Dietary Intake of Energy and Nutrients from Breakfast and Risk of Stroke in The Japanese Population:

The Circulatory Risk in Communities Study (CIRCS)

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Aims: The frequency of breakfast intake has been reported to be inversely associated with the risk of cardiovascular events; however, it is uncertain what the impact of the energy and nutrient intakes from breakfast are. We assessed the association between these intakes from breakfast and the risk of stroke prospectively.

Methods: In a baseline survey of four Japanese communities between 1981 and 1990, we enrolled 3 248 residents (1 662 men and 1 586 women) aged 40–59 years who were free from stroke and heart disease and who responded to the 24-hour dietary recall survey. We assessed the dietary intake at breakfast, lunch, dinner, and other times separately.

Results: During the median 25-year follow-up, 230 individuals (147 men and 83 women) developed stroke. After adjustment for age, community, other dietary intakes, and lifestyle and physiological factors, the multivariable-adjusted hazard ratios (95% confidence intervals) of intracerebral hemorrhage for the highest versus lowest quartiles of energy intake from breakfast were 0.38 (0.15–0.99) in men and 1.36 (0.36–5.10) in women. For the major nutrients, a higher saturated or monounsaturated fat intake at breakfast was associated with a reduced risk of intracerebral hemorrhage in men, and remained statistically significant after further adjustment for intake of other major nutrients from breakfast.

Conclusions: A higher intake of energy from breakfast, primarily saturated or monounsaturated fat, was associated with a reduced risk of intracerebral hemorrhage in Japanese men.

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Introduction

Breakfast is being recognized as an important meal for cardiometabolic health. In several recent studies, the eating of breakfast was associated with a lower risk of coronary heart disease[1], cerebral hemor-

rhage[2], and type 2 diabetes[3]. However, it is uncertain what the appropriate intake of energy and nutrients from breakfast in the prevention of cardiometabolic disease are.

The balance between energy in and energy out, that is, the calories obtained through eating and drinking and the calories burned through basal metabolism and physical activity, is important to maintain body weight and a healthy metabolism. Therefore, the national guidelines for dietary reference intakes recommend energy requirement values based on the energy expenditure per day[4-6]. In addition, they suggest the Recommended Dietary Allowance or the dietary goal for specific nutrients to prevent cardiometabolic disease[4, 5]. However, these values are daily quantities and proportions, and no guidelines have addressed whether it is more important to consume energy and dietary components at a specific meal for good health.

To the best of our knowledge, no study has investigated the association between the dietary intake of energy and nutrients from breakfast and the risk of cardiovascular disease. We aimed to use a long-term prospective cohort study of middle-aged Japanese men and women to examine whether the dietary intake of energy, fat, protein, and carbohydrate from breakfast was associated with the risk of the incidence of stroke.

Methods

Study Population

The surveyed population included residents from four communities: Ikawa (a rural community in Akita Prefecture in northeastern Japan), Minami-Takayasu (a suburb in Osaka Prefecture in mid-western Japan), Noichi (a rural community in Kochi Prefecture in western Japan), and Kyowa town (a rural community in Ibaraki Prefecture in mid-eastern Japan), who participated in a cardiovascular risk survey. The participants of the dietary survey were approximately 10% of the participants chosen as systematic samples in the annual cardiovascular risk surveys, and mostly participated in the dietary survey every 4 to 5 years. The present surveys were conducted from 1981 to 1990, and 3 289 participants aged 40–59 years responded to the dietary survey data using 24-hour dietary recall. For participants responding twice or more to the dietary survey during the baseline period, the initial survey data were used. After the exclusion of 41 participants with a history of stroke and/or coronary heart disease from the baseline survey, 3 248 individuals (1 662 men and 1 586 women) were included. We obtained informed consents for the existing data from representatives in communities, but not from each research participant since the current study is the secondary use of existing data obtained for public health practice on cardiovascular disease prevention in local communities. The ethics committees of the Osaka Center for Cancer and Cardiovascular Disease Prevention and of Osaka University approved this study.

