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Intakes of vegetables and related nutrients such as vitamin B complex, potassium, and calcium, are negatively correlated with risk of stroke in Korea

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Abstract

Consumption of vegetables and fruits is associated with a reduced risk of stroke, but it is unclear whether their protective effects are due to antioxidant vitamins or folate and metabolically related B vitamins. The purpose of the study was to test the hypothesis that intake of fruits and vegetables, which are major sources of antioxidant and vitamin B complex vitamins, reduces the risk of stroke. Cases consisted of patients diagnosed with first event of stroke (n = 69). Controls (n = 69) were age-, sex-, and body mass index-matched to cases. Multivariable-adjusted regression analysis showed that subjects who ate four to six servings of vegetable per day had a 32% reduction in the risk of stroke, and those with more than six servings per day had a reduction of 69% after adjusting for age, sex, BMI, and family history of stroke. Intakes of total fat, plant fat, calcium, potassium, vitamin B_1, vitamin B_2, vitamin B_6, niacin, and folate were significantly and negatively associated with the risk of stroke. Although the trend was not significant, stroke risk was reduced in the second quartile (1.21-2.66 servings per week) of fish intake. However, intake of fruits (average daily intake of 1.0 serving) and antioxidant vitamins such as carotene, vitamin C, and vitamin E was not associated with the risk of stroke. In conclusion, our observational study suggests that intake of fat and vegetables, rich sources of vitamin B complex, calcium, and potassium may protect against stroke.

Key Words: Fruit, human, stroke, vegetable, vitamin

Introduction

Stoke is the second leading cause of death worldwide [1] as well as in Korea [2], and thus prevention of stroke is a major public health priority. Modifiable lifestyle risk factors such as dietary intake could be related to the risk of stroke [3]. These include an inverse relationship between intake of fruits and vegetables and stroke risk [4-7]. Meta-analyses of cohort studies show that increased intake of fruits and vegetables is associated with a reduced risk of stroke, and provides support for the recommendation to consume more than five servings of fruits and vegetables per day, which is likely to cause a major reduction in stroke [4]. The potential protective effects of fruits and vegetables may be due to their antioxidant vitamins [3], folate contents, and metabolically related B vitamins such as vitamin B_{12}, vitamin B_6, and riboflavin [8].

Vitamin C, β-carotene, and vitamin E scavenge free radicals, and vitamin C protects membranes from peroxidation by regenerating their α-tocopherol components [9]. Free radical oxidation of LDL is thought to be an important contributor to the development of atherosclerosis, and thus antioxidants may slow or prevent this process and thereby decrease the risk of stroke. Observational studies have shown that decreased risk of stroke is associated with increased antioxidant intake [10]. This decreased risk is associated with some but not all antioxidant vitamins [11-13], and two randomized trials found no association between supplementation with β-carotene [14] and some other antioxidant vitamins [15] and a reduced risk of stroke. Thus, the evidence regarding antioxidant vitamin intake and risk of stroke remains equivocal.

There has been growing interest in protection against stoke by intake of folate and related B vitamins [16-17]. These effects may be mediated via homocysteine, the metabolism of which requires adequate status of all four relevant B vitamins [8]. Higher folate intakes were associated with reduced stroke risk in studies of Health Professionals [18], male Swedish smokers [16], and male Finnish smokers [19], but not in the Nurses Health study [20]. Thus, the role of folate in stroke has yet to be established, and data on the intake of other B vitamins and stroke are sparse.

Some studies have reported an association between food group intake and stroke risk, while others assessed only selected nutrients. The purpose of the present study was to examine the hypothesis that intake of fruits and vegetables, and also their nutrients such as antioxidant vitamins and folate and related B vitamin reduces the risk of stroke after adjusting for traditional risk factors in Korean population.

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Subjects and Methods

Subjects

We recruited patients admitted to Hanyang University Seoul Hospital for treatment of first event of stroke (n = 69) between May 2007 and January 2009 to participate in the present study. The 69 cases were age-, sex-, and body mass index-matched to healthy controls (n = 69). Subjects currently taking dietary supplementation were excluded from the study. This study was approved by the institutional review board of Hanyang University Seoul Hospital and written informed consent was obtained from all participants.

