Catechin intake might explain the inverse relation between tea consumption and ischemic heart disease: the Zutphen Elderly Study[1–3]

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ABSTRACT

Background: Epidemiologic studies suggest that tea consumption may reduce the risk of cardiovascular diseases, but results are inconsistent. Catechins, which belong to the flavonoid family, are the main components of tea and may be responsible for the alleged protective effect. Taking catechin sources other than tea into account might clarify the reported associations.

Objective: The objective was to evaluate the association between catechin intake and the incidence of and mortality from ischemic heart disease and stroke.

Design: We evaluated the effect of a high catechin intake by using data from the Zutphen Elderly Study, a prospective cohort study of 806 men aged 65–84 y at baseline in 1985.

Results: The mean (±SD) catechin intake at baseline was 72 ± 47.8 mg, mainly from black tea, apples, and chocolate. A total of 90 deaths from ischemic heart disease were documented. Catechin intake was inversely associated with ischemic heart disease mortality; the multivariate-adjusted risk ratio in the highest tertile of intake was 0.49 (95% CI: 0.27, 0.88; *P* for trend: 0.017). After multivariate adjustment, catechin intake was not associated with the incidence of myocardial infarction (risk ratio in the highest tertile of intake: 0.70; 95% CI: 0.39, 1.26; *P* for trend: 0.232). After adjustment for tea consumption and flavonol intake, a 7.5-mg increase in catechin intake from sources other than tea was associated with a tendency for a 20% reduction in ischemic heart disease mortality risk (*P* = 0.114). There was no association between catechin intake and stroke incidence or mortality.

Conclusion: Catechins, whether from tea or other sources, may reduce the risk of ischemic heart disease mortality but not of stroke. *Am J Clin Nutr* 2001;74:227–32.

KEY WORDS Catechin, tea, flavonoid, diet, ischemic heart disease, cerebrovascular disorders, stroke, epidemiology, cohort studies, elderly men, the Zutphen Elderly Study, Netherlands

INTRODUCTION

Epidemiologic studies suggest that tea may reduce the risk of cardiovascular and cerebrovascular diseases (1–5). However, published results are not consistent. Studies from both the United Kingdom (where there is a high intake of black tea) and the United States (where there is a relatively low intake of black tea) found no effect of tea consumption on ischemic heart disease (IHD) risk (6–8) or even a slightly increased risk (9). Tea is a rich source of flavonoids, the compounds that are held responsible for its alleged protective effect. More than 4000 different flavonoids have been identified (10). They occur ubiquitously in plant foods and can be categorized into 6 major subclasses: catechins, flavonols, flavones, flavanones, anthocyanidins, and isoflavonoids. To date, only comprehensive food-composition data on the subclasses of flavonols and flavones are available (11, 12). In several prospective studies, flavonols and flavones are related to a reduced risk of stroke (3) and death from cardiovascular disease (2, 13–15).

Catechins are the major components of tea; they constitute ≈30% of the dry weight of green tea and 9% of the dry weight of black tea (16). Several mechanisms by which catechins could prevent cardiovascular diseases are suggested; they were reviewed by Middleton and Kandaswami (17). Catechins may prevent LDL from oxidative damage either through their free radical–quenching and metal-chelating abilities (18, 19) or by recycling other antioxidants such as vitamin E (20, 21). Catechins interfere with several stages of the inflammatory process involved in atherosclerosis (22, 23) and may influence hemostatic indexes and reduce thrombosis (24). However, the relevance of these proposed mechanisms to the in vivo situation remains to be established.

Until now, an epidemiologic evaluation of catechins has been impossible because reliable data on the catechin content of foods were lacking. We developed a method (25) in which we determined 6 major catechins in foods: (+)-catechin, (+)-gallocatechin, (−)-epicatechin, (−)-epigallocatechin, (−)-epicatechin gallate, and (−)-epigallocatechin gallate in foods and beverages

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commonly consumed in the Netherlands (26, 27). Using these data we evaluated the effect of catechin intake on the risk of fatal and incident IHD and stroke in a cohort of elderly men.

