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Coffee and Tea Consumption and Risk of Stroke Subtypes in Male Smokers

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Background and Purpose—Coffee and tea consumption could potentially reduce the risk of stroke because these beverages have antioxidant properties, and coffee may improve insulin sensitivity. We examined the associations of coffee and tea consumption with risk of stroke subtypes.

Methods—We used prospective data from the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study, a cohort study of 26 556 male Finnish smokers aged 50 to 69 years without a history of stroke at baseline. Coffee and tea consumption was assessed at baseline using a validated food-frequency questionnaire. During a mean follow-up of 13.6 years, from 1985 through December 2004, 2702 cerebral infarctions, 383 intracerebral hemorrhages, and 196 subarachnoid hemorrhages were ascertained from national registries.

Results—After adjustment for age and cardiovascular risk factors, both consumption of coffee and tea was statistically significantly inversely associated with the risk of cerebral infarction but not intracerebral or subarachnoid hemorrhage. The multivariate relative risk of cerebral infarction for men in the highest category of coffee consumption ($\geq$8 cups/d) was 0.77 (95% CI, 0.66 to 0.90; *P* for trend <0.001) compared with those in the lowest category (<2 cups/d). The corresponding relative risk comparing men in the highest category of tea consumption ($\geq$2 cups/d) with those in the lowest category (nondrinkers) was 0.79 (95% CI, 0.68 to 0.92; *P* for trend=0.002).

Conclusions—These results suggest that high consumption of coffee and tea may reduce the risk of cerebral infarction among men, independent of known cardiovascular risk factors. (*Stroke*. 2008;39:1681-1687.)

Key Words: cerebral infarction ■ coffee ■ cohort study ■ epidemiology ■ stroke ■ tea

Coffee is one of the most widely consumed beverages worldwide. Because of the high coffee consumption, even small effects in persons could have a large impact on public health. Coffee consumption could plausibly influence the risk of cardiovascular disease because coffee has antioxidant properties[1] and may improve insulin sensitivity.[2–5] In addition, a recent study found that coffee consumption was inversely related to markers of inflammation and endothelial dysfunction in women with type 2 diabetes.[6] Whereas the relation between coffee consumption and risk of coronary heart disease has been studied extensively,[7] few studies have examined the association of coffee drinking with stroke risk and the studies that do exist were based on a small number of cases.[8–10] Only one study examined whether the association between coffee consumption and stroke risk differed between stroke subtypes.[10]

Tea is another widely consumed beverage with potential health benefits. Tea contains high amounts of polyphenols, which have antioxidant activities and prevent oxidation of low density lipoprotein (LDL) cholesterol in vitro and in vivo.[11–14] Oxidization of LDL particles promotes the formation of atherosclerotic lesions, leading to increased risk of cardiovascular disease.[15] Prospective studies on tea consumption in relation to stroke incidence[16,17] or mortality[8,18–20] have produced inconsistent results.

The purpose of this study was to evaluate the associations of coffee and tea consumption with risk of stroke subtypes among male smokers participating in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study cohort.

Methods

Study Population

The ATBC Study is a randomized, double-blind, placebo-controlled, primary prevention trial originally designed to determine whether α-tocopherol (50 mg/d), â-carotene (20 mg/d), or both could reduce cancer incidence in male smokers.[21] The cohort consists of 29 133 men, aged 50 to 69 years, who resided in southwestern Finland and smoked 5 or more cigarettes per day at baseline. Participants were recruited into the trial between 1985 and 1988 and the trial ended in April 1993, with registry-based follow-up continuing thereafter. Study eligibility was assessed before randomization; men who had

prior cancer (other than nonmelanoma skin cancer or carcinoma in situ) or other serious illness that might limit long-term participation, as well as those who received anticoagulant therapy or used supplements containing vitamin E (>20 mg/d), vitamin A (>20 000 IU/d), or â-carotene (>6 mg/d) were ineligible. Information on coffee and tea consumption was provided by 26 556 (93%) of the randomized participants who had no history of stroke at baseline.

Written informed consent was obtained from each participant before randomization. The study was approved by the institutional review boards of the National Public Health Institute of Finland and the US National Cancer Institute.