Dietary intake

Anthropometric data, medical history, and socioeconomic status were obtained from both medical chart reviews and interviews. The participants' usual dietary intakes were assessed using a semi-quantitative food frequency questionnaire (FFQ), which includes questions on 117 food items commonly consumed in Korean meals, obtained from the Korea Health and Nutrition Examination Survey (KHANES) in 1998. Patients or caregivers were asked to indicate how often, on average, they had consumed various foods during the year prior to the interview and asked about their usual consumption patterns, so as to exclude periods of illness or dieting. The portion size was determined depending on the median value of each food determined from the 24-h recall data obtained from the KHANES. For easy understanding of portion size, we provided pictures on serving size for food items. Three-dimensional food models and full-scale photographs were used to assist subjects in estimating portion size. Nutrient and food intake were analyzed by Can-Pro 3.0 (the Korean Nutrition Society, Seoul, Korea).

Laboratory measurements

Blood samples were collected in EDTA and SST blood tubes on the day of admission, centrifuged, and then divided into aliquots for storage at -80℃. Serum lipid profiles (TBA-30FR; Toshiba, Tokyo, Japan), blood chemicals (Coulter LH 750, Beckman Coulter, Inc., Fullerton, CA, USA), liver function (Variant Ⅱ, Bio-RAD, Hercules, CA, USA), and C-reactive protein (CRP) concentrations (IMMAGE Immunochemistry System; Beckman Coulter, Inc., Fullerton, CA, USA) were measured with auto analyzers.

Statistical analysis

Continuous variables were expressed using the mean and the standard errors of the mean to compare cases and controls using an independent t-test. Proportions of nominal variables were compared using the chi-square test. Multivariable logistic models were used to determine the independent effects on stroke status. Intake of nutrients and foods was categorized into quartiles based on control values. To prevent confounding, the following covariates were included in the models: age, sex, body mass index (BMI; kg/m^2), family history of stroke, and energy intake; and were selected by use of a backward variable selection method. A P value of < 0.05 was considered statistically significant. Statistical analysis was performed using SPSS, version 12.0 (SPSS Inc., Chicago, IL, USA).

Results

Stroke cases were significantly more likely to have a family history of stroke than controls (Table 1). Age, sex, BMI, education level, smoking, drinking, exercise, and family history of diabetes and hypertension were similar between cases and controls. In addition, there were no significant differences in liver function, lipid profile, CRP, and hemoglobin A1c.

Multivariable-adjusted regression analysis showed that intakes of total fat, plant fat, calcium, potassium, vitamin B_1, vitamin B_2, vitamin B_6, niacin, and folate were negatively correlated with the risk of stroke after adjusting for age, sex, BMI, and family history of stroke (Table 2). Although the trend was not significant, the risk of stroke was lower in the third quartile of protein intake, and the second and the third quartile of fiber

Table 1. Baseline characteristics of stroke cases and controls N (%)

	Controls (n = 69)	Cases (n = 69)	P value
Age (yr)[1]	57.4 ± 1.6	57.9 ± 1.6	0.816
Body mass index (kg/m^2)	23.5 ± 0.4	23.4 ± 0.4	0.808
Type of stroke			
Hemorrhagic stroke	0 (0)	34 (49.3)	
Ischemic stroke	0 (0)	35 (50.7)	
Female	26 (37.7)	26 (37.7)	1.000
Education level			
< Middle school	18 (27.7)	27 (40.3)	
Middle to high school	32 (49.2)	33 (49.2)	0.443
> High school	15 (23.0)	7 (10.5)	
Family history of hypertension	15 (21.7)	21 (30.4)	0.162
Family history of stroke	5 (7.2)	16 (23.2)	0.003
Family history of diabetes	11 (15.9)	11 (15.9)	0.214
Exercise	34 (49.3)	31 (44.9)	0.609
Smoking	37 (53.6)	36 (52.2)	0.865
Drinking	37 (53.6)	46 (66.7)	0.118
Hemoglobin A1c (%)	5.8 ± 0.2	5.9 ± 0.1	0.711
Aspartate aminotransferase (U/l)	28.4 ± 2.6	24.9 ± 1.7	0.267
Alanine aminotransferase (U/l)	31.7 ± 4.6	24.4 ± 2.0	0.149
Triacylglyceride (mg/dl)	113.2 ± 6.5	137.7 ± 12.7	0.089
Total cholesterol (mg/dl)	165.8 ± 5.2	169.3 ± 4.9	0.627
LDL-cholesterol (mg/dl)	95.1 ± 4.5	96.2 ± 4.8	0.868
HDL-cholesterol (mg/dl)	42.4 ± 1.5	42.9 ± 2.3	0.877
C-reactive protein (mg/dl)	1.3 ± 0.4	1.3 ± 0.3	0.968