SUBJECTS AND METHODS

Study population

The Zutphen Elderly Study is a prospective cohort study on risk factors for chronic diseases in elderly men. It is an extension of the Zutphen Study, the Dutch contribution to the Seven Countries Study. In 1985, a total of 555 men of the original Zutphen cohort recruited in 1960 were still alive and were invited to participate in the Zutphen Elderly Study. A random sample of all other men of the same age also living in Zutphen but not belonging to the original cohort was also invited to participate. This invitation resulted in a total target population of 1266 men aged 65–84 y, of whom 939 (74%) participated in the study; 876 completed a dietary questionnaire. Complete information on both diet and other risk factors was available for 806 men. The study was approved by the Medical Ethics Committee of the University of Leiden, Netherlands. Informed consent was obtained from all participants.

Data collection

Dietary and medical examinations were conducted between March and June 1985. Medical examinations were performed by trained physicians and included anthropometric measurements, blood sampling, blood pressure measurements, and detailed, validated questionnaires on smoking behavior and physical activity designed for retired men (28). The habitual diet in the month preceding the interview was determined by using a cross-check dietary history method adapted to the Dutch situation (29). Participants were interviewed at home by an experienced dietitian in the presence of the person who usually prepared the meals. If the respondent followed a prescribed diet, the type of diet was noted. The food intake data were encoded by the dietitians and converted into energy and nutrient data by using the 1985 release of the Dutch Food Table (30), updated with 1993 data for β-carotene and vitamin E, with flavonol and flavone data, and with catechin data. The flavonol and flavone contents of foods were previously determined by Hertog et al (11, 12). Flavones are a minor group of flavonoids compared with the flavonols; the term *flavonols* will be used here for the sum of both groups. Catechin, or total catechin, is defined as the sum of (+)-catechin, (+)-gallocatechin, (−)-epicatechin, (−)-epigallocatechin, (−)-epicatechin gallate, and (−)-epigallocatechin gallate. We determined these 6 catechins by reversed-phase HPLC with online ultraviolet and fluorescence detection (25). More than 120 commonly consumed plant foods and beverages in the Dutch diet were analyzed (26, 27). Each food was purchased at 3 outlets: a nationwide supermarket chain, an open-air street market, and a grocery. To take into account seasonal and year-to-year variability, each food was purchased in August and December 1997 and in April and August 1998, if available. Different brands and varieties of the most important catechin sources were analyzed and combined into average values, taking into account consumption levels.

Disease ascertainment

Information on the vital status of the participants until January 1995 was obtained from municipal population registries. Three men were lost to follow-up in 1991. Of these men, 2 had moved abroad and 1 had moved to an unknown destination. These men were included in the analyses but were censored at 31 December 1990. Causes of death were obtained from the Central Bureau of Statistics; between June 1990 and January 1995 information was also obtained from the participants' general practitioners. Information was verified with either hospital discharge data or written information from the general practitioner. Because it is often difficult to determine the underlying cause of death in elderly people, both the primary and secondary cause of death were included in the analyses. Coding of the causes of death followed the ninth revision of the *International Statistical Classification of Diseases* (31). In this classification, codes 410–414 refer to ischemic heart disease and codes 430–438 refer to cerebrovascular disease, further referred to as stroke.

The prevalence of disease at baseline and the time of the first clinical diagnosis of disease during follow-up were recorded at the examinations in 1985, 1990, 1993, and 1995 by using the standardized Rose and Blackburn questionnaire (32). Nonresponders at follow-up examinations received a short questionnaire on disease history. Data on the prevalence of angina pectoris (AP) at baseline and on the prevalence at baseline and the first clinical diagnosis during follow-up of myocardial infarction (MI) and stroke were verified from hospital discharge data and written information from the general practitioner. Data on first events, fatal or nonfatal (referred to as incidence), were uniformly coded by 3 physicians. At baseline there were 115 men (14%) with prevalent MI, who were excluded in the analysis of MI incidence. Prevalence of MI or AP at baseline was included as a covariate in the analyses of MI mortality. Similarly, the 39 men (5%) with prevalent stroke at baseline were excluded in the analyses of stroke incidence, and stroke at baseline was included as a covariate in the analyses of stroke mortality.