Assessment of Energy and Energy-Product Nutrient Intake

The details of the dietary survey protocol are reported elsewhere[7]. Briefly, we adopted the 24-hour dietary recall method to collect the dietary data. Excluded from the dietary survey were persons who had attended special events such as a festival or celebration on the day prior to the survey. The participants were interviewed by trained dietitians or nutritionists about what they had eaten for breakfast, lunch, dinner, and others during the 24 hours before the examination. Actual-sized food models, pictures of food materials and dishes, and/or real foods and dishes were used during the interview to help the recall. The interview took approximately 30 minutes per person.

The intake of energy and energy-product nutrients (protein, fat, and carbohydrate) from each meal (breakfast, lunch, dinner, and other) were calculated based on the Standard Tables of Food Composition in Japan, 2015 (7th revised edition)[8]. The original data for nutrients were encoded in the 4th edition of the food composition table, published in 1982. We calculated the energy and nutrient intake based on the 7th edition (with translation) because the analysis method used in the later edition provided more accurate results. The energy intake at breakfast was calculated for the evaluation of the quantity of the meal, and persons who skipped breakfast were assigned a zero. To evaluate the dietary components, the intake of protein, fat, and carbohydrate were assessed, and the intake of saturated fatty acids and mono- and polyunsaturated fatty acids were also calculated.

We evaluated the reliability of the dietary assessment among 133 participants (102 men and 31 women) who responded to two surveys using the 24-hour dietary recall, 1 year apart. Spearman's correlation coefficient (95% CI) of energy intake at breakfast was 0.54 (0.39–0.68) in men, and 0.36 (0.01–0.63) in women. Nutrient intake at breakfast had fair reliability in men but not in women: Spearman's rank correlation coefficients in men were 0.45 for protein, 0.38 for fat, 0.66 for carbohydrate, 0.41 for saturated fat, 0.31 for monounsaturated fat, and 0.49 for polyunsaturated fat; the corresponding values in women were 0.36 for protein, −0.16 for fat, 0.60 of carbohydrate, –0.13 for saturated fat, −0.23 for monounsaturated fat, and –0.01 for polyunsaturated fat.

Baseline Examination

The details of the Circulatory Risk in Communities Study (CIRCS) baseline examinations have been described in a previous report[9, 10]. Trained physicians used standard mercury sphygmomanometers and standardized epidemiological methods to measure blood pressure levels. Height in stocking feet and weight in light clothing was measured. Body mass index (BMI) was calculated as weight (kg) divided by the square of height (m^2). To ascertain the number of cigarettes smoked per day, usual weekly alcohol intake expressed as the unit go (a Japanese traditional unit of volume corresponding to 23 g of ethanol), and medications for hypertension, an interview was conducted. Diabetes was defined as a serum glucose level ≥ 126 mg/dL in the fasting or ≥ 200 mg/dL in the non-fasting state, or as use of medication for diabetes.

Follow-Up and Ascertainment of Stroke Endpoint

We followed the participants until the end of 2007 for Noichi, 2011 for Kyowa, 2012 for Osaka, and 2013 for Akita. The details of endpoint determination have been described elsewhere[11]. Death certificates, national insurance claims, reports from local physicians, reports from public health nurses and health volunteers, and an annual cardiovascular risk survey were used to ascertain the endpoint of stroke. To confirm the diagnosis, all the patients that were alive were telephoned, were visited, or were invited to take part in risk factor surveys, or a medical history was obtained from their families. In addition, the medical records in the local clinics and hospitals were reviewed. In case of death with cause-specific mortality from stroke (ICD-10 classification codes: I60-I61and I63-I64), histories were obtained from family members and/or attending physicians and the medical records were reviewed.

The criteria for stroke included a focal neurological disorder with rapid onset that persisted for at least 24 hours or until death[11]. The determination of stroke subtypes was performed primarily using computer tomography (CT) and magnetic resonance imaging (MRI) findings[12], which were available for 91% (210/230) of stroke cases. Strokes diagnosed clinically without any lesion on CT/MRI were classified based on the clinical criteria mentioned here[11, 13]. We used a modified criteria for coronary heart disease according to the World Health Organization Expert Committee[14] as described previously[9, 10]. A panel of two to four physicians participating in this study who were blinded to each individual's risk factor data made the final diagnosis of stroke and/or coronary heart disease.

Statistical Analyses

Analysis of covariance was used to test for differences in terms of baseline characteristics and the intake of energy and nutrients at breakfast as sex-specific, age-adjusted mean values.