Baseline Data Collection

At baseline, study participants completed questionnaires on general background characteristics, including medical, smoking, and physical activity histories.[21] Trained medical staff measured weight, height, and blood pressure using standard methods. Body mass index (BMI) was calculated by dividing the weight in kilograms by the square of height in meters. A blood sample was obtained from participants after an overnight fast and serum was stored at −70°C. Serum total cholesterol and high-density lipoprotein (HDL) cholesterol levels were determined enzymatically (CHOD-PAP method, Boehringer Mannheim).

Assessment of Coffee and Tea Consumption

At baseline, consumption of coffee and tea was assessed using a validated self-administered food frequency questionnaire.[22] Participants were asked to report their average number of cups of coffee and tea consumed per day or week during the previous year. They were also asked to indicate the usual cup size. A color picture booklet was used to aid in cup size estimation; for coffee there were 3 cup sizes commonly used in Finland, 70 mL, 110 mL, and 170 mL; and for tea 110 mL, 170 mL, and 220 mL. We converted the reported amount of coffee and tea consumed into cups per day using the size of a cup of medium size (110 mL for coffee and 170 mL for tea). The type of tea used was not asked because Finnish men rarely drink any tea other than black tea. In the autumn of 1990 (2 to 5 years after randomization), we asked about the usual method of preparing coffee at baseline with the answer categories: "usually filtered", "usually boiled", "usually instant", and "I don't drink coffee". Information on method of preparing coffee was available for 20 427 men. Among these, 14 513 reported drinking filtered coffee (71.1%), 4232 boiled coffee (20.7%), and 372 instant coffee (1.8%). We calculated the total intake of caffeine for each participant by summing the caffeine content of coffee and tea multiplied by the amount of consumption; for caffeine content we used 80 mg per 100 mL of coffee and 26 mg per 100 mL of tea.[23] In our validation study, the correlations coefficients between the food frequency questionnaire and food records were 0.72 for coffee and 0.69 for tea.[22]

Assessment of Stroke Cases

The study end point was first-ever stroke that occurred between the date of randomization and December 31, 2004. The strokes were further divided into cerebral infarction, intracerebral hemorrhage, subarachnoid hemorrhage, and unspecified stroke. The end points were identified by record linkage with the National Hospital Discharge Register and the National Register of Causes of Death. Both registers used the codes of the *International Classification of Diseases* (ICD): the 8th edition was used until the end of 1986, the 9th edition through the end of 1996, and the 10th edition thereafter. The end points comprised ICD-8 codes 430 to 434 and 436, ICD-9 codes 430 to 431, 433 to 434, and 436, and ICD-10 codes I60, I61, I63, and I64, excluding ICD-8 codes 431.01 and 431.91 representing subdural hemorrhage and ICD-9 codes 4330X, 4331X, 4339X, and 4349X denoting occlusion or cerebral or precerebral artery stenosis without cerebral infarction. In a reviewed sample, the diagnoses of cerebral infarction, subarachnoid hemorrhage, and intracerebral hemorrhage proved correct by strict preset criteria[24,25] in 90%, 79%, and 82% of the discharge diagnoses and in 92%, 95%, and 91% of the causes of death, respectively.[26]

Statistical Analysis

Person-time of follow-up for each participant was computed from the date of randomization to the date of occurrence of first stroke, death from any cause, or December 31, 2004, whichever came first. Cut points for coffee consumption were obtained by dividing the consumption into quintiles, and then finding the closest whole medium cup size (110 mL) frequency of use for each cutoff. By doing this, we created consumption categories that can be easily interpreted. For tea consumption, cut points for the categories had to be chosen differently because of the lower frequency and range of consumption; never consumption was used as the reference category and any consumption was divided into approximate tertiles. Cox proportional hazards models[27] were used to estimate relative risks (RRs) with 95% confidence intervals (CIs). The initial model was controlled for age at randomization and supplementation group (α-tocopherol, â-carotene, both, or placebo). In the main multivariate models, we further adjusted for smoking (number of cigarettes smoked per day), BMI, systolic and diastolic blood pressure, serum total cholesterol, serum HDL cholesterol, histories of diabetes and coronary heart disease, leisure-time physical activity, and alcohol intake. The multivariate model for coffee included tea consumption and that for tea included coffee consumption. Tests based on Schoenfeld residuals showed no evidence that proportional hazard assumptions were violated.