[1] Values for continuous variables are means ± standard error mean (SEM).

Table 2. Association of daily nutrient intake with the risk of stroke by multivariate regression analysis (odds ratios and 95% confidence interval)[1)]

	Quartile of nutrients intake				*P* for trend[2)]
	1	2	3	4	
Energy (g)					
No. of case/control	11/17	20/18	9/17	29/17	
Intake cutoff	≤ 1391.08	1391.08 < to ≤ 1807.80	1807.80 < to ≤ 2121.32	> 2121.32	0.158
OR (95% CI)	1.00	1.680 (0.564-5.009)	0.745 (0.209-23.653)	2.550 (0.851-7.641)	
Total protein (g)					
No. of case/control	15/17	20/18	12/17	22/17	
Intake cutoff	≤ 61.06	61.06 < to ≤ 83.96	83.96 < to ≤ 103.91	> 103.91	0.087
OR (95% CI)	1.00	0.616 (0.177-2.141)	0.201 (0.041-0.991)*	0.199 (0.027-1.444)	
Plant protein (g)					
No. of case/control	12/17	13/18	26/17	18/17	
Intake cutoff	≤ 31.07	31.07 < to ≤ 39.98	39.98 < to ≤ 55.00	> 55.00	0.801
OR (95% CI)	1.00	0.987 (0.285-3.414)	1.791 (0.432-7.428)	0.988 (0.165-5.917)	
Animal protein (g)					
No. of case/control	15/17	21/18	13/17	20/17	
Intake cutoff	≤ 24.82	24.82 < to ≤ 38.70	38.70 < to ≤ 51.68	> 51.68	0.338
OR (95% CI)	1.00	0.910 (0.297-2.791)	0.361 (0.092-1.424)	0.393 (0.093-1.661)	
Total fat (g)					
No. of case/control	16/17	19/18	19/17	15/17	
Intake cutoff	≤ 34.35	34.35 < to ≤ 48.67	48.67 < to ≤ 63.68	> 63.68	0.016
OR (95% CI)	1.00	0.711 (0.231-2.189)	0.262 (0.064-1.078)	0.126 (0.022-0.708)*	
Plant fat (g)					
No. of case/control	36/17	4/18	15/17	14/17	
Intake cutoff	≤ 18.37	18.37 < to ≤ 20.99	20.99 < to ≤ 27.23	> 27.23	< 0.001
OR (95% CI)	1.00	0.043 (0.009-0.210)**	0.153 (0.045-0.523)*	0.033 (0.006-0.175)**	
Animal fat (g)					
No. of case/control	10/17	19/18	20/17	20/17	
Intake cutoff	≤ 16.09	16.09 < to ≤ 26.09	26.09 < to ≤ 36.04	> 36.04	0.899
OR (95% CI)	1.00	1.271 (0.377-4.281)	1.621 (0.451-5.821)	1.047 (0.257-4.259)	
Carbohydrate (g)					
No. of case/control	11/17	10/18	21/17	27/17	
Intake cutoff	≤ 191.60	191.60 < to ≤ 247.21	247.21 < to ≤ 309.90	> 309.90	0.075
OR (95% CI)	1.00	0.751 (0.205-2.755)	2.219 (0.577-8.535)	3.684 (0.629-21.568)	
Fiber (g)					
No. of case/control	21/17	25/18	13/17	10/17	
Intake cutoff	≤ 20.29	20.29 < to ≤ 30.69	30.69 < to ≤ 37.59	> 37.59	0.734
OR (95% CI)	1.00	0.548 (0.177-1.701)	0.124 (0.028-0.556)*	0.076 (0.014-0.422)*	
Calcium (mg)					
No. of case/control	21/17	24/18	16/17	8/17	
Intake cutoff	≤ 404.57	404.57 < to ≤ 610.67	610.67 < to ≤ 784.58	> 784.58	<0.001
OR (95% CI)	1.00	0.558 (0.182-1.705)	0.205 (0.049-0.854)	0.030 (0.004-0.210)**	
Phosphorus (mg)					
No. of case/control	22/17	15/18	17/17	15/17	
Intake cutoff	≤ 1002.70	1002.70 < to ≤ 1261.36	1261.36 < to ≤ 1552.21	> 1552.21	0.251
OR (95% CI)	1.00	0.771 (0.048-1.611)	0.582 (0.017-1.394)	0.414 (0.002-1.121)	
Iron (mg)					
No. of case/control	16/17	15/18	21/17	17/17	
Intake cutoff	≤ 11.57	11.57 < to ≤ 15.66	15.66 < to ≤ 20.73	> 20.73	0.389
OR (95% CI)	1.00	0.475 (0.138-1.630)	0.689 (0.164-2.888)	0.313 (0.054-1.831)	
Sodium (mg)					
No. of case/control	17/17	18/18	25/17	9/17	
Intake cutoff	≤ 4078.64	4078.64 < to ≤ 5549.49	5549.49 < to ≤ 6943.38	> 6943.38	0.081
OR (95% CI)	1.00	0.418 (0.144-1.210)	1.167 (0.045-2.623)	0.052 (0.010-1.277)	

