical history was investigated by χ^2-tests (χ^2 [d.f.=3]=4.16, P=0.25).

a possible association of blood type B with exceptional longevity. Differences in ABO blood groups are determined by antigens in the glycocalyx on the surface of the erythrocyte. These antigens are present in most tissues as well as on erythrocytes. Therefore, differences in the glycocalyx expressed by cells might elicit differing responses in biomedical phenomena apart from hemagglutination. Henry et al. summarized patterns in which blood types may be associated with various diseases, stating that bacterial infections tend to attack individuals with blood type A, while viral infections tend to be associated with blood type O. Also, cancers and clotting disorders tend to be associated with blood type A, while autoimmune diseases and bleeding disorders are associated with blood type O (Henry and Samuelsson, 2000). According to these tendencies, blood type B individuals might be more likely to escape serious illnesses, and therefore show longevity. On the other hand, our findings imply that blood type B might contribute to longevity via biomedical mechanisms favorable for surviving serious diseases rather than

escaping them. In future, blood groups will need to be investigated from an aspect of glyconomics, or the study of sugar-modifications to proteins that affect structure and function.

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Association analysis between longevity in the Japanese population and polymorphic variants of genes involved in insulin and insulin-like growth factor 1 signaling pathways

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Abstract

Recent studies have demonstrated a significant association between mutations in genes involved in the insulin/IGF1 signaling pathway and extension of the life span of model organisms. In this study which compared 122 Japanese semisupercentenarians (older than 105) with 122 healthy younger controls, we examined polymorphic variations of six genes which are involved in insulin/IGF1 signaling. These genes were FOXO1A, INSR, IRS1, PIK3CB, PIK3CG, and PPARGC1A. We investigated the possible association of each gene locus and longevity by haplotype-based association analyses using 18 SNPs from public databases and the published literature. One INSR haplotype, which was comprised of 2 SNPs in linkage disequilibrium, was more frequent in semisupercentenarians than in younger controls.
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Keywords: Aging; Centenarian; Gene polymorphism; Insulin/IGF1 signaling; Longevity

1. Introduction

Recent studies using model organisms have demonstrated a significant association between mutations in genes involved in the insulin/insulin-like growth factor 1 (IGF1) signaling pathway and extension of the life span. The first examples of such genes were found in Caenorhabditis elegans (Kenyon et al., 1993). They include daf-2, an ortholog of the insulin/IGF1 receptor gene family, and daf-16, an ortholog of the forkhead transcription factors which regulate insulin/IGF1-induced gene transcription.

Another example is age-1 which is the C. elegans ortholog of the gene encoding the catalytic subunit of phosphoinositide-3-kinase, a protein involved in insulin/IGF1 signal

transduction (Morris et al., 1996). A long-lived mutant of the insulin-like receptor gene (InR) was also reported in Drosophila melanogaster (Tatar et al., 2001). At almost the same time, the ablation of the D. melanogaster gene chico, which encodes an insulin receptor substrate, was reported to extend the life span of the fly (Clancy et al., 2001). Regulations of life span by insulin receptor and IGF1 receptor were also reported in mice (Bluher et al., 2003; Holzenberger et al., 2003). Based on these studies, genes involved in the insulin/IGF1 signaling pathway are believed to play a role in longevity throughout evolution. In fact, polymorphic variations of the genes for insulin-like growth factor 1 receptor (IGF1R) and phosphoinositide-3-kinase have been reported to affect human longevity (Bonafe et al., 2003).

In this study, we compared 122 Japanese semisupercentenarians (SSCs) (older than 105) with 122 healthy younger controls. We examined polymorphic variations of the genes for six proteins, forkhead box O1A (FOXO1A), insulin

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Table 1
Subjects

Group	Number (male/female)	Mean age ± SD
SSC	122 (15/107)	106.8 ± 1.0
Control	122 (17/105)	33.3 ± 11.4

SSC, semisupercentenarian.

receptor (*INSR*), insulin receptor substrate 1 (*IRS1*), phosphoinositide-3-kinase, catalytic, beta polypeptide (*PIK3CB*), phosphoinositide-3-kinase, catalytic, gamma polypeptide (*PIK3CG*), and peroxisome proliferative activated receptor, gamma, coactivator 1, alpha (*PPARGC1A*), all of which are involved in insulin/IGF1 signaling.