To test for linear trends across increasing categories, we modeled consumption of coffee and tea as continuous variables in the models with the median value of each category. We also used restricted cubic spline regression to model coffee consumption as a continuous variable in relation to stroke risk. To assess possible effect modification, we conducted analyses stratified by age, cardiovascular risk factors, and supplementation group. The likelihood ratio test was used to assess the significance of multiplicative interactions. All probability values were 2-sided, and probability values <0.05 were considered statistically significant. Statistical analyses were performed using Stata, version 9.2 (StataCorp).

Results

Baseline characteristics of the study population by coffee and tea consumption are presented in Table 1. About 2.5% of participants reported that they never drank coffee, and about 64% were nondrinkers of tea. The mean (±SD) daily coffee consumption among drinkers was 5.7 cups (±3.1 cups). Men with higher coffee consumption were slightly younger, smoked more cigarettes daily, had lower systolic and diastolic blood pressure, were less likely to have a history of diabetes or coronary heart disease, were more likely to be physically active, and consumed less alcohol and tea than men with a low coffee consumption. Compared with nondrinkers of tea, those who consumed tea tended to smoke slightly fewer cigarettes daily, were somewhat more likely to be physically active, and consumed more alcohol but less coffee.

During 360 187 person-years of follow-up (mean 13.6 years), we ascertained 2702 cerebral infarctions, 383 intracerebral hemorrhages, 196 subarachnoid hemorrhages, and 84 unspecified strokes. After adjustment for age, supplementation group, and cardiovascular risk factors, both coffee consumption (Table 2) and tea consumption (Table 3) were statistically significantly inversely associated with risk of cerebral infarction but not of intracerebral or subarachnoid hemorrhage. The multivariate RRs of cerebral infarction for men in the highest compared with the lowest category of consumption were 0.77 (95% CI, 0.66 to 0.90) for coffee and 0.79 (95% CI, 0.68 to 0.92) for tea. Additional adjustment for consumption of fruits, vegetables, fish, and total fat did not appreciably alter the results for coffee (highest versus lowest

Table 1.   Baseline Characteristics by Categories of Coffee and Tea Consumption Among 26 556 Men in the ATBC Study*

	Coffee Consumption, cups/d†						Tea Consumption, cups/d†				
	<2	2 to 3	4 to 5	6 to 7	≥8	P‡	0	<0.5	0.5 to 1.9	≥2	P‡
Participants, n	2337	4487	7863	5766	6103	...	16 997	3615	3743	2201	...
Age, y	57.9	58.2	57.9	57.6	56.8	<0.001	57.7	57.5	57.7	57.6	0.91
Smoking, cigarettes/d	19.9	19.1	19.7	20.5	22.4	<0.001	20.9	20.1	19.4	19.4	<0.001
Body mass index, kg/m²	26.2	26.3	26.3	26.2	26.3	0.65	26.3	26.3	26.2	26.2	0.10
Systolic blood pressure, mm Hg	144.3	143.8	142.2	140.6	140.3	<0.001	142.0	141.4	142.0	142.0	0.76
Diastolic blood pressure, mm Hg	89.6	89.1	87.9	86.8	86.1	<0.001	87.5	87.6	87.8	87.9	0.07
Serum total cholesterol, mmol/L	6.06	6.21	6.23	6.31	6.30	<0.001	6.28	6.24	6.16	6.09	<0.001
Serum HDL cholesterol, mmol/L	1.26	1.22	1.19	1.18	1.17	<0.001	1.19	1.20	1.18	1.20	0.57
Diabetes, %	6.8	6.6	5.8	5.3	5.3	0.001	5.9	5.7	5.7	5.6	0.50
Coronary heart disease history, %	12.0	11.5	10.8	11.3	9.9	0.006	11.1	11.7	9.5	10.9	0.17
Physically active, %§	51.6	58.4	59.5	60.7	58.8	<0.001	57.3	61.2	62.2	59.9	<0.001
Daily intake											
Alcohol, g	27.3	22.8	18.4	15.2	13.7	<0.001	17.5	19.4	18.9	18.9	0.001
Coffee, cups	0.7	2.7	4.6	6.3	9.8	<0.001	6.1	5.2	4.4	3.5	<0.001
Tea, cups	1.3	0.6	0.4	0.3	0.2	<0.001	0	0.3	1.0	3.0	<0.001