Table 2. Continued

	Quartile of nutrients intake				P for trend[2)]
	1	2	3	4	
Potassium (mg)					
No. of case/control	20/17	16/18	21/17	12/17	
Intake cutoff	≤ 2744.50	2744.50 < to ≤ 3650.37	3650.37 < to ≤ 4537.86	> 4537.86	0.007
OR (95% CI)	1.00	0.387 (0.121-1.237)	0.293 (0.072-1.185)	0.077 (0.012-0.478)*	
Zinc (mg)					
No. of case/control	17/17	7/18	20/17	25/17	
Intake cutoff	≤ 7.43	7.43 < to ≤ 9.52	9.52 < to ≤ 12.03	> 12.03	0.646
OR (95% CI)	1.00	0.348 (0.089-1.357)	1.174 (0.291-4.792)	0.977 (0.137-6.945)	
Retinol (μg)					
No. of case/controls	14/17	12/18	20/17	23/17	
Intake cutoff	≤ 56.05	56.05 < to ≤ 81.84	81.84 < to ≤ 124.69	> 124.69	0.821
OR (95% CI)	1.00	0.632 (0.204-1.955)	1.220 (0.410-3.633)	0.961 (0.269-3.435)	
Carotene (μg)					
No. of case/controls	15/17	16/18	19/17	19/17	
Intake cutoff	≤ 2094.83	2094.83 < to ≤ 3574.01	3574.01 < to ≤ 5457.25	> 5457.25	0.201
OR(95% CI)	1.00	0.367 (0.203-1.326)	0.841 (0.974-1.143)	1.809 (0.775-2.361)	
Vitamin B_1 (mg)					
No. of case/control	18/17	20/18	16/19	15/15	
Intake cutoff	≤ 1.06	1.06 < to ≤ 1.40	1.40 < to ≤ 1.70	> 1.70	0.011
OR (95% CI)	1.00	0.599 (0.184-1.952)	0.163 (0.035-0.761)*	0.076 (0.010-0.593)*	
Vitamin B_2 (mg)					
No. of case/control	22/17	14/18	14/17	19/17	
Intake cutoff	≤ 1.01	1.01 < to ≤ 1.28	1.28 < to ≤ 1.70	> 1.70	0.008
OR (95% CI)	1.00	0.242 (0.072-0.813)*	0.162 (0.041-0.647)*	0.104 (0.020-0.548)*	
Vitamin B_6 (mg)					
No. of case/control	22/17	21/17	17/17	9/18	
Intake cutoff	≤ 1.89	1.89 < to ≤ 2.47	2.47 < to ≤ 3.17	> 3.17	0.050
OR (95% CI)	1.00	0.385 (0.096-1.552)	0.193 (0.035-0.963)*	0.185 (0.050-0.682)*	
Niacin (mg)					
No. of case/control	22/19	13/16	14/17	20/17	
Intake cutoff	≤ 14.54	14.54 < to ≤ 19.81	19.81 < to ≤ 23.68	> 23.68	0.040
OR (95% CI)	1.00	0.333 (0.099-1.125)	0.253 (0.064-0.995)*	0.169 (0.035-0.819)*	
Folate (μg)					
No. of case/control	28/17	20/18	15/17	6/17	
Intake cutoff	≤ 286.38	286.38 < to ≤ 412.38	412.38 < to ≤ 520.28	> 520.28	< 0.001
OR (95% CI)	1.00	0.357 (0.116-1.095)	0.094 (0.023-0.386)*	0.043 (0.008-0.229)**	
Vitamin C (mg)					
No. of case/control	15/17	11/18	24/17	19/17	
Intake cutoff	≤ 89.04	89.04 < to ≤ 125.87	125.87 < to ≤ 174.03	> 174.03	0.627
OR (95% CI)	1.00	0.495 (0.145-1.696)	1.691 (0.537-5.332)	1.096 (0.269-4.467)	
Vitamin E (mg)					
No. of case/control	17/17	15/18	11/17	26/17	
Intake cutoff	≤ 9.75	9.75 < to ≤ 13.43	13.43 < to ≤ 17.29	> 17.29	0.525
OR (95% CI)	1.00	0.719 (0.240-2.157)	0.339 (0.082-1.402)	0.608 (0.133-2.779)	