Statistical analysis

Baseline characteristics of the participants were compared between tertiles of catechin intake by using the chi-square test for categorical variables, one-way analysis of variance for normally distributed variables, and the Kruskal-Wallis test for skewed variables. Spearman rank correlation coefficients were calculated between catechin intake and other dietary factors. Correlation coefficients ranged from −0.27 for coffee to 0.23 for fiber. Risk ratios of fatal and nonfatal incidence of MI and stroke as well as death from IHD and stroke were estimated by Cox proportional hazards regression analysis by using the SAS procedure PHREG (release 6.12; SAS Institute, Inc, Cary, NC). After age-adjusted analyses, 2 multivariate models were tested. The first model was adjusted for baseline prevalence of the disease of interest (mortality analyses only), age, smoking status, total energy intake, body mass index, alcohol intake, and physical activity. The second model was additionally controlled for the following dietary factors: coffee consumption, fish consumption, vitamin C, vitamin E, β-carotene, saturated fatty acids, polyunsaturated fatty acids, dietary cholesterol, fiber, and prescribed diet (yes or no). Probability values for a linear trend were derived from tertile medians.

RESULTS

The mean (±SD) catechin intake of the 806 elderly men who participated in 1985 was 72 ± 47.8 mg/d (range: 0–355.4 mg/d). Only one subject had a catechin intake of 0. The major source of

TABLE 1
Baseline characteristics and dietary intakes of 806 elderly men by tertile of total catechin intake[1]

	Tertile of total catechin intake (mg/d)			
	Low (0–49.0)	Middle (49.1–85.8)	High (85.9–355.4)	P^2
No. of men	268	269	269	
No. of men with a history of MI or AP	54	55	57	
No. of men with a history of stroke	20	8	11	
Current smokers (%)	42.2	28.6	19.3	0.001
Never smokers (%)	15.7	16.4	23.4	0.038
Prescribed diet (%)	25.4	24.5	30.1	0.289
Age in 1985 (y)	70.8 ± 5.0[3]	71.9 ± 5.5	71.3 ± 5.2	0.088
Physical activity (min/wk)	657.6 ± 665.2	645.4 ± 617.4	735.4 ± 662.6	0.052
Serum total cholesterol (mmol/L)	6.18 ± 1.1	6.13 ± 1.2	6.03 ± 1.0	0.285
Serum HDL cholesterol (mmol/L)	1.15 ± 0.3	1.11 ± 0.3	1.11 ± 0.3	0.464
Systolic blood pressure (mm Hg)	150.2 ± 20.8	151.6 ± 21.3	150.6 ± 21.6	0.555
BMI (kg/m^2)	25.5 ± 3.5	25.3 ± 2.9	25.6 ± 3.0	0.602
Intake				
Catechin (mg/d)	25.3 ± 15.4	66.8 ± 10.7	124.0 ± 40.0	
Flavonol + flavone (mg/d)	14.0 ± 8.7	24.5 ± 7.8	38.9 ± 13.0	0.0001
Energy (MJ/d)	9.3 ± 2.2	9.3 ± 2.1	9.8 ± 2.1	0.010
Alcohol (g/d)	15.2 ± 18.4	11.9 ± 17.0	12.6 ± 15.6	0.189
Tea (mL/d)	122.9 ± 102.9	390.3 ± 84.9	768.7 ± 276.1	0.0001
Coffee (mL/d)	538.1 ± 340.2	403.1 ± 210.6	364.8 ± 229.5	0.0001
Fish (g/d)	22.1 ± 24.8	16.2 ± 18.8	17.0 ± 21.6	0.002
Fruit (g/d)	177.2 ± 146.0	202.4 ± 139.6	222.2 ± 133.2	0.0001
Vegetables (g/d)	168.8 ± 73.8	173.8 ± 67.0	185.8 ± 73.8	0.011
Vitamin C (mg/d)	87.7 ± 48.3	95.9 ± 42.9	104.7 ± 46.6	0.0001
Vitamin E (mg/d)	8.1 ± 2.6	8.3 ± 2.5	8.7 ± 2.6	0.030
β-Carotene (mg/d)	1.3 ± 0.7	1.4 ± 0.6	1.5 ± 0.6	0.001
Saturated fatty acids (g/d)	43.7 ± 15.6	43.2 ± 13.8	44.3 ± 14.2	0.686
Polyunsaturated fatty acids (g/d)	15.9 ± 8.5	15.9 ± 7.8	16.6 ± 8.1	0.355
Dietary cholesterol (mg/d)	336.6 ± 117.9	335.9 ± 110.7	341.4 ± 127.2	0.842
Fiber (g/d)	23.7 ± 7.7	25.0 ± 6.5	27.5 ± 7.9	0.0001

