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Plant foods and the risk of cerebrovascular diseases: a potential protection of fruit consumption

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Studies on the association between plant foods and cerebrovascular diseases have given contradictory results suggesting the existence of some effect-modifying factors. The present study determines whether the consumption of plant foods (i.e. fruits and berries, vegetables, and cereals) predicts a decreased cerebrovascular disease incidence in a population with low fruit and vegetable and high wholegrain intake. This cohort study on 3932 men and women was based on data from the Finnish Mobile Clinic Health Examination Survey, conducted in 1968–72. The participants were 40–74 years of age and free of cardiovascular diseases at baseline. Data on the plant food consumption were derived from a 1-year dietary history interview. During a 24-year follow-up 625 cases of cerebrovascular diseases occurred, leading to either hospitalisation or death. An inverse association was found between fruit consumption and the incidence of cerebrovascular diseases, ischaemic stroke and intracerebral haemorrhage. The adjusted relative risks (RR) between the highest and lowest quartiles of intake of any cerebrovascular disease, ischaemic stroke and intracerebral haemorrhage were 0·75 (95 % CI 0·59, 0·94), 0·73 (95 % CI 0·54, 1·00) and 0·47 (95 % CI 0·24, 0·92), respectively. These associations were primarily due to the consumption of citrus fruits and occurred only in men. Total consumption of vegetables or cereals was not associated with the cerebrovascular disease incidence. The consumption of cruciferous vegetables, however, predicted a reduced risk of cerebrovascular diseases (RR 0·79; 95 % CI 0·63, 0·99), ischaemic stroke (RR 0·67; 95 % CI 0·49, 0·92) and intracerebral haemorrhage (RR 0·49; 95 % CI 0·25, 0·98). In conclusion, the consumption of fruits, especially citrus, and cruciferous vegetables may protect against cerebrovascular diseases.

Plant foods: Cerebrovascular diseases: Ischaemic stroke: Intracerebral haemorrhage

It has been suggested that the consumption of plant foods such as fruits and berries, vegetables and cereals provides protection against cerebrovascular diseases. These foods are rich sources of fibre, K and antioxidant compounds, which through different mechanisms may have protective effects against stroke[1]. Although a recent meta-analysis suggested a reduced risk of stroke for those with an ample daily consumption of fruits or vegetables[2], the original cohort studies examining the prediction of fruit and vegetable consumption on the risk of stroke have given inconsistent results[3–13]. Studies linking wholegrain or bran consumption with the risk of cerebrovascular diseases are also inconclusive, with some suggesting a reduced risk[14,15] and others no association[4,5,16].

Since some of the risk factors of ischaemic stroke and haemorrhagic stroke differ, the possible effects of fruits and vegetables on the development of these diseases may also be different. Most cohort studies to date have considered either total stroke or ischaemic stroke as the sole outcome variable, and few have considered haemorrhagic strokes. The results from these studies are inconsistent, suggesting either an inverse association between fruit or vegetable intake and haemorrhagic stroke incidence[6,7] or no significant association[8,9]. It has been suggested that the intake of cereal fibre and total stroke or haemorrhagic stroke are inversely associated[4,17], but no studies on the consumption of different types of cereals and haemorrhagic stroke exist.

The inconsistency of the published results suggests that the possible protection may be either present only for some plant foods (or certain nutrients in them or their combination), or at specific levels of the plant food intake, or only in some subpopulations (for example, sex, age or lifestyle). For this reason we initiated the present study, which focuses on the prediction of plant food intake, including fruits and berries, vegetables and cereals, on the incidence of cerebrovascular diseases and its subgroups, ischaemic stroke and intracerebral haemorrhage, in subpopulations of a Finnish cohort with a low intake of fruits and vegetables and high intake of wholegrain cereals.

Methods

Subjects

The present study was based on the Finnish Mobile Clinic Health Examination Survey, carried out during 1968–72.

Abbreviations: DBP, diastolic blood pressure; ICD-8, International Classification of Diseases, eighth revision; SBP, systolic blood pressure.

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The survey included a dietary history interview of 10 054 men and women, aged 15 years and over. After excluding those under 40 or over 74 years of age and those suffering from cardiovascular diseases before baseline examination, the final cohort comprised 3932 men and women.

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki. Data on population samples held at the National Institute for Health and Welfare can be used on the basis of the law on Personal Data and the legislation applying to the National Institute for Health and Welfare.