1) OR and 95% CI were analyzed by logistic regression. OR for energy intake was adjusted for age, sex, BMI, and family history of stroke; ORs for nutrients were adjusted for the same variables and energy.
2) Estimates of p values for a linear trend were based on linear scores derived from the medians of quartile of nutrient intake among controls.
* $P < 0.05$ from the first quartile by logistic regression analysis
** $P < 0.01$ from the first quartile by logistic regression analysis

intake. However, intake of antioxidant vitamins, such as carotene, vitamin C, and vitamin E was not associated with the risk of stroke.

Intake of vegetables was negatively associated with the risk of stroke by multivariable-adjusted regression analysis after adjusting for age, sex, BMI, and family history of stroke (Table

Table 3. Association of food intake with the risk of stroke by multivariate regression analysis (odds ratios and 95% confidence interval)[1)]

(servings/week)	Quartile of nutrients intake				P for trend[2)]
	1	2	3	4	
Grain					
No. of case/control	7/17	20/18	22/17	21/17	
Intake cutoff	≤ 12.82	12.82 < to ≤ 17.95	17.95 < to ≤ 23.21	> 23.21	0.164
OR (95% CI)	1.00	1.110 (0.298-2.138)	2.709 (0.792-4.268)	2.183 (0.455-4.458)	
Fruit					
No. of case/controls	15/17	14/18	27/17	14/17	
Intake cutoff	≤ 2.59	2.59 < to ≤ 5.20	5.20 < to ≤ 11.00	> 11.00	0.850
OR (95% CI)	1.00	0.445 (0.152-1.305)	0.936 (0.351-2.498)	0.605 (0.197-1.852)	
Seafood					
No. of case/control	26/18	13/19	19/17	14/18	
Intake cutoff	≤ 2.80	2.80 < to ≤ 5.58	5.58 < to ≤ 12.04	> 12.04	0.234
OR (95% CI)	1.00	0.370 (0.103-1.329)	0.921 (0.311-2.731)	0.460 (0.139-1.518)	
Fish					
No. of case/control	25/17	15/18	18/18	11/16	
Intake cutoff	≤ 1.21	1.21 < to ≤ 2.66	2.66 < to ≤ 6.00	> 6.00	0.161
OR (95% CI)	1.00	0.265 (0.085-0.830)*	0.453 (0.158-1.295)	0.358 (0.116-1.104)	
Vegetable					
No. of case/control	29/17	20/18	13/17	7/17	
Intake cutoff	≤ 19.81	19.81 < to ≤ 30.31	30.31 < to ≤ 42.99	> 42.99	0.043
OR (95% CI)	1.00	1.200 (0.378-3.808)	0.687 (0.606-0.875)*	0.311 (0.100-0.963)*	
Milk					
No. of case/control	24/17	15/18	19/18	11/16	
Intake cutoff	≤ 0.10	0.10 < to ≤ 1.12	1.12 < to ≤ 2.95	> 2.95	0.119
OR (95% CI)	1.00	0.714 (0.253-2.011)	0.637 (0.251-1.682)	0.004 (0.000-27.278)	
Meat					
No. of case/control	12/17	16/18	17/17	24/17	
Intake cutoff	≤ 2.44	2.44 < to ≤ 4.46	4.46 < to ≤ 7.64	> 7.64	0.188
OR (95% CI)	1.00	1.090 (0.336-3.528)	1.361 (0.409-4.524)	1.967 (0.622-6.215)	

[1)] OR and 95% CI were analyzed by logistic regression. OR for food intake was adjusted for age, sex, BMI, energy, and family history of stroke.
[2)] Estimates of p values for a linear trend were based on linear scores derived from the medians of quartile of nutrient intake among controls.
* $P < 0.05$ from the first quartile by logistic regression analysis

3). The trend was not significant, but stroke risk was reduced in the second quartile of fish intake. There was no association between intake of grain, fruits, seafood, milk and meat, and the risk of stroke.