2. Materials and methods

2.1. Subjects

A total of 122 Japanese SSCs (107 female, 15 male, mean age 106.8 ± 1.0 years) were recruited from 2002 to

present for this study (Table 1). Forty-six SSCs were living at home and 76 were institutionalized. None were in an acute care situation and none were receiving tube feeding. The gender matched control subjects comprised 122 healthy volunteers (105 female, 17 male, mean age 33.3 ± 11.4 years, range 19–63) recruited from hospital and institutional workers, medical and nursing school students, and bank clerks. The control subjects were free from diseases such as coronary artery disease, stroke, diabetes, and cancer. Smoking and alcohol consumption was moderate to nil. All subjects enrolled in this study were Japanese. Twenty milliliters of non-fasting venous blood was collected from all subjects, and genomic DNA was prepared from peripheral leukocytes according to standard protocols. Written informed consent was obtained from all participants directly, or by proxy. This study was approved by the ethics committees of the medical school of Keio University and RIKEN Yokohama Institute.

2.2. Single nucleotide polymorphisms (SNPs) typing

Twelve SNPs in the *FOXO1A*, *INSR*, *IRS1*, *PIK3CB* and *PIK3CG* gene loci (3, 6, 1, 1, and 1 SNPs, respectively) were

Table 2
Polymorphisms in six genes and association study of SSCs and controls using allelic frequencies

SNP ID	Location (function)	Minor allele frequency		χ^2	P	dbSNP rs#	Contig position	Reference
		SSC	Control					
FOXO1A (NT_024524)								
FO1	Intron	0.357 (87/244)	0.385 (94/244)	0.430	0.512	2297626	22214002	
FO2	Intron	0.299 (73/244)	0.328 (80/244)	0.467	0.495	2297627	22213931	
FO3	Intron	0.131 (32/244)	0.160 (39/244)	0.808	0.369	–	22123190	Bonafe et al. (2003)
FO4	Intron	–	0.332 (61/184)	–	–	3751436	22115038	
INSR (NT_011255)								
IN1	Intron	0.230 (56/244)	0.201 (49/244)	0.595	0.441	3745544	7207939	
IN2	Intron	0.102 (25/244)	0.143 (35/244)	1.900	0.168	3745546	7151816	
IN3	Intron	0.430 (105/244)	0.516 (126/244)	3.625	0.057	3745548	7092703	
IN4	Intron	0.234 (57/244)	0.303 (74/244)	3.016	0.083	2252673	7090418	
IN5	Exon (syn)	0.340 (83/244)	0.287 (70/244)	1.609	0.205	1799817	7065297	
IN6	Intron	0.459 (112/244)	0.508 (124/244)	1.182	0.277	2288404	7064986	
IRS1 (NT_005403)								
IR1	Exon (syn)	0.344 (84/244)	0.332 (81/244)	0.082	0.774	1801123	77870455	
IR2	Exon (R971G)	0.045 (11/244)	0.029 (7/244)	0.923	0.337	1801278	77869956	Bonafe et al. (2003)
PIK3CB (NT_005612)								
3B1	Promoter	0.037 (9/242)	0.041 (10/244)	0.047	0.829	361072	44973698	Bonafe et al. (2003)
3B2	Promoter	–	–	–	–	–	44973642	Bonafe et al. (2003)
3B3	Intron	0.475 (116/244)	0.434 (106/244)	0.826	0.363	2305268	44879227	
PIK3CG (NT_079596)								
3G1	Intron	0.270 (66/244)	0.332 (81/244)	2.190	0.139	3779501	5908409	
PPARGC1A (NT_006316)								
PP1	Exon (S482G)	0.492 (119/242)	0.525 (128/244)	0.525	0.469	8192678	14491020	Ek et al. (2001)
PP2	Exon (M612T)	0.169 (41/242)	0.148 (36/244)	0.436	0.509	3736265	14490065	Ek et al. (2001)

Syn, synonymous change.