Baseline examination

All the participants completed a questionnaire that was sent to their home, which was then checked at the baseline examination. The questionnaire yielded information on the respondent's occupation, previous and current diseases, use of medicines, lifestyle, i.e. leisure-time physical activity (high physical activity *v.* low physical activity) and smoking. Subjects were classified according to smoking status as never smokers, ex-smokers, smokers of cigars or pipe only, smokers of fewer than fifteen cigarettes per d, and smokers of fifteen cigarettes or more per d. Those who had never smoked and ex-smokers were combined to form a category of non-smokers. A health examination included measurement of height and weight, from which the BMI was calculated. A BMI of under 28 kg/m^2 was considered to represent normal weight and a BMI over 28 kg/m^2 overweight. Blood pressure was registered using the auscultatory method after a 5 min rest[18]. Four hypertension categories were formed on the basis of systolic blood pressure (SBP), diastolic blood pressure (DBP) and antihypertensive medication[19]. Individuals with SBP $\geq$ 170 mmHg and DPB $\geq$ 100 mmHg and individuals using antihypertensive medication were considered definitely hypertensive. Individuals with SBP $\geq$ 160 mmHg and DBP $\geq$ 95 mmHg but not defined as definitely hypertensive were considered to have mild hypertension, and those with SBP $<$ 140 mmHg and DBP $<$ 90 mmHg were considered normotensive. All individuals with intermediate values were considered to have borderline hypertension. The serum cholesterol level was determined with an autoanalyser modification of the Liebermann–Burchard reaction[20]. Known cases of diabetes were identified from information given by the participants and a modified glucose tolerance test was carried out to diagnose new diabetes cases at baseline[21,22].

Dietary assessment

At a baseline dietary history interview, the subjects were asked about their usual diet during the previous year[23]. The interview was carried out by trained staff, which consisted of personnel with an education in home economics or nutrition. A preformed questionnaire accompanied by food models was utilised to help in estimating of the amounts of food consumed. The questions were mostly open-ended, so subjects could also describe their diet freely and in detail. Subjects reported their food consumption on a daily, weekly or monthly basis. The ingredients of mixed foods were broken down into their components using a recipe file and the consumption of fruits and berries, vegetables, and cereals as well as subgroups of them, and separate food items were calculated per d. Energy intake was calculated based on the intake of protein, fat and available carbohydrate according to Finnish food composition tables[24].

Repeatability of the dietary history method was estimated after 4–8 months (short term) and 4–7 years (long term) by repeating the interview[23]. The intra-class correlation coefficients for short-term repeatability were 0·63 for total vegetables without potatoes (0·50 for cruciferous vegetables, 0·44 for legumes and 0·59 for root vegetables), 0·62 for cereals, 0·64 for fruits and 0·36 for berries. The corresponding coefficients for long-term repeatability were 0·47 for vegetables without potatoes (0·35 for cruciferous vegetables, 0·26 for legumes and 0·39 for root vegetables), 0·39 for cereals, 0·41 for fruits and 0·10 for berries.

Morbidity and mortality

Disease events leading to hospitalisation were identified by linking data from the Finnish Hospital Discharge Register from 1970–94 to the dietary data[25]. Information on mortality was based on death certificates obtained for all the deceased from Statistics Finland[22]. The primary diagnoses of hospital records and the principal causes of death were classified as cerebrovascular diseases using the three digit codes 344 or 430–438 of the International Classification of Diseases, eighth revision (ICD-8)[26]. The diagnoses were further classified as total strokes (ICD-8 codes 430–438, 344) including all acute strokes, subarachnoidal haemorrhages and other, undefined strokes; ischaemic stroke (ICD-8 codes 432–434) and intracerebral haemorrhage (ICD-8 code 431). During the 24-year follow-up 625 cases (334 in men and 291 in women) of cerebrovascular disease occurred, of which fifty-eight were intracerebral haemorrhages (ICD-8 code 431) and 335 were thrombotic or embolic occlusions in precerebral or cerebral arteries (ICD-8 codes 432–434), defined in the present study as ischaemic strokes. The rest of the 232 cases were other or undefined cerebrovascular diseases.

Statistical methods

The relative risks of cerebrovascular diseases between quartiles of different plant food intake (fruits and berries, vegetables, and cereals) were estimated using Cox's model[27]. The follow-up time was defined as the time from the baseline examination to the date of hospitalisation for cerebrovascular disease, death or the end of follow-up, whichever came first. Adjustments for variables that fulfilled the criteria for confounding factors[28] were made by including them in the models. Three main models were defined: (1) a model adjusted for age (continuous) and sex; (2) model 1 further adjusted for the non-dietary risk factors of BMI (continuous), smoking (non-smokers, current smokers), physical activity (high, low), serum cholesterol (continuous), hypertension (normotensive, borderline hypertensive, mildly hypertensive, definitely hypertensive) and total energy intake (continuous); (3) model 2 further adjusted by including all three plant food groups (fruits and berries, vegetables, and cereals) simultaneously. A test for trend was carried out based on the likelihood ratio test by including the quartile of plant food intake as a continuous variable in the model.