*Values are means unless otherwise indicated. All variables, except age, are standardized to the age distribution of the cohort.
†One cup of coffee=110 mL; one cup of tea=170 mL.
‡P value for trend across categories of consumption.
§Moderate or heavy activity at leisure time.

category: RR, 0.78; 95% CI, 0.66 to 0.90) or tea (corresponding RR, 0.82; 95% CI, 0.70 to 0.95). Spline regression analysis demonstrated a dose-response relationship between coffee consumption and risk of cerebral infarction (Figure). We obtained similar results when we censored the participants who developed acute myocardial infarction or diabetes during follow-up.

As shown in Table 4, the inverse relation between coffee consumption and risk of cerebral infarction was persistent in subgroup analysis according to history of diabetes and coronary heart disease, systolic and diastolic blood pressure, alcohol intake, and cigarettes smoked per day. We did not identify any statistically significant interactions between coffee consumption and these covariates. The

Table 2.   Relative Risks of Stroke Subtypes by Coffee Consumption Among 26 556 Men in the ATBC Study, 1985–2004

	Coffee Consumption, cups/d					
	<2	2 to 3	4 to 5	6 to 7	≥8	P for Trend
Cerebral infarction						
Cases, n	267	503	847	545	540	
Relative risk (95% CI)*	1.0	0.92 (0.79 to 1.06)	0.87 (0.76 to 1.00)	0.76 (0.66 to 0.88)	0.75 (0.65 to 0.87)	<0.001
Relative risk (95% CI)†	1.0	0.91 (0.79 to 1.06)	0.88 (0.77 to 1.02)	0.77 (0.66 to 0.90)	0.77 (0.66 to 0.90)	<0.001
Intracerebral hemorrhage						
Cases, n	41	64	124	63	91	
Relative risk (95% CI)*	1.0	0.76 (0.51 to 1.12)	0.83 (0.58 to 1.18)	0.57 (0.39 to 0.85)	0.83 (0.57 to 1.20)	0.47
Relative risk (95% CI)†	1.0	0.80 (0.54 to 1.20)	0.92 (0.64 to 1.32)	0.66 (0.44 to 1.00)	0.98 (0.66 to 1.47)	0.39
Subarachnoid hemorrhage						
Cases, n	14	26	84	43	49	
Relative risk (95% CI)*	1.0	0.94 (0.49 to 1.80)	1.28 (0.72 to 2.28)	1.14 (0.62 to 2.08)	1.22 (0.67 to 2.21)	0.47
Relative risk (95% CI)†	1.0	0.91 (0.47 to 1.76)	1.24 (0.68 to 2.25)	1.10 (0.59 to 2.07)	1.18 (0.63 to 2.20)	0.51

*Adjusted for age and supplementation group.
†Adjusted for age, supplementation group, No. of cigarettes smoked daily, body mass index, systolic and diastolic blood pressure, serum total cholesterol, serum HDL cholesterol, histories of diabetes and coronary heart disease, leisure-time physical activity, alcohol intake, and tea consumption.

Table 3. Relative Risks of Stroke Subtypes by Tea Consumption Among 26 556 Men in the ATBC Study, 1985–2004

	Tea Consumption, cups/d				
	0	<0.5	0.5 to 1.9	≥2	P for Trend
Cerebral infarction					
Cases, n	1760	365	378	199	
Relative risk (95% CI)*	1.0	0.93 (0.83 to 1.04)	0.92 (0.83 to 1.03)	0.85 (0.73 to 0.98)	0.02
Relative risk (95% CI)†	1.0	0.93 (0.83 to 1.04)	0.89 (0.80 to 1.00)	0.79 (0.68 to 0.92)	0.002
Intracerebral hemorrhage					
Cases, n	244	47	53	39	
Relative risk (95% CI)*	1.0	0.87 (0.63 to 1.18)	0.94 (0.70 to 1.26)	1.20 (0.86 to 1.69)	0.37
Relative risk (95% CI)†	1.0	0.86 (0.63 to 1.18)	0.90 (0.66 to 1.22)	1.10 (0.77 to 1.58)	0.66
Subarachnoid hemorrhage					
Cases, n	137	25	21	13	
Relative risk (95% CI)*	1.0	0.82 (0.54 to 1.26)	0.67 (0.42 to 1.06)	0.72 (0.41 to 1.27)	0.11
Relative risk (95% CI)†	1.0	0.84 (0.54 to 1.28)	0.68 (0.43 to 1.08)	0.76 (0.42 to 1.37)	0.15

*Adjusted for age and supplementation group.