selected from the JSNP database (http://snp.ims.u-tokyo. ac.jp/) using the criteria that minor allele frequencies were more than 10% in the Japanese population. Five SNPs in the *FOXO1A*, *IRS1* and *PIK3CB* gene loci (1, 1, 1, and 2 SNPs, respectively) were from Bonafe et al. (2003). Additionally 2 non-synonymous SNPs in the *PPARGC1A* gene locus were selected from Ek et al. (2001) (Table 2). The genomic DNA sequences of *FOXO1A*, *INSR*, *IRS1*, *PIK3CB*, *PIK3CG*, and *PPARGC1A* were obtained from the National Center for Biotechnology Information (NCBI, USA) (accession numbers NT_024524, NT_011255, NT_005403, NT_005612, NT_079596, and NT_006316, respectively). For each polymorphism not obtained from JSNP, we ensured that there was a sufficiently high frequency in our subjects by testing 24 control subjects. Polymorphisms were typed by DNA sequencing using the BigDye Terminator cycle sequencing kit and an ABI Prism 3700 DNA analyzer (Applied Biosystems, Foster City, CA, USA) or by real-time pyrophosphate DNA sequencing (Ronaghi et al., 1996, 1998) using a PSQ 96 system (Pyrosequencing AB, Uppsala, Sweden) according to the manufacturer's instructions.

2.3. Statistical analysis

The chi-square test was performed between SSCs and control subjects for each allelic and haplotypic frequency. Statistical significance was inferred when $P<0.05$. Pairwise linkage disequilibrium (LD) was estimated as $D=x_{11}-p_1q_1$, where x_{11} is the frequency of haplotype A_1B_1, and p_1 and q_1 are the frequencies of alleles A_1 and B_1 at locus A and B, respectively. A standardized LD coefficient, r, is given by $D/(p_1p_2q_1q_2)^{1/2}$ where p_2 and q_2 are the frequencies of the other alleles at locus A and B, respectively (Hill and Robertson, 1968). Lewontin's coefficient D' is given by D/D_{max}, where $D_{max}=min[q_1p_2,p_1q_2]$ when $D>0$ (Lewontin, 1964). Haplotype frequencies for multiple loci were estimated by the expectation-maximization method.

Computations were performed using SNPAlyze software (Dynacom, Mobara, Japan).

3. Results

3.1. Pairwise LD in 5 genes

Among the SNPs not from the JSNP database, 3B2 in *PIK3CB* was not polymorphic in our 24 control samples (Table 2). Consequently this SNP was excluded from further experiments. The 92 healthy controls were genotyped for each of the 17 selected SNPs. The strength of LD for each SNP pair within each gene was measured using the $|D'|$ and the r^2 values (Fig. 1). This figure shows that FO1 and FO4 in *FOXO1A* locus are in very tight LD with each other ($r^2=$ 0.789). FO1 was selected as the representative SNP for this SNP pair and was examined in further analysis. FO4 was excluded from further analysis.
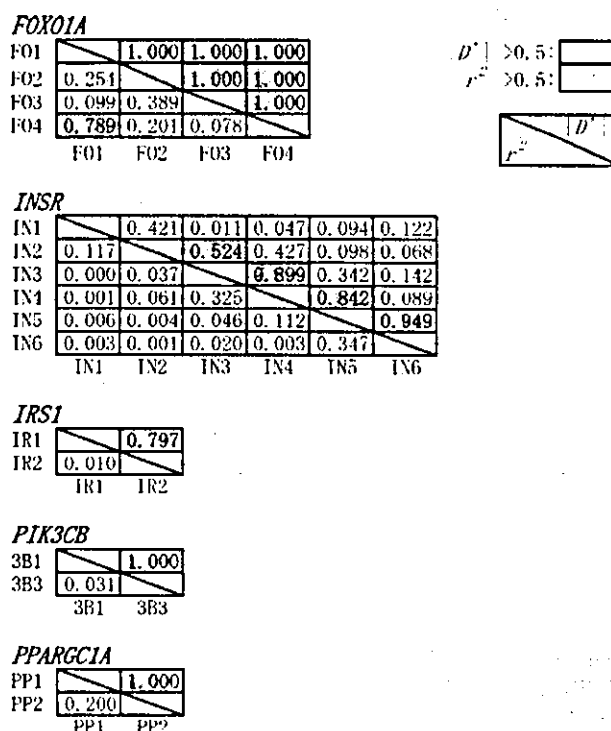

Fig. 1. Pairwise LD in *FOXO1A*, *INSR*, *IRS1*, *PIK3CB*, and *PPARGC1A* evaluated by $|D'|$ and r^2 estimations. The LD between all pairs of SNPs was evaluated by measuring $|D'|$ and r^2 values. Designated SNP IDs are shown in Table 2. Pairwise LD was determined in 92 younger controls. SNP pairs in high LD ($|D'|>0.5$, $r^2>0.5$) are shown as gray boxes. Upper right triangles show values of $|D'|$ and lower left triangles show values of r^2.