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Potential effect-modifying factors (i.e. sex and hypertension) were studied by including interaction terms between them and the different plant foods in the model. Finally, exclusion of the first 4 years of follow-up was carried out to control for the potential effect of undiagnosed cerebrovascular diseases at baseline on results. The analyses were performed by using SAS 9 (SAS Institute Inc., Cary, NC, USA).

Results

Individuals who experienced a stroke during the follow-up tended to be older and to have a higher BMI, higher serum cholesterol levels and hypertension (Table 1). Older age, smoking and low physical activity were associated with a lower consumption of fruit and berries (Table 2). Older age and low physical activity were also related to a lower consumption of vegetables. Furthermore, there was a higher prevalence of diabetes among those with the lowest vegetable intake. Those who consumed the fewest cereals were older and more often smokers, and had lower physical activity, higher serum cholesterol level, and a higher prevalence of hypertension and diabetes. Compared with women, men tended to eat fewer fruits and berries, and vegetables, but more cereals (Table 3).

Fruits and berries

An inverse association was found between total consumption of fruits and berries and subsequent incidence of cerebrovascular diseases (Table 4). This association was especially strong for fruits. The relative risk between the highest and lowest quartiles of fruit consumption was 0·75 (95 % CI 0·59, 0·94; *P* for trend=0·006). The association was similar both for ischaemic stroke and intracerebral haemorrhage, the corresponding relative risks being 0·73 (95 % CI 0·54, 1·00; *P*=0·03) and 0·47 (95 % CI 0·24, 0·92; *P*=0·02), respectively. These associations were mainly due to the intake of citrus fruits (including juices) and no significant association was found for other fruits or berries. All results persisted after exclusion of cases occurring during the first 4 years of follow-up and after inclusion of cases occurring during the first 15 and first 20 years of follow-up (data not shown).

A study of the interactions between fruit and berry consumption and sex revealed a statistically significant interaction for cerebrovascular diseases (*P*=0·02) and ischaemic stroke incidence (*P*=0·02) but not for intracerebral haemorrhage (*P*=0·78). The relative risks were 0·58 (95 % CI 0·42, 0·80) for all cerebrovascular diseases combined and 0·55 (95 % CI 0·36, 0·85) for ischaemic stroke in men and 1·14 (95 % CI 0·83, 1·57) and 1·30 (95 % CI 0·84, 1·99) in women. No significant interaction for hypertension was found (*P*>0·47).

Vegetables

The total consumption of vegetables, with or without potatoes, was not associated with the incidence of cerebrovascular diseases, ischaemic stroke or intracerebral haemorrhage (Table 5). Of the vegetable subgroups, the consumption of cruciferous vegetables was, however, inversely associated with the risk of all three types of cerebrovascular diseases. The relative risks for cerebrovascular diseases, ischaemic stroke and intracerebral haemorrhage between the highest and lowest quartiles of these vegetables were 0·79 (95 % CI 0·63, 0·99; *P*=0·04), 0·67 (95 % CI 0·49, 0·92; *P*=0·009)

Table 1. Age- and sex-adjusted levels of selected variables for individuals who did and did not experience some type of stroke during follow-up

(Mean values or percentages)

	Type of stroke				
Variable	Ischaemic stroke (*n* 335)	Intracerebral haemorrhage (*n* 58)	Undefined strokes (*n* 232)	No stroke (*n* 3307)	*P**
Age (years)†	55·5	53·1	56·2	51·2	<0·01
Sex (% males)‡	54·0	54·0	52·6	51·9	0·84
BMI (kg/m²)	27·0	26·8	26·5	26·4	0·08
Current smoking (%)	34·0	28·0	31·0	31·5	0·65
High physical activity (%)	53·0	52·5	58·1	57·2	0·41
Serum cholesterol (mmol/l)	6·9	6·8	7·2	7·0	0·04
Hypertension (%)	23·8	25·1	23·2	15·1	<0·01
Diabetes (%)	3·2	3·2	2·6	2·5	0·87
Dietary intake					
Energy					
kJ/d	10 586	10 418	10 418	10 544	0·95
kcal/d	2530	2490	2490	2520	0·95
Cereals (g/d)	273	272	274	277	0·95
Vegetables (g/d)§	329	347	320	328	0·63
Fruits (g/d)‖	99	85	99	100	0·73
Berries (g/d)¶	15	17	17	17	0·75

* Significance of the differences between the groups.
† Adjusted for sex.
‡ Adjusted for age.
§ Including potatoes.
‖ Including fresh, dried and canned fruits, and juices.
¶ Including only fresh berries.