Discussion

Consumption of vegetables and B complex vitamins, such as B_1, B_2, B_6, niacin, and folate was associated with reduced risk of stroke after adjusting for BMI, sex, age, energy intake, and family history of stroke. However, risk of stroke was not related to the intake of fruits and antioxidant vitamins. Compared to subjects who ate less than four vegetable servings per day, those who ate four to six servings per day exhibited a 32% reduction in the risk of stroke, and those who ate more than six servings per day exhibited a reduction of 69%. The present study adds to the growing evidence that increased vegetable consumption is protective against stroke [5-7,18-19], and provides support for recommendations encouraging the public to consume more than four servings of vegetables per day.

The potential protective effect of vegetables on stroke is thought to be mediated through reductions in homocysteine concentration. Elevated homocysteine concentration is considered a risk factor for arterial endothelial dysfunction [21]. Plasma homocysteine is very responsive to intervention with B-vitamins required for its metabolism: folate, and to a lesser extent, vitamin B_6, and riboflavin [8,12]. Previous studies showed that intake of folate between 300 μg and 821 μg reduced the risk of stroke [17-19,21-22], and the present study also observed a 90% stroke risk reduction in subjects with daily folate intake of more than 412 μg. In addition, intakes of vitamin B_6, riboflavin and niacin were negatively associated with the risk of stroke in the present study. There is growing evidence that niacin inhibits vascular inflammation by decreasing endothelial reactive oxygen species production and subsequent LDL oxidation and inflammatory cytokine production, key events involved in atherogenesis [23]. Another B vitamin, vitamin B_{12} may also protect against stroke by mediating homocysteine metabolism, but unfortunately our database did not contain vitamin B_{12} content of foods.

Vegetables are also rich sources of potassium and calcium, which have been shown to lower blood pressure. Since high blood pressure is the major cause of stroke, the effects of potassium and calcium on blood pressure may contribute to the reduced risk of stroke with an increased vegetable intake [24] Higher dietary calcium and potassium intake are inversely correlated with the risk of stroke or stroke mortality [25-26], and the Systolic Hypertension in the Elderly Study indicated that low serum potassium was associated with increased stroke incidence [27]. Randomized controlled trials have shown fruit and vegetable consumption to significantly lower systolic and diastolic blood pressure [28-29], and thus possibly preventing stroke. The present study also showed a negative association between intake of calcium and potassium and stroke risk.