We calculated person-years of follow-up as the duration from the date of the baseline survey to the date when the participants developed stroke or coronary heart disease, when they moved out of the community, or the date of death, whichever came first. The Cox's proportional hazards regression model was used calculate the age- and community-adjusted, and multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for incidence of stroke. Reference groups were those within the lowest quartile of energy intake at breakfast. The adjustment variables were age (years), community, and dietary factors. We adjusted for energy intake from other meals (lunch, dinner, and other) in the analysis for energy intake from breakfast. We adjusted for energy and each nutrient intakes from other meals, and also protein, saturated fat, and carbohydrate intakes from breakfast mutually in the analysis for major nutrients from breakfast. Because of the high correlations between saturated and monounsaturated fat (Spearman's correlation coefficient = 0.88) and between monounsaturated and polyunsaturated fat (Spearman's correlation coefficient = 0.80), these fats were not mutually adjusted. Since one incident case only of intracerebral hemorrhage was observed in the highest quartile of fat intake from breakfast, the analysis for fat intake from breakfast was not presented. Finally, the further adjustment variables included lifestyle factors [smoking status (never, former, current 1–20 or >20 cigarettes/day) and drinking status (never, former, current <46 or ≥ 46 g ethanol/day)] and, then, physiological factors [BMI (kg/m^2, sex-specific quartile category), serum triglycerides (mmol/L, sex-specific quartile category), total cholesterol (mmol/L), systolic blood pressure (mmHg), use of antihypertensive medication (yes or no), and diabetes (yes or no)]. During the examination of the associations between nutrient intakes from breakfast and risk of intracerebral hemorrhage, physiological factors were not adjusted because physiological factors such as blood lipids could be intermediate factors in the associations. Two-sided P values less than 0.05 were considered to be statistically significant. SAS version 9.4 (SAS Institute Inc., Cary, NC, USA) was used to perform all the statistical analyses.

Results

During the median 24.6-year follow-up (interquartile range: 20.1, 27.2), 230 persons (147 men and

83 women) developed stroke. Persons who moved out of the communities or died during follow-up numbered 163 (5.0%) and 793 (24.4%), respectively and were censored at the time of these events.

Table 1 lists sex-specific, age-adjusted mean values and the proportions of cardiovascular risk factors and dietary intake at baseline according to the quartiles of energy intake from breakfast. The numbers of participants who skipped breakfast were 20 (1.2%) men and 18 (1.1%) women. Compared with the participants with the lowest quartile of dietary energy intake at breakfast, those consuming more energy had lower age-adjusted mean values for diastolic blood pressure and serum total cholesterol in both sexes and included a lower proportion of current male smokers. In both sexes, breakfast energy intake was positively associated with total daily energy intake, and also with total daily and breakfast intakes of protein, fat, and carbohydrate intake.

Breakfast energy intake was inversely associated with an age- and community- adjusted risk of intracerebral hemorrhage in men; however, such a trend was not observed in women (**Table 2**). After further adjustment for dietary factors, the multivariable-adjusted HRs (95% CIs) of intracerebral hemorrhage for the highest versus lowest quartiles of energy intake from breakfast were 0.44 (0.18–1.08; *P*-trend = 0.08) in men and 1.60 (0.44–5.78; *P*-trend = 0.29) in women. The associations after further adjustment for lifestyle and also physiological factors were in the same direction: the multivariable-adjusted HRs were 0.38 (0.15–0.99; *P*-trend = 0.04) in men and 1.36 (0.36–5.10; *P*-trend = 0.45) in women. There was no significant association between breakfast energy intake and risk of total stroke, subarachnoid hemorrhage, or ischemic stroke in either sex.

In the analysis for major nutrients from breakfast, we evaluated the associations of intakes of protein, saturated, monounsaturated, and polyunsaturated fats, and carbohydrate from breakfast with risk of intracerebral hemorrhage in men (**Table 3**). After adjustment for age, community, dietary factors and lifestyle factors, the multivariable-adjusted HRs (95% CIs) of intracerebral hemorrhage for the highest versus the lowest quartiles of each nutrient intake from breakfast were 1.12 (0.35–3.62; *P*-trend = 0.65) for protein, 0.22 (0.06–0.79; *P*-trend = 0.008) for saturated fat, 0.21 (0.05–0.86; *P*-trend = 0.06) for monounsaturated fat, 1.39 (0.47–4.13; *P*-trend = 0.43) for polyunsaturated fat, and 0.59 (0.22–1.58; *P*-trend = 0.16) for carbohydrate. The total daily saturated or monounsaturated fat intake was not associated with risk of intracerebral hemorrhage in men (data not shown).