Table 2. Age- and sex-adjusted levels of selected variables in the lowest and highest quartiles of intake of fruits and berries, vegetables or cereals (Mean values or percentages)

	Fruits and berries			Vegetables			Cereals		
Variable	1 (lowest)	4 (highest)	P*	1 (lowest)	4 (highest)	P*	1 (lowest)	4 (highest)	P*
Age (years)†	52·8	51·2	< 0·01	54·2	50·2	< 0·01	53·3	51·0	< 0·01
Sex (% males)‡	52·7	51·4	0·95	53·1	51·2	0·85	52·2	51·9	0·99
BMI (kg/m^2)	26·4	26·5	0·40	26·4	26·4	0·51	26·9	26·3	< 0·001
Current smoking (%)	38·8	28·3	< 0·01	29·2	33·4	0·11	35·9	26·8	< 0·01
High physical activity (%)	44·4	68·6	< 0·01	55·9	54·0	0·08	62·7	51·5	< 0·01
Serum cholesterol (mmol/l)	6·9	7·1	0·04	7·0	7·0	0·71	7·1	6·8	< 0·001
Hypertension (%)	16·4	17·1	0·60	15·9	17·5	0·74	19·4	15·1	0·03
Diabetes (%)	2·6	3·3	0·34	3·7	2·0	0·05	3·7	2·0	0·06
Dietary intake (g/d)									
Energy									
kJ/d	9749	11590	< 0·01	8996	12385	< 0·01	7991	13640	< 0·01
kcal/d	2330	2770	< 0·01	2150	2960	< 0·01	1910	3260	< 0·01
Cereals	259	286	< 0·01	241	316	< 0·01	145	445	< 0·01
Vegetables§	299	361	< 0·01	175	517	< 0·01	286	378	< 0·01
Fruits‖	15	226	< 0·01	77	117	< 0·01	106	99	0·04
Berries¶	7	28	< 0·01	13	20	< 0·01	14	20	< 0·01

* *P* value for trend.
† Adjusted for sex.
‡ Adjusted for age.
§ Including potatoes.
‖ Including fresh, dried and canned fruits, and juices.
¶ Including only fresh berries.

and 0·49 (95 % CI 0·25, 0·98; *P*=0·04), respectively. In the case of ischaemic stroke, also the consumption of legumes and the consumption of root vegetables were associated with a reduced risk of the disease. The relative risk between the extreme quartiles was 0·72 (95 % CI 0·54, 0·96; *P*=0·02) for legumes and 0·72 (95 % CI 0·53, 0·98, *P*=0·03) for root vegetables. No significant associations were found for the intake of potatoes. The associations that were found remained after exclusion of the cases occurring during the first 4 years of follow-up and after inclusion of cases occurring during the first 15 and first 20 years of follow-up (data not shown). No significant interaction between the consumption of all vegetables combined and the potential effect-modifying factors sex and hypertension was detected (data not shown).

Cereals

Neither the consumption of whole grain nor refined grain was associated with the incidence of all cerebrovascular diseases combined, ischaemic stroke or intracerebral haemorrhage (Table 6). Exclusion of the cases that occurred during the first 4 years of follow-up and after inclusion of cases occurring during the first 15 and first 20 years of follow-up (data not shown) did not alter the results (data not shown). No significant sex or hypertension interaction was found (data not shown). To study whether the associations observed for fruits and berries, vegetables and cereals were independent of each other, we entered all three food groups simultaneously in the same model. All the results remained unchanged. For example, the relative risks of cerebrovascular diseases between the highest and lowest quartiles of the consumption of fruits and berries, vegetables and cereals after inclusion of the variables in the same model were 0·83 (95 % CI 0·65, 1·04), 0·95 (95 % CI 0·74, 1·21) and 1·10 (95 % CI 0·82, 1·47), respectively.

Discussion

Fruits and berries

The present cohort study showed an inverse association between fruit consumption and risk of cerebrovascular diseases, ischaemic stroke and intracerebral haemorrhage in a population of Finnish men and women combined with a relatively low fruit intake (about 70 % of the median value of other countries)[29]. The findings concerning cerebrovascular diseases and ischaemic stroke are in accordance with the majority of previous studies[5,10,11], but not all[9]. At variance with the present study, however, the only study on

Table 3. Intakes (g/d) of selected plant foods in men and women (Mean values and ranges)

	Men		Women	
Variable	Mean	Range	Mean	Range
Fruits and berries*	127	0–1094	180	0–1325
Fruits†	78	0–1007	124	0–1082
Berries‡	14	0–308	19	0–246
Citrus fruits§	34	0–740	58	0–1040
Other fruits	43	0–522	66	0–876
Vegetables‖	99	0–535	115	1–800
Potatoes	263	2–1072	176	0–896
Cruciferous vegetables	10	0–269	11	0–188
Legumes	7	0–101	5	0–43
Root vegetables	30	0–356	42	0–579
Cereals	319	10–1535	230	20–1092
Whole grains	223	0–1321	151	0–963
Refined grains	93	0–567	76	0–457

* Including fresh, dried and canned fruits, fresh berries, and juices, jams and marmalades.
† Including fresh, dried and canned fruits, and juices.
‡ Including only fresh berries.
§ Including juices.
‖ Excluding potatoes.