3.2. Allele and haplotype frequency distributions in young people and semisupercentenarians

An additional 122 SSCs and 30 healthy younger controls were genotyped for an association analysis using 16 SNPs in six genes (Table 2). Two SNPs (IN3 and IN4) in *INSR* showed a weak difference between SSCs and controls. These SNPs are in LD with each other ($|D'|=0.899$) and are within 2.4 kb of each other (Fig. 1).

Haplotypes were constructed on the basis of the genotype data from these SNPs in *INSR*. The expectation-maximization algorithm, with phase-unknown samples, was used to estimate haplotype frequencies. The MM haplotype (M: major allele) was more frequent in SSCs (57.0%) than in controls (47.3%) ($P=0.030$) (Table 3).

Table 3
Case control study of SSCs and controls using estimated haplotype frequencies in *INSR*

Haplo-type ID	SNP ID		Frequency		χ^2	P
	IN3	IN4	SSC	Control		
1	M	M	0.570	0.473	4.729	0.030
2	m	M	0.197	0.224	0.603	0.437
3	M	m	0.000	0.011	3.019	0.082
4	m	m	0.234	0.292	2.076	0.150

M, major allele; m, minor allele.

4. Discussion

To date many genetic variations in the *INSR* locus have been reported to be associated with diseases including diabetes mellitus, leprechaunism, and Rabson–Mendenhall syndrome (Online Mendelian Inheritance in Man # 147670). To our knowledge this is the first report showing associations between genetic polymorphisms of *INSR* and human longevity. Through a study of Japanese centenarians, we found the prevalence of diabetes mellitus in centenarians to be significantly lower than that in the general population (manuscript in preparation). A common variant in the *PPARGC1A* gene has been reported to be associated with type II diabetes mellitus (Ek et al., 2001). The PPARGC1A protein interacts with FOXO1 in an insulin-regulated mechanism of gluconeogenesis (Puigserver et al., 2003). The risk variant (PP1 in Table 2) present frequently in both SSCs and controls (about 50%) and no association with the common variation and longevity was found in this study.

Although a significant association was observed between the IN3-M/IN4-M haplotype in *INSR* and longevity, both SNPs are located in introns and the functional implication of this haplotype association remains uncertain. Very recently a polymorphic variation of *IGF1R* was reported to affect human longevity in the Italian population (Bonafe et al., 2003) but the functional implication of the polymorphic variation also remains to be elucidated. It is noteworthy that both INSR and IGF1R are members of the insulin receptor tyrosine kinase family. Further comprehensive studies of the *INSR* locus, especially on the region including IN3 and IN4, together with the *IGF1R* locus are needed to identify the causal variations that enable or prevent human longevity and to clarify the molecular mechanisms of human longevity.

Acknowledgements

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2. 転倒予防を中心とした地域での取り組みについて

芳賀　博

はじめに

　今後の人口の高齢化，とくに後期高齢者の増加とあいまって要介護，要支援者の増大が懸念されている．このような状況の中，21世紀における新たな高齢者保健福祉施策においては，「介護サービス基盤の整備」に加え「介護予防や生きがい活動支援」が，車の両輪として推進されるべきことが提唱されることとなった．すなわち，いわゆる“元気高齢者”に対して積極的な保健福祉サービスを展開することで活力ある高齢者像の構築を目指すと共に，将来において要介護状態に陥ることがないように，そのリスクを少しでも軽減しようとするものである．しかしながら，現時点においては地域における要介護予防への取り組みは緒についたばかりである．

転倒が高齢者のQOLに及ぼす影響

　ところで，要介護状態の主な原因は，何であろうか．国民生活基礎調査（1998年）によれば，第1位が脳血管疾患（29.3%），第2位　高齢による衰弱（12.1%），第3位　骨折・転倒（10.4%），以下　痴呆（10.1%），リウマチ・関節炎（6.6%）などと続く．要介護状態の予防は，第1に脳血管疾患の予防にあることは間違いないことであり，老人保健事業等による脳血管疾患対策の推進が引き続き求められている．しかし，寿命の延伸に伴い，高齢による衰弱や転倒・骨折が要介護の原因として注目されるようになってきた．