Discussion

We found that energy intake from breakfast was inversely associated with risk of intracerebral hemorrhage in middle-aged men in this community-based, long-term cohort study. For the nutritional components of breakfast, we observed an inverse association between higher fat (primarily saturated and monounsaturated fat) intake and risk of intracerebral hemorrhage.

Since 1975, the proportion of persons who skip breakfast has increased in Japan[15]. Skipping breakfast has been associated with an increased risk of incident coronary heart disease in US men[1] as well as an increased risk of total cardiovascular disease and stroke, more specifically intracerebral hemorrhage, in Japanese[2]. Our study used the qualitative nutritional data to extend the evidence from previous studies. In the present study, we found no association of dietary intake of energy and nutrients from breakfast with the risk of stroke in women. The reasons for the lack of association may be two-fold. One is the lower reliability of breakfast energy for women compared with men and the low reliability of breakfast intake of fat (saturated, monounsaturated and polyunsaturated fat). The other is the half smaller number of stroke cases for women compared with men, resulting in the low statistical power to detect the association.

In the present study, the median quantities of major nutrient intakes from breakfast were 14.6 g (16.1 g in men and 13.1 g in women) for protein, 8.2 g (8.3 g and 8.2 g, respectively) for fat, 1.9 g (1.9 g in both sexes) for saturate fat, 2.4 g (2.4 g in both sexes) for monounsaturated fat, 2.1 g (2.2 g and 2.0 g, respectively) for polyunsaturated fat, and 69.8 g (85.0 g and 59.5 g, respectively) for carbohydrate, which characterized the typical Japanese breakfast as being extremely low-fat. The traditional Japanese breakfast pattern was characterized by mainly rice, miso soup, and vegetable pickles, while the westernized breakfast pattern with high fat was characterized by bread or rice, eggs, milk/milk products, and meats.

Our finding of an inverse association between saturated fat intake from breakfast and the risk of intracerebral hemorrhage is in line with the results from previous cohort studies in US women[16] and Japanese men and women[17-19]. In these studies, a low dietary intake of saturated fat was associated with an increased risk of intracerebral hemorrhage. The intake of saturated fat and animal protein among the Japanese and US populations were largely different, and there was hardly an overlap in their distributions[17].

Regarding the pathophysiologic mechanism of intracerebral hemorrhage, we consider the morning

Table 1. Baseline characteristics of participants according to the quartiles of energy intake from breakfast