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Table 4. Multivariate relative risks (RR) of cerebrovascular diseases, ischaemic stroke and intracerebral haemorrhage with 95 % confidence intervals by quartiles of fruit and berry intake

Stroke type...	Cerebrovascular diseases			Ischaemic stroke			Intracerebral haemorrhage		
Variable	Cases (*n*)	RR*	95 % CI	Cases (*n*)	RR*	95 % CI	Cases (*n*)	RR*	95 % CI
Fruits and berries†									
1st quartile	186	1		106	1		26	1	
2nd quartile	150	0·79	0·64, 0·98	83	0·77	0·57, 1·03	12	0·43	0·22, 0·86
3rd quartile	144	0·77	0·61, 0·96	72	0·70	0·52, 0·96	12	0·40	0·19, 0·82
4th quartile	145	0·81	0·64, 1·02	83	0·84	0·62, 1·14	15	0·55	0·28, 1·08
P value for trend			0·06			0·18			0·05
Fruits‡									
1st quartile	177	1		101	1		27	1	
2nd quartile	168	0·94	0·76, 1·17	92	0·89	0·67, 1·19	12	0·38	0·19, 0·76
3rd quartile	145	0·80	0·64, 1·01	78	0·78	0·57, 1·05	12	0·41	0·20, 0·81
4th quartile	135	0·75	0·59, 0·94	73	0·73	0·54, 1·00	14	0·47	0·24, 0·92
P value for trend			0·006			0·03			0·02
Citrus fruits§									
1st tertile	234	1		129	1		29	1	
2nd tertile	213	0·99	0·82, 1·19	117	0·96	0·75, 1·24	20	0·70	0·39, 1·25
3rd tertile	178	0·77	0·63, 0·93	98	0·79	0·60, 1·03	16	0·54	0·29, 1·01
P value for trend			0·01			0·08			0·05
Other fruits‖									
1st quartile	162	1		90	1		20	1	
2nd quartile	172	1·09	0·88, 1·36	99	1·12	0·84, 1·49	18	0·88	0·46, 1·67
3rd quartile	137	0·85	0·68, 1·07	71	0·79	0·58, 1·08	11	0·53	0·25, 1·12
4th quartile	149	0·93	0·74, 1·17	82	0·94	0·69, 1·28	15	0·72	0·36, 1·44
P value for trend			0·20			0·27			0·19
Berries¶									
1st quartile	180	1		101	1		20	1	
2nd quartile	152	0·84	0·67, 1·04	84	0·83	0·62, 1·11	15	0·74	0·38, 1·44
3rd quartile	140	0·83	0·66, 1·04	77	0·82	0·61, 1·11	13	0·65	0·32, 1·32
4th quartile	153	0·92	0·73, 1·15	82	0·90	0·66, 1·21	17	0·84	0·43, 1·66
P value for trend			0·42			0·45			0·53

* Multivariate model: adjusted for age, sex, BMI, smoking, physical activity, serum cholesterol level, blood pressure and energy intake.
† Quartiles for total fruit and berry intake (including juices, jams and marmalades) (g/d): men, 0–47, 48–101, 102–174, 175–1094; women, 0–81, 82–151, 152–238, 239–1325.
‡ Quartiles for fruit intake (including fresh, dried and canned fruits, and juices) (g/d): men, 0–12, 13–52, 53–118, 119–1007; women, 0–36, 37–94, 95–168, 169–1082.
§ Tertiles for citrus fruit intake (including juices) (g/d): men, 0, 1–36, 37–740; women, 0–8, 11–67, 69–1040.
‖ Quartiles for other fruit intake (excluding citrus fruits) (g/d): men, 0–3, 4–21, 22–57, 58–522; women, 0–10, 11–42, 43–94, 95–876.
¶ Quartiles for (fresh) berry intake (g/d): men, 0–2, 3–9, 10–18, 19–308; women, 0–5, 6–12, 13–23, 24–246.

haemorrhagic strokes in men and women combined did not find any association between fruit consumption and risk of haemorrhagic stroke[9]. In line with previous studies on ischaemic strokes[10,11], the strongest association was found with citrus fruits, which are known to be a major source of flavonoids[30].