　高齢者にとっての転倒は，再転倒への不安や恐怖をあおり，高齢者の生活行動を制約するようになるばかりでなく，骨折などのケガを契機として「寝たきり」の誘引となることも知られている．老人保健事業第4次計画においても「転倒予防」は，「要介護予防」の重要な柱の一

Community based intervention study for prevention of falling among the elderly
Hiroshi Haga：東北文化学園大学医療福祉学部
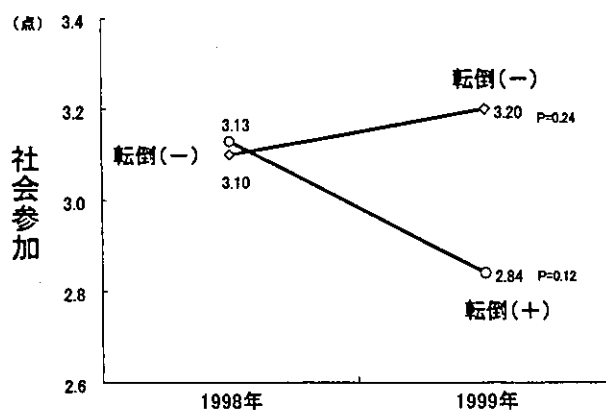
図1　転倒が社会参加に及ぼす影響（北海道O町）

つともなっている．

　演者ら[1]は，転倒が高齢者の心身に及ぼす影響について検討しているが，転倒後に社会参加の程度が減少すること，これに伴い週1回以上の交流のある友人数も減少すること，また，転倒は高齢者の社会参加（図1）も低下させることなどが明らかとなった．しかし，骨折などのケガがなければ，すぐには日常生活動作（手段的自立）の低下まではきたさないことも明らかにされた．

地域で実施可能な転倒予防プログラム開発の必要性

　転倒予防のための介入研究は，欧米では多くの実績が報告されているものの，わが国における地域での高齢者の転倒予防に関する研究は緒についたばかりである．金成ら[2]は，転倒予防に関する国内外の論文のレビューを行い，「日本でも転倒予防を目的としたさまざまな事業・研究が各地で行われつつあるが，有効性を立証した研究報告は見つからなかった」と指摘している．しかも，希望者を募ってのいわゆる転倒予防教室のような介入の試みはみられても地域の高齢者全体の転倒リスクの軽減や
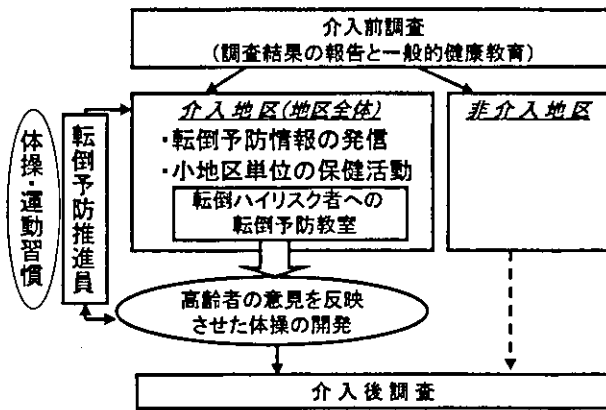
図2　プログラム開発の流れ

図3　介入前後の転倒率の変化

転倒率の低下を目指した介入研究の試みは極めて少ない．

　全国自治体を対象とした転倒予防事業に関する調査[3]では，転倒予防事業を実施している市町村は全体の半数程度に留まっており，予防事業を妨げている要因として最も多かったのは「指導プログラムがわからない」であった．地域で実施可能な効果的な介入プログラム（Community based intervention programme）の開発が望まれている．

地域での転倒予防プログラム開発の試み[4]

　演者らは，地域への介入方法として，i) 高齢者の意見を反映したプログラム　ii) 住民参加型の活動　iii) 地域に根ざしたタイムリーな情報発信　iv) 自治体での実施が可能なプログラムの4つを基本として転倒予防プログラムの開発と実践・評価を進めている．

　1) 研究の対象と介入プログラムの流れ（図2）

　宮城県北部に位置する三本木町において，転倒の危険が高くなる75歳以上の後期高齢者を対象とした．地域のまとまりを考慮して「介入地区」と「非介入地区」を設定．本研究は，介入前の調査（2000年8月），介入の実施（2001年1〜7月），介入後の調査（2001年8月）からなる．介入前後の調査は，会場での体力測定と質問紙による面接聞き取り調査及び会場に不参加の者には戸別訪問による面接聞き取り調査のみ実施した．介入地区には，特別な介入プログラムを実施，非介入地区には一般的な保健活動を展開した．