	Q1 (low)	Q2	Q3	Q4 (high)	P for difference
Men					
Number at risk	415	416	416	415	
Range of energy intake from breakfast, kcal	0–381	382–518	518–657	657–1,729	
Age, years	48.4	49.3	49.1	49.0	0.12
Body mass index, kg/m^2	23.3	23.2	23.5	23.7	0.02
Systolic blood pressure, mmHg	136	133	135	132	0.01
Diastolic blood pressure, mmHg	84	83	83	82	0.01
Antihypertensive medication use, %	13	10	11	11	0.51
Serum total cholesterol, mmol/L	4.99	4.89	4.77	4.86	0.004
Serum triglycerides, mmol/L	2.00	1.88	1.81	1.77	0.10
Diabetes, %	7	5	6	7	0.43
Current smoker, %	64	60	58	53	0.01
Current drinker, %	73	74	73	73	0.99
Daily intakes					
Energy, kcal/day	2023	2201	2465	2932	<0.001
Protein, g/day (% of energy)	68 (14)	74 (14)	80 (13)	93 (13)	<0.001 (<0.001)
Fat, g/day (% of energy)	44 (19)	46 (19)	48 (18)	58 (18)	<0.001 (0.003)
Carbohydrate, g/day (% of energy)	284 (57)	315 (58)	364 (60)	444 (61)	<0.001 (<0.001)
Sodium, mg/day	3453	3819	3972	4672	<0.001
Intakes from breakfast					
Energy, kcal	276	448	584	821	<0.001
Protein, g (% of energy)	9 (12)	15 (14)	19 (13)	26 (13)	<0.001 (<0.001)
Fat, g (% of energy)	5 (16)	8 (17)	11 (17)	16 (18)	<0.001 (0.09)
Saturated fat, g (% of energy)	2 (5)	2 (5)	3 (5)	4 (5)	<0.001 (0.04)
Monounsaturated fat, g (% of energy)	2 (5)	3 (5)	3 (5)	5 (6)	<0.001 (0.21)
Polyunsaturated fat, g (% of energy)	1 (4)	2 (5)	3 (4)	4 (5)	<0.001 (<0.001)
Carbohydrate, g (% of energy)	48 (66)	75 (67)	100 (68)	137 (67)	<0.001 (0.34)
Sodium, mg	584	976	1100	1475	<0.001
Women					
Number at risk	396	397	397	396	
Range of energy intake from breakfast, kcal	0–297	297–388	388–493	582–1,465	
Age, years	49.0	49.4	49.7	49.0	0.27
Body mass index, kg/m^2	24.0	23.9	23.8	23.8	0.90
Systolic blood pressure, mmHg	133	132	133	131	0.57
Diastolic blood pressure, mmHg	81	80	80	78	0.01
Antihypertensive medication use, %	11	14	14	8	0.06
Serum total cholesterol, mmol/L	5.26	5.13	5.17	5	<0.001
Serum triglycerides, mmol/L	1.46	1.48	1.51	1.53	0.77
Diabetes, %	2	3	2	2	0.78
Current smoker, %	5	5	4	5	0.92
Current drinker, %	9	7	8	7	0.61
Daily intakes					
Energy, kcal/day	1484	1659	1787	2168	<0.001
Protein, g/day (% of energy)	53 (14)	59 (14)	65 (15)	76 (14)	<0.001 (0.11)
Fat, g/day (% of energy)	36 (22)	41 (22)	46 (23)	55 (23)	<0.001 (0.03)
Carbohydrate, g/day (% of energy)	229 (62)	257 (62)	273 (61)	334 (62)	<0.001 (0.14)
Sodium, mg/day	2956	3219	3422	4217	<0.001
Intakes from breakfast					
Energy, kcal	224	341	436	622	<0.001
Protein, g (% of energy)	7 (13)	12 (14)	16 (15)	23 (15)	<0.001 (<0.001)
Fat, g (% of energy)	4 (15)	7 (19)	11 (23)	17 (24)	<0.001 (<0.001)
Saturated fat, g (% of energy)	1 (5)	2 (6)	3 (6)	4 (6)	<0.001 (<0.001)
Monounsaturated fat, g (% of energy)	1 (5)	2 (6)	4 (8)	6 (8)	<0.001 (<0.001)
Polyunsaturated fat, g (% of energy)	1 (4)	2 (5)	3 (6)	5 (6)	<0.001 (<0.001)
Carbohydrate, g (% of energy)	39 (67)	56 (66)	66 (60)	93 (60)	<0.001 (<0.001)
Sodium, mg	530	780	936	1353	<0.001

Value were presented as means or proportions, adjusted for age.
% of energy was proportion of breakfast energy intake using the following energy-conversion values; protein 4 kcal/g, fat 9 kcal/g, and carbohydrate 4 kcal/g.

Table 2. Age- and multivariable-adjusted HRs (95%CIs) of stroke according to quartiles of energy intake from breakfast by sex