The present study supports the hypothesis whereby fruit consumption has a protective effect on stroke incidence[1]. Fruits have been found to reduce blood pressure[31,32], the major risk factor in stroke[33]. Nutrients that potentially contribute to this reduction include K, vitamin C and dietary fibre[34–36]. In addition to its antihypertensive effect, it has been suggested that in animal models K prevents stroke through other mechanisms, such as inhibiting free radical formation, proliferation of arterial smooth muscles and obstruction of blood vessels[37]. Fruits may also prevent atherosclerosis through vitamins C and E, and other biologically active compounds such as flavonoids. Beside other possible effects, they all work as antioxidants inhibiting blood-clot formation[38] by protecting fatty acids in cell membranes from oxidation. Fruits might also lower serum cholesterol or the homocysteine level. Potential nutrients contributing to these effects are dietary fibre for serum cholesterol[39] and folic acid for serum homocysteine, which is a possible risk factor for stroke[40].

Unlike in the majority of previous studies[4,6,8,9,12,13,15], we found an association between fruit intake and cerebrovascular diseases in men but not in women. In the case of ischaemic stroke, we found an inverse association between fruit intake and disease risk in men, whereas previous studies found a reduced risk either in women[11], both in men and in women[6] or in neither[7,9]. Studies on fruit intake and haemorrhagic stroke risk have yielded similar results, which suggests an inverse association in men[7] congruently to the present study, or both in men and in women[6] or no association at all[9]. The inverse association observed in the present study was mainly due to an elevated risk in the lowest quartile of fruit intake in men. The intake in that category was much lower for men (0–12 g/d) than for women (0–36 g/d).

Vegetables

The total consumption of vegetables, with or without potatoes, was not associated with the risk of cerebrovascular diseases in the present study. Some of the previous studies, however,

Table 5. Multivariate relative risks (RR) of cerebrovascular diseases, ischaemic stroke and intracerebral haemorrhage with 95 % confidence intervals by quartiles of vegetable intake

Stroke type...	Cerebrovascular diseases			Ischaemic stroke			Intracerebral haemorrhage		
Variable	Cases (*n*)	RR*	95 % CI	Cases (*n*)	RR*	95 % CI	Cases (*n*)	RR*	95 % CI
Vegetables 1†									
1st quartile	185	1		100	1		17	1	
2nd quartile	137	0·77	0·61, 0·96	73	0·76	0·56, 1·03	11	0·60	0·27, 1·32
3rd quartile	155	0·91	0·73, 1·13	88	0·94	0·70, 1·26	15	0·93	0·46, 1·91
4th quartile	148	0·93	0·73, 1·17	83	0·92	0·67, 1·27	22	1·48	0·74, 2·96
P value for trend			0·78			0·88			0·16
Vegetables 2‡									
1st quartile	171	1		108	1		14	1	
2nd quartile	145	0·90	0·72, 1·12	73	0·70	0·52, 0·95	13	0·96	0·45, 2·07
3rd quartile	150	1·02	0·82, 1·28	76	0·78	0·58, 1·06	19	1·45	0·71, 2·95
4th quartile	154	1·11	0·88, 1·41	85	0·92	0·68, 1·25	18	1·45	0·69, 3·03
P value for trend			0·24			0·69			0·19
Potatoes§									
1st quartile	182	1		91	1		19	1	
2nd quartile	152	0·89	0·71, 1·10	83	0·97	0·72, 1·31	14	0·75	0·37, 1·51
3rd quartile	139	0·84	0·67, 1·05	82	0·98	0·73, 1·33	12	0·66	0·31, 1·38
4th quartile	147	0·86	0·68, 1·09	86	1·01	0·74, 1·39	19	1·03	0·52, 2·07
P value for trend			0·16			0·92			0·99
Cruciferous vegetables‖									
1st quartile	203	1		119	1		29	1	
2nd quartile	166	0·90	0·73, 1·10	89	0·81	0·61, 1·07	11	0·40	0·20, 0·80
3rd quartile	134	0·86	0·69, 1·07	72	0·75	0·56, 1·01	13	0·53	0·27, 1·04
4th quartile	122	0·79	0·63, 0·99	64	0·67	0·49, 0·92	12	0·49	0·25, 0·98
P value for trend			0·04			0·009			0·04
Legumes¶									
1st quartile	185	1		111	1		14	1	
2nd quartile	144	0·89	0·72, 1·12	76	0·79	0·59, 1·06	16	1·34	0·64, 2·79
3rd quartile	135	0·81	0·64, 1·01	75	0·74	0·55, 1·00	16	1·31	0·62, 2·74
4th quartile	161	0·86	0·69, 1·07	82	0·72	0·54, 0·96	19	1·44	0·70, 2·96
P value for trend			0·12			0·02			0·36
Root vegetables**									
1st quartile	163	1		103	1		16	1	
2nd quartile	162	0·99	0·79, 1·23	89	0·84	0·63, 1·12	14	0·85	0·41, 1·75
3rd quartile	159	0·97	0·78, 1·21	82	0·77	0·57, 1·03	17	1·01	0·51, 2·02
4th quartile	141	0·92	0·73, 1·17	70	0·72	0·53, 0·98	18	1·08	0·54, 2·19
P value for trend			0·50			0·03			0·72