†Adjusted for age, supplementation group, No. of cigarettes smoked daily, body mass index, systolic and diastolic blood pressure, serum total cholesterol, serum HDL cholesterol, histories of diabetes and coronary heart disease, leisure-time physical activity, alcohol intake, and coffee consumption.

association also did not differ significantly by strata of age, smoking years, BMI, serum total or HDL cholesterol, physical activity, or supplementation group (data not shown). Likewise, the inverse association between tea consumption and cerebral infarction did not vary significantly by age, cardiovascular risk factors, or supplementation group.

Coffee is a source of magnesium, which may improve insulin sensitivity.[28,29] To examine whether the observed inverse association between coffee consumption and cerebral infarction may be explained by magnesium, we included magnesium intake in the multivariate model. The inverse association for coffee was only slightly attenuated (highest versus lowest category: RR, 0.80; 95% CI, 0.68 to 0.95), suggesting that other components of coffee contributed to the observed inverse association.

We also evaluated whether the used method of preparing coffee affected the association between coffee consumption

and risk of cerebral infarction. The multivariate RRs associated with a 4 cups increment in coffee consumption per day was similar for filtered coffee (RR, 0.93; 95% CI, 0.86 to 1.01) and boiled coffee (RR, 0.87; 95% CI, 0.77 to 0.99; the number of cases reporting consumption of filtered and boiled coffee was 1355 and 483, respectively).

To address the possibility of increased exposure misclassification over time, we divided the follow-time into less than 10 years and 10 or more years of follow-up. Results did not vary appreciably by follow-up time.

Caffeine intake also showed an inverse association with cerebral infarction. Compared with men in the lowest quintile of caffeine intake (median, 189 mg/d), the RR of cerebral infarction for men in the highest quintile (median, 880 mg/d) was 0.76 (95% CI, 0.68 to 0.87; P for trend <0.001) after adjusting for age and supplementation group and 0.83 (95% CI, 0.73 to 0.94; P for trend=0.003) after further adjustment for cardiovascular risk factors.
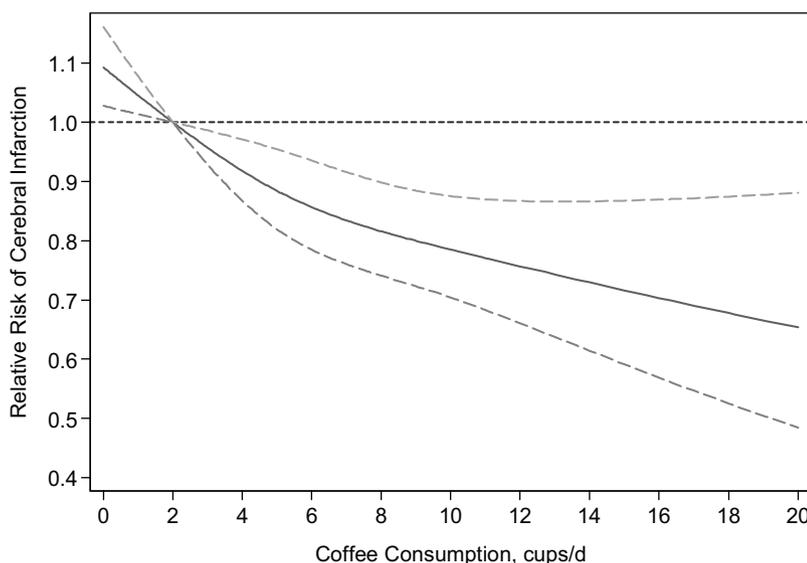

Figure. Relative risk of cerebral infarction according to coffee consumption. Relative risks are calculated by restricted cubic spline Cox proportional hazards model and are adjusted for all variables included in the most adjusted model in Table 2. Solid curve represents point estimates, and dashed curves represent 95% confidence intervals.