	Q1 (low)	Q2	Q3	Q4 (high)	*P*-trend
Men					
Median (range) intake, kcal	306 (0–381)	447 (382–518)	582 (518–657)	770 (657–1,729)	
Person-years	8726	9253	9439	9464	
Total stroke					
No of events	37	38	34	38	
Age- and community-adjusted HR	1.00	0.80 (0.50–1.25)	0.69 (0.43–1.10)	0.75 (0.47–1.18)	0.19
+ Dietary factors*	1.00	0.81 (0.52–1.29)	0.73 (0.46–1.18)	0.85 (0.53–1.37)	0.46
+ Lifestyle factors†	1.00	0.85 (0.54–1.34)	0.78 (0.49–1.27)	0.88 (0.54–1.43)	0.57
+ Physiological factors‡	1.00	0.90 (0.56–1.44)	0.73 (0.45–1.19)	0.92 (0.56–1.50)	0.56
Intracerebral hemorrhage					
No of events	15	13	12	8	
Age- and community-adjusted HR	1.00	0.66 (0.31–1.39)	0.59 (0.27–1.26)	0.38 (0.16–0.90)	0.03
+ Dietary factors*	1.00	0.68 (0.32–1.43)	0.64 (0.29–1.39)	0.44 (0.18–1.08)	0.08
+ Lifestyle factors†	1.00	0.71 (0.34–1.51)	0.69 (0.31–1.51)	0.43 (0.17–1.08)	0.08
+ Physiological factors‡	1.00	0.73 (0.34–1.58)	0.55 (0.24–1.23)	0.38 (0.15–0.99)	0.04
Subarachnoid hemorrhage					
No of events	5	1	2	6	
Age- and community-adjusted HR	1.00	0.16 (0.02–1.36)	0.28 (0.05–1.48)	0.83 (0.25–2.77)	0.99
+ Dietary factors*	1.00	0.16 (0.02–1.36)	0.29 (0.05–1.51)	0.85 (0.24–3.03)	0.97
+ Lifestyle factors†	1.00	0.14 (0.02–1.24)	0.25 (0.05–1.31)	0.84 (0.23–3.03)	0.98
+ Physiological factors‡	1.00	0.22 (0.02–1.99)	0.28 (0.05–1.60)	1.32 (0.33–5.28)	0.69
Ischemic stroke					
No of events	17	24	20	23	
Age- and community-adjusted HR	1.00	1.11 (0.59–2.07)	0.91 (0.47–1.74)	1.02 (0.54–1.92)	0.87
+ Dietary factors*	1.00	1.14 (0.61–2.13)	0.98 (0.51–1.89)	1.18 (0.61–2.28)	0.75
+ Lifestyle factors†	1.00	1.21 (0.65–2.28)	1.10 (0.57–2.14)	1.26 (0.65–2.44)	0.59
+ Physiological factors‡	1.00	1.35 (0.70–2.59)	1.11 (0.56–2.19)	1.40 (0.71–2.76)	0.48
Women					
Median (range) intake, kcal	245 (0–297)	342 (297–388)	433 (388–493)	582 (493–1,465)	
Person-years	9500	9183	9309	9422	
Total stroke					
No of events	17	22	19	25	
Age- and community-adjusted HR	1.00	1.28 (0.68–2.41)	1.02 (0.53–1.98)	1.36 (0.73–2.54)	0.48
+ Dietary factors*	1.00	1.26 (0.67–2.38)	1.00 (0.52–1.94)	1.26 (0.66–2.42)	0.66
+ Lifestyle factors†	1.00	1.25 (0.66–2.37)	0.93 (0.48–1.81)	1.26 (0.66–2.42)	0.70
+ Physiological factors‡	1.00	1.28 (0.67–2.44)	0.95 (0.49–1.85)	1.25 (0.65–2.41)	0.74
Intracerebral hemorrhage					
No of events	4	2	5	8	
Age- and community-adjusted HR	1.00	0.51 (0.09–2.80)	1.24 (0.33–4.68)	2.14 (0.63–7.33)	0.12
+ Dietary factors*	1.00	0.48 (0.09–2.65)	1.14 (0.30–4.33)	1.60 (0.44–5.78)	0.29
+ Lifestyle factors†	1.00	0.49 (0.09–2.71)	1.03 (0.26–3.99)	1.61 (0.45–5.84)	0.29
+ Physiological factors‡	1.00	0.50 (0.09–2.80)	1.13 (0.29–4.39)	1.36 (0.36–5.10)	0.45
Subarachnoid hemorrhage					
No of events	2	7	5	5	
Age- and community-adjusted HR	1.00	3.44 (0.71–16.6)	2.39 (0.46–12.4)	2.26 (0.43–11.8)	0.58
+ Dietary factors*	1.00	3.41 (0.70–16.5)	2.36 (0.45–12.3)	2.18 (0.40–11.9)	0.62
+ Lifestyle factors†	1.00	3.31 (0.68–16.0)	2.37 (0.45–12.4)	2.20 (0.41–11.9)	0.60
+ Physiological factors‡	1.00	3.58 (0.72–17.6)	2.44 (0.47–12.7)	2.27 (0.41–12.5)	0.56
Ischemic stroke					
No of events	11	13	8	11	
Age- and community-adjusted HR	1.00	1.15 (0.51–2.58)	0.62 (0.25–1.56)	0.87 (0.38–2.04)	0.47
+ Dietary factors*	1.00	1.17 (0.52–2.63)	0.65 (0.26–1.64)	0.99 (0.41–2.38)	0.65
+ Lifestyle factors†	1.00	1.17 (0.52–2.62)	0.60 (0.24–1.53)	0.97 (0.40–2.35)	0.60
+ Physiological factors‡	1.00	1.15 (0.50–2.61)	0.59 (0.23–1.50)	1.04 (0.43–2.53)	0.66