　2) 転倒予防推進員の養成

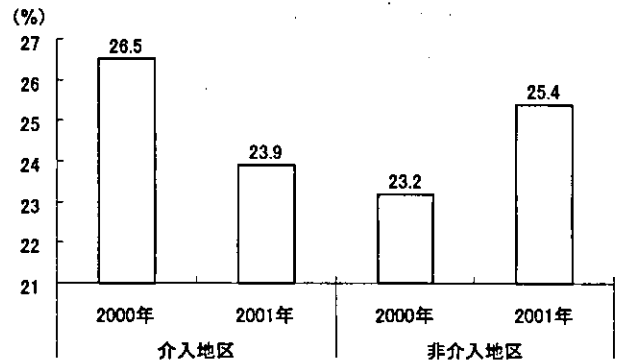　転倒予防プログラムの中核的な推進役として高齢（60歳以上）ボランティアを位置付け，転倒予防教室への参加呼びかけと補助，転倒予防に関する知識の普及や体操

の普及，ミニコミ紙の編集などの役割を担ってもらっている．本格的な介入に先立ちボランティア養成のための研修会（3回）の実施とその後の研究者・保健師と転倒予防推進員との定例会（隔月）の開催を通じて新たな体操，レクリエーションプログラムの紹介を行うと共に推進員相互の交流を図り活動の継続を支援している．

　3) 中央会場での転倒予防教室と体操の開発

　介入地区の対象者のうち，介入前の調査データに基づき転倒の危険性の高い者を対象として転倒予防教室を開催した．2001年1月から1回/2週，計12回開催した．教室の内容は，転倒予防や体力づくりに関する健康教育，体操，レクリエーションから構成された．また，参加者に対して家庭での運動習慣が定着するように体操やウオーキングの実施有無と実施時間を毎日記録してもらうように促した．

　さらに，教室の一環として参加者の意見を取り入れた三本木町独自の転倒予防体操（SUN体操）の開発も併せて行った．これはプログラムの前半6回で30種類（毎回5種類）の体操を体験してもらい，参加者と転倒予防推進員による評価（上手にできたか，楽しくできたか，きついところがあればどこか，自宅でもできそうか等）に基づいて，研究者らが10種類から成るオリジナルな体操として試案を作成し，第7回目の教室において一連の体操として実施してもらい，最終的に完成にいたったものである．転倒予防教室の後半5回は，運動プログラムに加えて，散歩をしながらの歩道上の危険箇所の探索とそれに基づく転倒防止マップづくりや転倒予防のための標語づくりなども組み込まれた．

　4) 介入地区全体へのプログラムの提供

　小地区単位で行う地区全体への介入は，本研究の中心的課題でもあり，以下の3つの要素をその柱としている．i) 地区集会所を利用しての転倒予防推進員によるSUN

体操やウォーキングの普及，ii) 研究者，保健師による介入前調査のデータを用いた小地区単位の転倒予防を中心とする健康学習，iii) 転倒予防のための情報や転倒予防教室での出来事等を介入地区全体に紹介するためのミニコミ紙（ダウンストッパー通信）の全戸配付（毎月）から成る．通信紙の編集は転倒予防推進員及び保健師の意見を取り入れ研究者が行っている．また，SUN 体操普及のための簡易マニュアル(カラー A3 版)を作成し，各戸配布した．さらに，体操の仕方を解説，実演したビデオの作成も行い転倒予防推進員に携帯してもらい体操の普及に役立ててもらうことにした．

　5) 介入プログラムの効果

　転倒の割合：介入地区では介入前の 26.5% から介入後の 23.9% へと 2.6 ポイントの低下を示した．一方，非介入地区の転倒率は，逆に介入前の 23.2% から介入後の 25.4% へと 2.2 ポイントの上昇を示していた（図 3）．

　体力の変化：介入地区と非介入地区の体力レベルの低下に着目して検討すると，握力，長座位体前屈，最大歩行速度では，介入地区の加齢にともなう低下幅は非介入地区より少なく，Up&Go では介入地区で改善傾向にある様子が示された．

　6) まとめ：住民の研究計画，実施過程への参加のもとに行われる介入プログラムは，参加的アクションリサーチとして地域での健康づくりの手法として重要視されている．高齢ボランティアを中核とする転倒予防活動が，地域高齢者の転倒率の改善や老化に伴う体力レベルの低下を緩和する効果を有することが示唆されたといえよう．