* Multivariate model: adjusted for age, sex, BMI, smoking, physical activity, serum cholesterol level, blood pressure and energy intake.
† Quartiles for total vegetable intake including potatoes (g/d): men, 9–252, 253–337, 338–448, 449–1354; women, 10–203, 204–273, 274–353, 354–1026.
‡ Quartiles for total vegetable intake excluding potatoes (g/d): men, 0–44, 45–84, 85–137, 138–535; women, 1–56, 57–95, 96–150, 151–800.
§ Quartiles for potato intake (g/d): men, 2–169, 170–239, 240–326, 327–1072; women, 0–108, 109–156, 157–223, 224–896.
‖ Quartiles for cruciferous vegetable intake (g/d): men, 0–1, 2–6, 7–13, 14–269; women, 0–2, 3–7, 8–15, 16–188.
¶ Quartiles for legume intake (g/d): men, 0–2, 3–5, 6–9, 10–101; women, 0–1, 2–3, 4–6, 7–43.
** Quartiles for root vegetable intake (g/d): men, 0–5, 6–17, 18–40, 41–356; women, 0–11, 12–29, 30–56, 57–579.

found an inverse association between total or some individual vegetable consumption and cerebrovascular disease incidence[6,8,9], whereas others reported no significant association[4,5,12,13]. The results were also inconsistent for ischaemic and haemorrhagic stroke. Only a few studies found an inverse association for ischaemic[6,7] or haemorrhagic stroke[7], whereas the majority found no significant association between vegetable consumption and either type of stroke[6,9,10,11].

Study of vegetable subgroups showed that a higher cruciferous vegetable intake was associated with a lower risk of both ischaemic stroke and intracerebral haemorrhage. Previous studies on the relationship between cruciferous vegetables (or a single cruciferous vegetable, such as broccoli) and total stroke[13] or ischaemic stroke[10,11] have given inconsistent results. In the case of ischaemic stroke, Joshipura *et al.* [11] found a reduced stroke risk for a higher intake of cruciferous vegetables, whereas Johnsen *et al.* [10] did not.

The present study gives limited support to the general hypothesis that the consumption of vegetables gives protection against stroke. One reason for the lack of association in the present study might be the comparatively low consumption of vegetables in Finland in general. At the time of the baseline examination of the present study, the intake of vegetables was only about 20 % that of the median intake of vegetables in previous study populations in other countries[29]. Furthermore, fresh vegetables, which contain more beneficial nutrients, became more available only after the baseline examination[41]. Nevertheless, our findings suggest that the consumption of cruciferous vegetables may be of benefit against cerebrovascular diseases. Cruciferous vegetables are an important source of flavonoids, as are citrus fruits[30], the consumption of which was also found to be inversely associated with the risk of cerebrovascular diseases. These results are in agreement with the findings from previous studies on flavonoids and risk of cerebrovascular diseases in this same study population[42,43].

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Table 6. Multivariate relative risks (RR) of cerebrovascular diseases, ischaemic stroke and intracerebral haemorrhage with 95 % confidence intervals by quartiles of total cereal, wholegrain and refined grain intake

Stroke type...	Cerebrovascular diseases			Ischaemic stroke			Intracerebral haemorrhage		
Variable	Cases (*n*)	RR*	95 % CI	Cases (*n*)	RR*	95 % CI	Cases (*n*)	RR*	95 % CI
Cereals†									
1st quartile	166	1		92	1		15	1	
2nd quartile	159	1·09	0·87, 1·36	81	0·96	0·71, 1·31	25	1·72	0·88, 3·36
3rd quartile	152	1·09	0·86, 1·39	91	1·12	0·81, 1·53	9	0·64	0·27, 1·53
4th quartile	148	1·09	0·82, 1·45	80	0·97	0·66, 1·43	16	1·14	0·47, 2·78
P value for trend			0·53			0·84			0·61
Whole grains‡									
1st quartile	157	1		87	1		15	1	
2nd quartile	156	0·98	0·78, 1·23	85	0·95	0·70, 1·29	16	1·01	0·49, 2·08
3rd quartile	161	1·18	0·93, 1·48	88	1·11	0·81, 1·51	18	1·31	0·64, 2·68
4th quartile	151	1·12	0·87, 1·45	84	1·06	0·75, 1·50	16	1·19	0·53, 2·67
P value for trend			0·19			0·53			0·52
Refined grains§									
1st quartile	175	1		97	1		21	1	
2nd quartile	158	0·93	0·74, 1·15	79	0·81	0·60, 1·10	15	0·70	0·36, 1·36
3rd quartile	148	0·88	0·70, 1·10	90	0·95	0·71, 1·28	14	0·66	0·33, 1·33
4th quartile	144	0·88	0·69, 1·14	78	0·85	0·61, 1·19	15	0·66	0·31, 1·42
P value for trend			0·27			0·53			0·26