Table 4. Multivariate Relative Risks of Cerebral Infarction by Coffee Consumption Stratified by Stroke Risk Factors at Baseline*

	Cases, n	<2	2 to 3	4 to 5	6 to 7	≥8	P for Trend	P for Interaction
				Coffee Consumption, cups/d				
Diabetes								
No	2432	1.0	0.90 (0.77 to 1.06)	0.87 (0.75 to 1.01)	0.78 (0.66 to 0.92)	0.77 (0.65 to 0.90)	0.001	
Yes	270	1.0	1.05 (0.68 to 1.62)	1.04 (0.69 to 1.57)	0.75 (0.47 to 1.20)	0.75 (0.46 to 1.21)	0.06	0.27
Coronary heart disease								
No	2286	1.0	0.99 (0.84 to 1.17)	0.92 (0.78 to 1.07)	0.83 (0.70 to 0.99)	0.82 (0.69 to 0.97)	0.002	
Yes	416	1.0	0.65 (0.45 to 0.92)	0.78 (0.56 to 1.08)	0.55 (0.38 to 0.79)	0.57 (0.39 to 0.83)	0.006	0.31
Systolic blood pressure								
<140 mm Hg	973	1.0	0.92 (0.70 to 1.20)	0.87 (0.68 to 1.12)	0.77 (0.59 to 1.00)	0.79 (0.60 to 1.03)	0.04	
≥140 mm Hg	1729	1.0	0.92 (0.77 to 1.10)	0.90 (0.76 to 1.07)	0.79 (0.65 to 0.95)	0.76 (0.63 to 0.93)	0.001	0.65
Diastolic blood pressure								
<90 mm Hg	1247	1.0	0.96 (0.76 to 1.22)	0.89 (0.71 to 1.12)	0.81 (0.64 to 1.02)	0.84 (0.66 to 1.07)	0.10	
≥90 mm Hg	1455	1.0	0.88 (0.72 to 1.06)	0.88 (0.73 to 1.06)	0.75 (0.61 to 0.92)	0.70 (0.57 to 0.87)	<0.001	0.41
Alcohol consumption								
<15 g/d	1492	1.0	1.00 (0.79 to 1.27)	0.93 (0.75 to 1.16)	0.79 (0.63 to 0.99)	0.80 (0.64 to 1.01)	0.003	
≥15 g/d	1210	1.0	0.84 (0.69 to 1.03)	0.84 (0.69 to 1.01)	0.76 (0.62 to 0.94)	0.74 (0.59 to 0.92)	0.01	0.96
Cigarettes smoked daily								
<20	960	1.0	0.94 (0.74 to 1.21)	0.97 (0.76 to 1.23)	0.97 (0.75 to 1.25)	0.76 (0.57 to 1.00)	0.04	
≥20	1742	1.0	0.89 (0.74 to 1.08)	0.84 (0.70 to 1.00)	0.67 (0.56 to 0.82)	0.76 (0.63 to 0.91)	0.001	0.82

*Relative risks are adjusted for all variables included in the most adjusted model in Table 2.

Discussion

In this prospective cohort study of male smokers, we observed significant inverse associations of coffee and tea consumption with risk of cerebral infarction. When compared to participants with low or no consumption of these beverages, those who consumed 8 or more cups of coffee per day and 2 or more cups of tea per day had their risk of cerebral infarction lowered by 23% and 21%, respectively. These associations were independent of other known risk factors.

Few previous prospective studies have examined the relation between coffee consumption and risk of stroke. In a study of Finnish patients with type 2 diabetes, those who consumed 3 or more cups of coffee per day had a statistically nonsignificant 27% lower risk of death from stroke (n=210 cases) compared with those who consumed 2 or fewer cups of coffee per day (RR, 0.73; 95% CI, 0.92 to 1.05).[8] In contrast, in a study of nonsmoking and hypertensive men enrolled in the Honolulu Heart Program with 25 years of follow-up and 76 total stroke cases, the risk of thromboembolic stroke was higher for men who consumed 3 cups of coffee per day compared to nondrinkers (RR, 2.1; 95% CI, 1.2 to 3.7).[10] Coffee drinking was not associated with risk of total stroke in a cohort of US Health Professionals, but the number of cases in that study was small (n=52).[9] These disparate results might reflect different study populations with different associations in smokers and nonsmokers.