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〈原　著〉

都市在住の高齢者におけるソーシャル・サポートと抑うつ症状の関連性

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栗山　進一[2)]　　鈴木　寿則[2)]　　大森　　芳[2)]　　寳澤　　篤[2)]

海老原　覚[3)]　　荒井　啓行[3)]　　辻　　一郎[2)]

〈要　約〉　都市在住の高齢者におけるソーシャル・サポートと抑うつ症状の関連を明らかにするため，仙台市T地区の70歳以上住民に対し総合機能評価を平成14年7月から8月に行った．対象2,730人のうち1,198人が参加し，聞き取り調査を受けた．ソーシャル・サポートに関しては，村岡ら（1996）の調査票により (i) 困ったときの相談相手，(ii) 体の具合の悪いときの相談相手，(iii) 家事などの日常生活を援助してくれる人，(iv) 具合の悪いとき病院に連れて行ってくれる人，(v) 寝込んだとき身の回りの世話をしてくれる人の有無を尋ねた．抑うつ症状の評価は Geriatric Depression Scale（GDS）30項目を用い，GDS に回答した1,170人のうち，Mini-Mental State Examination（MMSE）が18点以上で研究に同意した1,146人を解析対象とした．GDS 10点以下を非抑うつ群，11点以上または抗うつ剤服用者を抑うつ群とした．ソーシャル・サポートの欠如と抑うつ症状の出現に関する多変量補正オッズ比（95%信頼区間）を (i) から (v) の各項目について，多重ロジスティック回帰分析により算出した．その際，年齢，配偶者の有無，同居人数，既往疾患数，教育レベル，認知機能，運動能力，痛み，主観的健康度を補正した．抑うつ群は男性134人（27.9%），女性259人（38.9%）であった．質問 (i) から (v) まで各々の「ある」者に比べて「ない」者では抑うつ症状出現のオッズ比（95%信頼区間）は，男性では (i) 2.5（1.5～4.1），(ii) 1.9（1.1～3.2），(iii) 2.7（1.7～4.4），(iv) 1.9（1.1～3.2），(v) 2.8（1.6～4.9）と全項目で有意に上昇した．女性では (i) 1.2（0.8～1.8），(ii) 1.2（0.8～1.8），(iii) 1.4（1.0～2.0），(iv) 1.6（1.1～2.3），(v) 2.0（1.4～2.9）と (iii)，(iv)，(v) の項目で有意にオッズ比が上昇した．都市部高齢者では男女ともソーシャル・サポートの欠如と抑うつ症状との間に有意な関連があった．しかも男性では，関連するソーシャル・サポートの種類と関連の強さの両面において影響が顕著であった．

Key words：高齢者，Geriatric Depression Scale，抑うつ症状，ソーシャル・サポート

緒　言

高齢者の抑うつ症状の出現には，役割意識や人間関係の喪失などの心理社会的背景と脳の器質的変化や慢性身体疾患などの身体的背景が関連している[1)]．このうち，高齢者の心理社会的背景に影響を及ぼすものの1つに，地域社会の中での孤立や人間関係の希薄化によるソーシャル・サポート不足があげられる[2)]．

ソーシャル・サポートは，人と人の結びつき，他者か

らの援助や情報提供を意味し，社会における対人関係の機能的側面を示すと定義される[2)3)]．これまでの海外の研究では，ソーシャル・サポートの不足が死亡リスクの増大，身体的健康状態の悪化，高齢者の抑うつ症状のリスク増大と関連すると報告されている[4)～9)]．また，わが国においても，村岡ら，青木ら，Hashimoto らがソーシャル・サポートと高齢者の抑うつ症状の関連を指摘している[10)～12)]．

しかし，地域在住高齢者の抑うつ症状に関するわが国の研究は，比較的緊密な人間関係が期待される農村地域や非都市部で実施されたものが多く，孤立や人間関係の希薄化がより深刻化していると思われる都市部での調査はきわめて少ない[10)11)13)～16)]．特に，ソーシャル・サポートと抑うつ症状に関する先行研究は3件あるが，都市部の高齢者を対象としたものは在宅介護を受けている対象者を調査した1件のみである[12)]．また，高齢者の男性は退職後に役割意識や人間関係が希薄になりやすく，一方，