The result of the unclassified type of stroke was not shown because of the small number of cases (1 for men and 2 for women).
*Further adjusted for energy intake from other meals. †Further adjusted for smoking and drinking status. ‡Further adjusted for body mass index, serum triglycerides, serum total cholesterol, systolic blood pressure, antihypertensive medication use, and diabetes.

Table 3. Multivariable-adjusted HRs (95% CIs) of intracerebral hemorrhage according to quartiles of protein, saturated, monounsaturated and polyunsaturated fat, and carbohydrate intakes from breakfast in men

	Q1 (low)	Q2	Q3	Q4 (high)	P-trend
Protein					
Median (range) intakes, g	8.0 (0.0–11.1)	13.6 (11.1–16.1)	18.6 (16.1–22.3)	27.4 (22.4–71.5)	
Person-years	8812	9492	9240	9338	
No of events	15	13	13	7	
Age- and community-adjusted HR	1.00	0.67 (0.32–1.42)	0.70 (0.33–1.49)	0.35 (0.14–0.88)	0.03
+ Dietary factors*	1.00	0.93 (0.42–2.08)	1.31 (0.54–3.18)	1.04 (0.32–3.38)	0.73
+ Lifestyle factors†	1.00	1.03 (0.46–2.31)	1.41 (0.57–3.47)	1.12 (0.35–3.62)	0.65
Saturated fat					
Median (range) intakes, g	0.5 (0.0–0.8)	1.2 (0.8–1.9)	2.5 (1.9–4.0)	6.0 (4.0–22.1)	
Person-years	9181	9149	9266	9285	
No of events	17	19	8	4	
Age- and community-adjusted HR	1.00	1.10 (0.57–2.12)	0.48 (0.21–1.12)	0.26 (0.09–0.77)	0.003
+ Dietary factors*	1.00	1.09 (0.54–2.22)	0.44 (0.17–1.17)	0.24 (0.07–0.83)	0.01
+ Lifestyle factors†	1.00	1.19 (0.58–2.43)	0.44 (0.17–1.18)	0.22 (0.06–0.79)	0.008
Monounsaturated fat					
Median (range) intakes, g	0.4 (0.0–0.9)	1.7 (0.9–2.4)	3.2 (2.4–4.5)	6.4 (4.5–19.6)	
Person-years	9166	9229	9069	9417	
No of events	15	18	12	3	
Age- and community-adjusted HR	1.00	1.15 (0.58–2.29)	0.79 (0.37–1.69)	0.21 (0.06–0.73)	0.01
+ Dietary factors*	1.00	1.16 (0.56–2.41)	0.80 (0.34–1.90)	0.22 (0.05–0.89)	0.05
+ Lifestyle factors†	1.00	1.20 (0.58–2.50)	0.84 (0.35–2.00)	0.21 (0.05–0.86)	0.06
Polyunsaturated fat					
Median (range) intakes, g	0.7 (0.0–1.3)	1.7 (1.3–2.2)	2.8 (2.2–3.6)	5.0 (3.6–18.5)	
Person-years	9173	9168	9104	9437	
No of events	11	14	14	9	
Age- and community-adjusted HR	1.00	1.19 (0.54–2.62)	1.19 (0.54–2.63)	0.76 (0.31–1.85)	0.59
+ Dietary factors*	1.00	1.43 (0.62–3.26)	1.68 (0.69–4.07)	1.31 (0.45–3.83)	0.52
+ Lifestyle factors†	1.00	1.44 (0.63–3.29)	1.83 (0.74–4.50)	1.39 (0.47–4.13)	0.43
Carbohydrate					
Median (range) intakes, g	48.5 (0.0–62.7)	73.4 (62.7–85.0)	98.6 (85.1–112.9)	134.7 (113.1–297.9)	
Person-years	8630	9287	9418	9547	
No of events	14	14	8	12	
Age- and community-adjusted HR	1.00	0.73 (0.34–1.53)	0.36 (0.15–0.87)	0.55 (0.25–1.22)	0.07
+ Dietary factors*	1.00	0.72 (0.34–1.55)	0.39 (0.16–0.99)	0.63 (0.24–1.65)	0.18
+ Lifestyle factors†	1.00	0.74 (0.34–1.61)	0.42 (0.16–1.07)	0.59 (0.22–1.58)	0.16