[1] MI, myocardial infarction; AP, angina pectoris.
[2] Differences between catechin intake tertiles were tested: chi-square test for categorical variables; one-way ANOVA for normally distributed variables (serum total cholesterol, BMI, and vitamin E, saturated fatty acid, dietary cholesterol, fiber, and total energy intakes); and Kruskal-Wallis test for all other variables.
[3] $\bar{x}$ ± SD.

catechins in this population was black tea (87%). Other foods that contributed substantially to catechin intake were apples (8%) and chocolate (3%). Other fruit and legumes were minor sources, whereas vegetables contributed no catechins. For participants in the lowest tertile of catechin intake (<49.1 mg/d) compared with all participants, tea was a less important source (71%), whereas apples (17%) and chocolate (7%) were more important. Of the individual catechins, (−)-epicatechin gallate (34%), (−)-epigallocatechin gallate (26%), and (−)-epicatechin (21%) contributed most to the catechin intake.

At baseline, participants who belonged to the highest tertile of catechin intake were less likely to be current smokers, were more likely to have never smoked, and tended to be more physically active (**Table 1**). They had higher intakes of total energy, fiber, vitamin C, vitamin E, and β-carotene. They ate more fruit and vegetables but ate less fish and drank less coffee. Because tea was the most important source of catechins in this population, tea consumption increased dose-dependently with catechin intake (r = 0.98).

After 10 y of follow-up (6025 person-years), 374 men (46%) had died. Of these men, 90 had IHD as a primary or secondary cause of death and 47 men died of stroke. Age-adjusted catechin intake showed a statistically significant inverse association with the risk of death from IHD (**Table 2**). The risk ratio in the highest tertile of catechin intake was 0.48 (95% CI: 0.28, 0.82). Adjustment for prevalence of MI or AP at baseline, age, physical activity, total energy intake, body mass index, alcohol intake, and smoking status (model 1) and dietary factors (model 2) did not essentially change the relation, nor did additional adjustment for serum total or HDL cholesterol, systolic blood pressure, prevalent hypertension, or prevalent diabetes (data not shown).

Prevalence of MI or AP at baseline was an important determinant of mortality. Catechin intake was inversely associated with IHD mortality both in subjects free of disease at baseline and in subjects with prevalent disease at baseline; there was no statistically significant interaction between catechin intake and baseline disease. When catechin intake was modeled as a continuous variable, an increase in intake of 1 SD (50 mg) was associated with a 25% decrease in risk (95% CI: 0.56, 0.99). Fifty milligrams of catechins is equivalent to 1 cup black tea (200 mL) plus a small piece of dark chocolate (20 g) or to 2 large apples. The age-adjusted association of catechin intake with fatal or nonfatal incidence of MI was not as strong as that with IHD mortality (Table 2). After adjustment for potential confounders, the risk ratio of incidence of MI in the highest tertile of catechin intake was 0.70 (95% CI: 0.39, 1.26) and was no longer statistically significant.