* Multivariate model: adjusted for age, sex, BMI, smoking, physical activity, serum cholesterol level, blood pressure and energy.
† Quartiles for cereal intake (g/d): men, 10–223, 224–295, 296–390, 391–1535; women, 20–156, 157–210, 211–285, 286–1092.
‡ Quartiles for wholegrain intake (g/d): men, 0–139, 140–201, 202–279, 280–1321; women, 0–89, 90–134, 135–194, 195–963.
§ Quartiles for refined grain intake (g/d): men, 0–50, 51–82, 83–124, 125–567; women, 0–43, 44–68, 69–99, 100–457.

Cereals

It has been suggested that the consumption of cereals, especially wholegrain, reduces the risk of chronic diseases[44,45]. Possible mechanisms could be a reduction in serum cholesterol, blood pressure and weight, mediated through cereal fibre, PUFA and different vitamins in grains[35,46]. However, we did not find any association between the consumption of cereals, whether wholegrain or refined, and the incidence of cerebrovascular diseases. In previous studies the results have been inconsistent, suggesting that some factors may modify the possible beneficial effects of cereals. A reduced risk of stroke was only found for women when bran was added to their food[15]. In the case of ischaemic stroke, one study[14] found an inverse relationship for wholegrain consumption in women. Other studies[4,5,16] found no significant association between the consumption of cereals, wholegrain bread or bran cereals and cerebrovascular disease or ischaemic stroke.

Methodological issues

There were several advantages in the present study: the prospective study design with a long follow-up giving enough outcomes of a disease with a long latency period; a comprehensive follow-up through nationwide, population-based registries; the possibility for separate consideration of ischaemic strokes and intracerebral haemorrhages; a study population consisting of both men and women; the use of the dietary history interview method for measuring food intake. An additional advantage of the present study was the possibility to explore the existence of potential effect-modifying factors, enabled by a study population of sufficient size and a sufficiently long follow-up period.

There remain, however, some methodological issues that may have affected the results. First, it cannot be excluded that the associations observed are due to the presence of some other healthy dietary factors or the absence of some unhealthy factors related to the consumption of plant foods. Although plant foods are generally considered to be healthy, the beneficial health effect may become masked by unhealthier accompaniments (for example, adding full-fat dairy products to wholegrain products or preserving vegetables in salty liquids and fruit and berries in excess sugar). The associations may also be related to lifestyle, which might be healthier among high consumers of fruits and vegetables, or due to residual confounding, for example, alcohol consumption, which was left out of the analysis because of insufficient data. Second, during the 24-year follow-up, considerable changes in the diet of the Finnish population occurred[41]. The consumption of fresh fruits doubled and the consumption of vegetables tripled as a result of improved availability, better storage facilities, and, presumably, an improved level of health education. These changes may have caused conservative estimates of the strength of associations between plant food intake and the incidence of cerebrovascular diseases. Finally, methodological issues related to the dietary history interview may have caused conservative estimates of the strength of associations. The short- and long-term reliability of the variables studied were, however, reasonably high and thus allowed the relevant associations to be revealed[23].

Conclusions

In conclusion, the results of the present study suggest that fruit consumption, especially citrus fruit, may provide protection against all cerebrovascular diseases, as well as against ischaemic stroke and intracerebral haemorrhage in men but

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not in women. Furthermore they suggest that the consumption of cruciferous vegetables, but not general consumption of vegetables, may reduce the risk of the same disease. Consumption of cereals did not, however, predict a reduced risk of cerebrovascular diseases. These results thus support the hypothesis that the dietary intake of plant foods reduces the risk of cerebrovascular diseases. The present results, however, indicate that the reduction may be due to selected plant foods. Because of the inconsistency of the findings between men and women and type of plant food in the present study and in studies carried out in different settings, further studies on plant foods and the risk of cerebrovascular diseases and the mechanisms behind their association are needed.

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A. M. participated in the interpretation of the data and in the drafting of the manuscript, and conducted the statistical analyses. P. K. participated in the analysis and interpretation of the data, in the acquisition, and in the drafting of the manuscript, and supervised the conducting of the study. J. M. participated in the analysis and the interpretation of the data and in the critical revision of the manuscript. M. A. L. provided statistical expertise and participated in the analysis and the interpretation of the data, and in the writing of the manuscript. M. H. participated in the study concept and design, the acquisition of data, and the critical revision of the manuscript. R. J. participated in the study concept and design, the acquisition and interpretation of data, and the critical revision of the manuscript.

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