*Further adjusted for energy and each nutrient intakes from other meals, and also protein, saturated fat and carbohydrate intakes from breakfast mutually.
†Further adjusted for smoking and drinking status.

elevation of blood pressure to be part of the association between higher energy intake from breakfast and a decreased risk of intracerebral hemorrhage because our finding is consistent with that of a previous study in which blood pressure elevation in the morning was associated with an increased risk of intracerebral hemorrhage; however, it was not associated with total and ischemic strokes[20]. Typical patterns of blood pressure in most persons show that blood pressure increases rapidly within an hour before morning awakening and peaks at 2 to 3 hours after awakening[21], and plasma cortisol levels also peak prior to or upon awakening[22]. Because breakfast eaters had lower cortisol levels compared to those who skipped breakfast[23], persons ingesting a higher energy intake may have lower cortisol levels and a suppressed peak of morning blood pressure surge, which may lead to a lower risk of intracerebral hemorrhage. Potential mediators such as systolic blood pressure at daytime, as well as BMI, blood lipids, and diabetes were unlikely to affect our find-

ings because the adjustment for these factors did not alter the HRs substantially.

The major strengths of this study include its prospective design and the involvement of a large cohort from a general population over a long follow-up duration. In addition, we were able to evaluate the energy and nutrient intake per meal by 24-hour dietary recall. However, generally, this method has an intrinsic disadvantage of low reliability because it evaluates the diet for 1 day only. Therefore, we assessed the reliability of the estimated values of energy intake among subsamples and confirmed them fairly reliable for ranking individual energy and nutrient intakes in men.

We identified several limitations. First, we used data from a single 24-hour recall period for energy and nutrient intakes, and no consideration was given to any subsequent change in diet. The reliability for energy intake, examined 1 year apart, was good in men and was moderate in women and was also moderate for major nutrients in men, although the Spearman's correlation coefficients examined one year apart in our study were slightly lower than those estimated from semi-quantitative food frequency questionnaires in established large cohort studies. The correlation coefficients were 0.54 for breakfast energy, 0.38 for breakfast fat, and 0.41 for breakfast saturated fat among men in the present study; in the Nurses' Health Study, 0.63 for total energy, 0.57 for fat, and 0.55 for saturated fat; and in the Health Professionals Follow-up Study, 0.65 for total energy, 0 .66 for fat, and 0.69 for saturated fat[24, 25]. Second, the participants of dietary survey (n=3 248, 65% and 8% current smoker in men and women, respectively) smoked less than the non-participants (n=6 967, 59% and 5%, respectively); however, blood pressure and serum lipid levels did not differ between them. Third, because of the relatively small number of incident cases of intracerebral hemorrhage in this study, the CIs of the HRs were large, although we observed the significant association of intakes of energy, saturated and monounsaturated fats from breakfast with risk of intracerebral hemorrhage. Fourth, it is possible that, because of other health behaviors and risk factors, individuals with low intakes of energy, saturated, and monounsaturated fats from breakfast were at a high risk of intracerebral hemorrhage. Although this likelihood was decreased by the multivariable adjustment for potential confounding variables, we cannot eliminate the impact of residual confounding or unmeasured variables such as the timing of meal and physical activity.

In conclusion, higher energy intake, primarily saturated or monounsaturated fat intake from breakfast, was associated with a lower risk of intracerebral hemorrhage in men.

The CIRCS Investigators

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Conflicts of Interest

The authors declare no conflict of interest.

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