TABLE 2
Risk ratios (RRs) of death from ischemic heart disease and fatal or nonfatal first myocardial infarction in 806 elderly men by tertile of total catechin intake

	Tertile of total catechin intake (mg/d)			
	Low (0–49.0)	Middle (49.1–85.8)	High (85.9–355.4)	*P* for trend
Ischemic heart disease mortality				
No. of men	268	269	269	—
No. of person-years	1908	2039	2078	—
No. of deaths	38	31	21	—
Age-adjusted RR	1.00	0.71 (0.44, 1.15)[1]	0.48 (0.28, 0.82)	0.007
RR-adjusted model 1[2]	1.00	0.73 (0.45, 1.19)	0.46 (0.26, 0.80)	0.006
RR-adjusted model 2[3]	1.00	0.76 (0.46, 1.26)	0.49 (0.27, 0.88)	0.017
Myocardial infarction incidence				
No. of men	230	231	230	—
No. of person-years	1537	1625	1646	—
No. of cases	36	33	21	—
Age-adjusted RR	1.00	0.85 (0.53, 1.37)	0.54 (0.32, 0.93)	0.026
RR-adjusted model 1[2]	1.00	0.90 (0.56, 1.46)	0.63 (0.36, 1.10)	0.103
RR-adjusted model 2[3]	1.00	0.96 (0.58, 1.59)	0.70 (0.39, 1.26)	0.232

[1] 95% CIs in parentheses.
[2] Adjusted for prevalent myocardial infarction or angina pectoris at baseline (mortality analyses only), age, physical activity, total energy intake, BMI, alcohol intake, and smoking status.
[3] Adjusted for above covariates plus prescribed diet and intakes of fish, coffee, saturated fatty acids, polyunsaturated fatty acids, dietary cholesterol, fiber, vitamin C, vitamin E, and β-carotene.

Catechin intake was not associated with the risk of death from stroke nor with the fatal or nonfatal incidence of stroke (**Table 3**).

Catechin intake was highly correlated with both tea consumption ($r = 0.98$) and the intake of flavonols ($r = 0.85$). Therefore, it was impossible to examine the effect of catechin intake on IHD risk after adjustment for flavonol and tea intakes. It was considered important, however, to examine whether flavonols, or some other component of tea, could be responsible for the observed protective effect of a high catechin intake on IHD mortality, rather than catechins as such. If catechins were indeed responsible for the observed protective effect of tea, then catechins from sources other than tea would be expected to be inversely associated with IHD risk as well. Catechin intake from sources other than tea was relatively independent of tea intake ($r = 0.11$) and of flavonol intake from sources other than tea ($r = 0.44$). Also, tea intake was independent of flavonols from sources other than tea ($r = 0.08$). These variables and potential confounders were entered into the model simultaneously (**Table 4**). Tea intake was nearly significantly associated with a reduced risk of IHD death. For catechins from sources other than tea, the risk ratio was 0.80 for an increase of 7.5 mg (SD) in the intake of catechins.

DISCUSSION

In this population of elderly men, age-adjusted catechin intake was inversely related to IHD mortality and MI incidence. Adjustment for cardiovascular disease risk factors, including diet, attenuated the association with MI incidence but not with mortality.