Our findings for tea consumption are consistent with results from the Zutphen study among 552 Dutch men followed over a 15-year period.[16] In that study, high consumption of tea was associated with a significant lower risk of stroke (n=42 cases; ≥4.7 cups/d versus <2.6 cups/d: RR, 0.31; 95% CI, 0.12 to 0.84). No significant relation between tea consumption and stroke mortality was observed in 3 cohort studies (with 131,[19] 210,[8] and 275[18] total stroke cases) conducted in the United States.

Two prospective studies have examined the relation between green tea consumption and mortality from stroke. In a cohort of 5910 nondrinking and nonsmoking Japanese women, the incidence of stroke (n=174 cases) during a 4-year follow-up was about 2-times higher in those who drank less than 5 cups of green tea daily than in those who drank 5 or more cups daily.[17] Likewise, in another cohort of 40 530 Japanese men and women followed up for 11 years, green tea consumption was significantly inversely related to mortality from cerebral infarction (n=197 cases; ≥5 cups/d versus <1 cup/d: RR, 0.49; 95% CI, 0.33 to 0.73) but not intracerebral or subarachnoid hemorrhages.[20]

Beneficial effects of consumption of coffee and tea with regard to risk of cerebral infarction are biologically plausible because coffee and tea contain phenolic compounds with antioxidant properties[1,11] that may prevent atherosclerosis. In the ATBC Study, we previously found that daily supplementation with α-tocopherol, a dietary antioxidant, significantly decreased the incidence of cerebral infarction but increased the risk of subarachnoid hemorrhage and had no effect on intracerebral hemorrhage.[30] This finding suggests that antioxidants may play a role in reducing the risk of cerebral infarction but not hemorrhagic stroke. Coffee and tea are major sources of caffeine, which was inversely associated with the risk of cerebral infarction in this study. However, this association may reflect the correlation between caffeine intake and other potentially protective factors in coffee and tea rather than a direct association between caffeine and cerebral infarction.

Evidence from observational studies suggests that coffee drinking is inversely associated with inflammation and endothelial dysfunction[6] and that coffee consumption may decrease postprandial hyperglycemia,[31,32] improve insulin sensitivity,[2–5,33] and reduce the risk of type 2 diabetes.[34] In a recent large cohort study, type 2 diabetes was associated with an increased risk of ischemic stroke but not hemorrhagic stroke.[35] Intake of coffee components has also been shown to improve glucose metabolism in rats.[36–39] With regard to tea, a recent randomized controlled trial in healthy men showed that black tea consumption reduces platelet activation and plasma C-reactive protein (a marker of systemic inflammation).[40] In prospective studies, high blood concentrations of C-reactive protein have associated with an increased incidence of ischemic stroke[41–44] but not hemorrhagic stroke.[41] Hence, this may be one potential explanation why tea consumption was significantly inversely related to risk of cerebral infarction only.

Our study has several strengths. The prospective design precluded the possibility of recall bias and the large number of stroke cases provided high statistical power to detect associations. The extensive information on cardiovascular risk factors allowed comprehensive adjustment for potential confounders. In addition, our fairly homogenous cohort of male smokers provided high internal validity.

A limitation of this study is that coffee and tea consumption was measured only at baseline. Although the validity of the dietary questionnaire for coffee and tea was demonstrated, changes in coffee and tea consumption during follow-up may have attenuated the observed associations. Another limitation is the small number of nondrinkers of coffee, which made it impossible to evaluate the effect of any coffee consumption versus none. As in any observational study, we cannot entirely rule out the possibility that the observed associations were attributable to confounding by other risk factors. On average, men with high coffee consumption had lower blood pressure, lower alcohol intake, and were less likely to have a history of diabetes or coronary heart disease than men with a low coffee consumption. However, our results persisted in multivariate models adjusting for these and other risk factors. Moreover, the observed relationships were consistent within different subgroups, which further supports the idea that confounding by these factors was unlikely to explain our results. Finally, because the ATBC Study consists entirely of male smokers, our results may not be generalizable to women or to nonsmokers.

In summary, in this large prospective study of male smokers, high consumption of coffee and tea was associated with a significant decreased risk of cerebral infarction. These findings warrant confirmation in other populations, particularly in women and nonsmokers.

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Disclosures

None.

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