Other mechanistic effects of vegetable consumption on stroke risk may be due to antioxidant vitamins, such as vitamin C, vitamin E, and β-carotene. In the Iowa Women's Health Study [11] and the Rotterdam Study [30], antioxidants were shown to prevent stroke possibly by reducing lipid oxidation of LDL cholesterol [9-10]. However, prospective studies of nurses in the United States [20] and the Netherlands [12] observed a non-significant association between the risk of stroke and intake of vitamin E, and between risk of stroke and serum concentration of vitamin E [13]. An intervention study on the intake of vitamin C, vitamin E, and carotenoids failed to show any beneficial effect on stroke incidence or mortality [14]. The present study showed that intake of vitamin C, vitamin E, and carotene was not associated with the risk of stroke. Although these observational studies produced inconsistent results, it does not mean that there is no association between antioxidants and stroke. The results may reflect the fact that the combination of photochemicals contained in vegetables may have a greater cumulative effect than a single antioxidant.

The lack of an association between intake of fruits and the risk of stroke is difficult to explain. In recent analyses from the Life Span Study cohort [6], Nurses' Health Study [5] and the Health Professionals' follow-up study [7], fruit intake was associated with a reduction in the risk of stroke. Meta-analyses of nine independent cohorts reported that the average intake of fruits was two to four servings per day, and that the risk of stroke was reduced for those who ate at least three to five servings of fruit per day [4]. However, in our study, fruit intake was low in general, with an average daily intake of one serving. Sex, age, geographical origin, collection method for dietary information, subtypes of stroke, and cutoff-points of nutrient intake may influence the conclusions of various studies.

Previous studies of dietary fat intake and stroke have produced mixed results. The Northern Manhattan Study reported that increased daily total fat intake, especially above 65 g, significantly increased risk of stroke [31], but a number of prospective cohort studies performed in Japanese samples showed that higher intake of fat (median 47 g daily) was associated with decreased stroke risk [32-34], suggesting that the very lowest levels of fat intake are associated with a higher stroke risk. The present study supported that a higher intake of fat reduced the risk of stroke in a cohort with lower levels of fat intake. The average daily intake of total fat in this study was 51 g, lower than 65-70 g that the United States Department of Health guidelines recommend for adults [35].

Several previous studies reported a significant inverse association between fish intake and risk of total stroke, particularly ischemic stroke [36-37]. Possible mechanisms for protection against stroke by fish intake include inhibition of platelet aggregation, lowered blood viscosity, suppressed formation of leukotrienes, and reduction of plasma fibrinogen and blood pressure [38]. In the present study, the average intake of fish was 3.5 servings per week, and although there was no significant trend, stroke risk was significantly reduced in the second quartile of fish intake (1.2-2.7 servings per week). Our previous study showed that the average intake of n-3 fatty acids among Korean adults was 1.2 g/d [39], lower than in Eskimos but higher than American and European samples. Additionally, we found that erythrocyte n-3 fatty acids could protect against hemorrhagic stroke and ischemic stroke, particularly in the case of small-artery occlusion [40].

Limitations of the present study include the questionnaire used for baseline dietary assessment. The food catalog included in the questionnaire was limited, and may not have captured the total intake of nutrients and food groups among our participants, which may have caused underreporting of certain food categories. Our findings do not demonstrate causality since the observed relationships may be due to residual confounding from other factors associated with stroke risk, such as differences in socioeconomic status not accounted for by adjustment for clinical and environmental risk factors. In addition, the numbers of subjects included in this study was small, and the generalizability of the present data to other populations is unknown.

In conclusion, our observational study suggests that intake of fat and vegetables, rich sources of vitamin B complex, calcium, and potassium may protect against stroke. Larger clinical trials are necessary to confirm the causality between vegetable intake and risk of stroke, and to clarify the mechanisms through which a high intake of vegetables may protect against stroke.

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