TABLE 3
Risk ratios (RRs) of death from stroke and fatal or nonfatal first stroke in 806 elderly men by tertile of total catechin intake

	Tertile of total catechin intake (mg/d)			
	Low (0–49.0)	Middle (49.1–85.8)	High (85.9–355.4)	*P* for trend
Stroke mortality				
No. of men	268	269	269	—
No. of person-years	1908	2039	2078	—
No. of deaths	17	15	15	—
Age-adjusted RR	1.00	0.73 (0.37, 1.47)[1]	0.74 (0.37, 1.48)	0.404
RR-adjusted model 1[2]	1.00	0.81 (0.39, 1.65)	0.78 (0.37, 1.62)	0.508
RR-adjusted model 2[3]	1.00	1.02 (0.48, 2.16)	0.81 (0.36, 1.83)	0.606
Stroke incidence				
No. of men	255	256	256	—
No. of person years	1724	1784	1824	—
No. of cases	27	36	25	—
Age-adjusted RR	1.00	1.24 (0.75, 2.04)	0.85 (0.49, 1.46)	0.516
RR-adjusted model 1[2]	1.00	1.26 (0.76, 2.09)	0.83 (0.48, 1.46)	0.482
RR-adjusted model 2[3]	1.00	1.40 (0.83, 2.36)	0.92 (0.51, 1.68)	0.749

[1] 95% CIs in parentheses.
[2] Adjusted for prevalent stroke at baseline (mortality analyses only), age, physical activity, total energy intake, BMI, alcohol intake, and smoking status.
[3] Adjusted for above covariates plus prescribed diet and intakes of fish, coffee, saturated fatty acids, polyunsaturated fatty acids, dietary cholesterol, fiber, vitamin C, vitamin E, and β-carotene.

TABLE 4
Intakes of tea, catechins from sources other than tea, and flavonols and flavones from sources other than tea and mutually independent risk ratios (RRs) of ischemic heart disease mortality in 806 elderly men

Intake	Intake	RR-adjusted model 2[1]	*P*
Tea (mL)	427.7 ± 318.7[2]	0.78	0.056
Catechins not from tea (mg)[3]	9.5 ± 7.2	0.80	0.114
Flavonols + flavones not from tea (mg)[4]	10.6 ± 7.6	0.93	0.581

[1] Risk ratios were per an SD increase in intake (320 mL tea, or 7.5 mg catechins or flavonols not from tea). Adjusted for prevalent myocardial infarction or angina pectoris at baseline, age, physical activity, prescribed diet, smoking status, BMI, and intakes of total energy, alcohol, fish, coffee, saturated fatty acids, polyunsaturated fatty acids, dietary cholesterol, fiber, vitamin C, vitamin E, and β-carotene.

[2] $\bar{x}$ ± SD.

[3] (+)-Catechin, (+)-gallocatechin, (−)-epicatechin, (−)-epigallocatechin, and (−)-epicatechin gallate.

[4] Quercetin, kaempferol, myricetin, luteolin, and apigenin.

We observed a significantly lower IHD mortality risk (by 51%) in the highest tertile of catechin intake. The risk of stroke mortality or incidence was not associated with the intake of catechins.

We found that subjects with a high catechin intake were more likely to have never smoked, were less likely to be a current smoker, were more physically active, and had higher intakes of total energy, fiber, fruit and vegetables, vitamins C and E, and β-carotene. It could therefore be hypothesized that a high catechin intake is merely an indicator of a healthy lifestyle. However, adjustment for these variables and additional adjustment for pack-years of smoking and socioeconomic status did not affect the risk ratios for IHD mortality or MI incidence, nor did an analysis restricted to former and never smokers, adjusted for all risk factors and pack-years of smoking. Nevertheless, we cannot rule out residual confounding as an explanation for the protective effect of catechin intake on IHD mortality.

The use of updated dietary data instead of only baseline data has been advocated to reduce measurement error due to intraindividual variation (33). In our study, dietary data were collected at baseline and in 1990. Thus, we repeated our analysis with updated catechin intake data. The results with updated models did not essentially differ from those presented using baseline data only. The men in our study were relatively old; therefore, it is likely that there was little variation over time in their dietary habits. Also, our dietary history method yielded information on the habitual diet. A validation study performed 12 mo after the initial investigation showed that the reproducibility of the dietary history method was sufficient (29).

Because of the high correlations between catechin, flavonol, and tea intakes, it is impossible to clearly discern their effects on IHD risk in this population. Tea consumption was nearly significantly inversely associated with IHD mortality ($P = 0.056$). After adjustment for tea consumption, a 7.5-mg increase in catechin intake from sources other than tea was associated with a tendency for a 20% reduction in risk (NS). The risk reduction of a 7.5-mg increase in flavonol intake was small (7%) and far from significant. These findings suggest that catechins, whether from tea or other sources, may lower the risk of IHD mortality and that, in this population, catechins may be more important than flavonols. Including catechins from sources other than tea might clarify the inconsistencies in reported health effects of tea, particularly in populations in which tea drinking is relatively low (6, 7, 13, 15).

The results of the present study cannot, however, explain the lack of effect of tea consumption reported in the United Kingdom by Woodward and Tunstall-Pedoe (8) and the increased risk reported by Hertog et al (9). Black tea consumption in these populations is twice that of the subjects in our study; therefore, it is unlikely that catechins from sources other than tea played a major role. It has been suggested that the addition of milk to tea, a habit that is common in the United Kingdom but not in the Netherlands, could explain the lack of a protective effect in the UK studies (9). However, milk proteins do not impede the absorption of catechins from the gut (34), which makes this explanation unlikely. The catechin content of tea infusions is influenced by the brewing method and type of tea used, which differ notably between countries and may partially explain the reported differences in effect. Another explanation for the UK findings could be residual confounding. In contrast with tea consumption in most other countries, tea consumption in the United Kingdom is positively associated with a less healthy lifestyle (eg, smoking and fat intake) and with lower social class (8, 9). Residual confounding by inaccurately measured or unmeasured confounders has been suggested as a likely explanation for the reported increased risk of IHD in the Caerphilly Study (9).

Studies on flavonols reported a slightly stronger protective effect on IHD mortality than on MI incidence (2) or a trend toward a protective effect on IHD mortality limited to those who had previously had cardiovascular disease (15). As a consequence, it was suggested that flavonols could possibly influence IHD through platelet aggregation and thrombosis, rather than through reducing atherosclerosis. In our study, we found a similar result for catechins. However, tea was found to protect against the development of severe atherosclerosis, as assessed by radiographic films of the abdomen, in a population-based follow-up study among >6000 men and women (4). Also, we did not find an effect of catechins on stroke risk, which would be expected if platelet aggregation and thrombosis were involved in the causal pathway. An alternative explanation of our findings may therefore be that causes of death were recorded more reliably than were nonfatal events, resulting in larger measurement error and thus weaker associations. Although we took great care to confirm morbidity data from questionnaires with hospital discharge data or written information from the general practitioner, we cannot completely disregard this possibility as an explanation. The number of cases in our study was relatively small and misclassification of a few cases could have attenuated the strength of the association.

To our knowledge, Keli et al (3), using data from the original Zutphen Study cohort, were the first to report on the relation between stroke risk and tea or flavonol intake. They found an inverse association between tea and flavonol intake and incident stroke. We did not find such an effect of catechins in the Zutphen Elderly Study. The power of detecting an effect of catechin intake on stroke risk was low because of the small number of cases of both incident and fatal stroke, but there was also a small number of cases in the study by Keli et al (3). Possibly, the older age of the men in our study played a role in the observed differences, but more research is needed to clarify the relation between stroke risk and intake of flavonoids.

The present prospective study is the first to examine the relation between catechin intake and cardiovascular diseases. In our study of elderly men in the Netherlands, catechin intake was inversely

associated with IHD mortality but not with MI incidence or stroke. The results suggest that catechins other than flavonols could explain the inverse relation between tea consumption and IHD mortality. However, the ability of our study to discern the effects of catechins, flavonols, and tea was limited. More research is needed to verify our results, particularly in populations with a lower intake of tea, to determine whether catechins or other constituents of tea are indeed protective against IHD.

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