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CORRESPONDENCE

Research Correspondence

Chocolate Consumption and Risk of Stroke in Women

To the Editor: Ample evidence indicates that chocolate may have beneficial effects on the cardiovascular system. Chocolate consumption has been shown to reduce systolic and diastolic blood pressure in short-term randomized feeding trials (1), and has been demonstrated to improve endothelial and platelet function and to ameliorate insulin resistance (2). Moreover, flavonoids in chocolate possess strong antioxidant activity and can suppress oxidation of low-density lipoprotein cholesterol (3).

We examined the association between chocolate consumption and risk of stroke in the population-based Swedish Mammography Cohort. In the autumn of 1997, 39,227 women completed a questionnaire that included approximately 350 items concerning diet and other lifestyle factors (4). We excluded women with a missing national identification number, those with implausible values for total energy intake, and those with a history of cancer, stroke, coronary heart disease, or diabetes mellitus before baseline. That left 33,372 women, age 49 to 83 years, for analysis. The study was approved by the Ethical Review Board at the Karolinska Institutet (Stockholm, Sweden). Chocolate consumption was assessed using a self-administered food-frequency questionnaire. Women were asked to indicate how often on average they had consumed chocolate and 95 other foods during the previous year. There were 8 pre-defined consumption categories ranging from never to ≥3 times a day. In the 1990s, approximately 90% of chocolate consumption in Sweden was milk chocolate, containing approximately 30% cocoa solids (5). The food-frequency questionnaire has been validated, and the Spearman correlation coefficient between chocolate intake estimated from the questionnaire and the intake estimated from 28 days of weighted diet records (4 1-week records completed approximately 3 months apart) was 0.4 (A. Wolk, unpublished data, 1992).

Incident cases of first stroke that occurred between January 1, 1998 (information on exact date of returning of the questionnaire was not available), and December 31, 2008, were ascertained by linkage with the Swedish Hospital Discharge Registry. The stroke events were classified as cerebral infarction (International Classification of Diseases-10th revision [ICD-10] code I63), intracerebral hemorrhage (I61), subarachnoid hemorrhage (I60), and unspecified stroke (I64). Information on dates of death was obtained from the Swedish Cause of Death Registry. The Swedish Hospital Discharge Registry provided information on diagnoses of atrial fibrillation (ICD-10 code I48). Cox proportional hazards models with age as the time scale was used to estimate relative risk (RR) and 95% confidence interval (CI) of stroke by exact quartiles of chocolate consumption based on the distribution in the cohort. Entry time was defined as a subject's age in months at start of follow-up, and exit time was defined as a subject's age in months at stroke diagnosis, death, or end of follow-up. The analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, North Carolina). All p values were 2-sided.

During a mean follow-up of 10.4 years, we ascertained 1,549 events of stroke, including 1,200 cerebral infarctions, 224 hemorrhagic strokes, and 125 unspecified strokes. Chocolate consumption was inversely associated with risk of total stroke, cerebral infarction, and hemorrhagic stroke (Table 1). The multivariable RRs for a 50 g/week increase of chocolate consumption were 0.86 (95% CI: 0.77 to 0.96) for total stroke, 0.88 (95% CI: 0.77 to 0.99) for cerebral infarction, and 0.73 (95% CI: 0.54 to 0.99) for hemorrhagic stroke. The difference in risk estimates for cerebral infarction and hemorrhagic stroke was not significant ($p = 0.28$). The association for total stroke persisted after excluding the first year of follow-up (50 g/week increase in intake RR: 0.86; 95% CI: 0.76 to 0.96). In stratified analysis by hypertension, the multivariable RRs of total stroke for 50 g per week increment of chocolate consumption were 0.89 (95% CI: 0.73 to 1.09) for women with a history of hypertension and 0.85 (95% CI: 0.74 to 0.97) for women without hypertension.

Our findings are broadly consistent with those from previous smaller studies, which observed either a statistically significant (136 stroke cases) (6) or a nonsignificant (111 or 469 stroke cases) (5,7) inverse association between chocolate consumption and total stroke. In the present study, only women in the highest quartile of chocolate consumption (median 66.5 g/week) had a significantly reduced risk of stroke, suggesting that higher intakes are necessary for a potential protective effect. The reason for the stronger association observed for hemorrhagic stroke than for cerebral infarction is unclear.

Strengths of this study include its prospective and population-based design, the nearly complete follow-up of participants through linkage with population-based Swedish registers, and the large number of stroke cases. A limitation is that chocolate consumption was self-reported, which will inevitably lead to some measurement error. Because of the prospective design, any misclassification of chocolate consumption is most likely to be nondifferential, leading to an attenuation of the true association between chocolate consumption and stroke. Although we adjusted for major risk factors for stroke, we cannot exclude the possibility that our results may have been affected by residual or unmeasured confounding. However, the similar results in the age-adjusted and multivariable models argue against the possibility of strong residual confounding.

In summary, results from this cohort of women suggest that a high chocolate consumption is associated with a lower risk of stroke.

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Table 1 Relative Risks and 95% Confidence Intervals of Total Stroke and Stroke Subtypes by Quartiles of Chocolate Consumption Among 33,372 Women in the Swedish Mammography Cohort, 1998 to 2008

	Chocolate Consumption, g/week				p Value for Trend†
	<8.9 (8.8)*	8.9–14.0 (14.0)	14.1–45.0 (28.5)	>45.0 (66.5)	
Total stroke					
Person-yrs	118,542	86,019	96,848	45,545	
Cases, n	926	206	303	114	
Age-adjusted	1.00	1.02 (0.84–1.22)	0.91 (0.80–1.05)	0.80 (0.66–0.98)	0.003
Multivariable model‡	1.00	1.04 (0.86–1.25)	0.94 (0.82–1.08)	0.80 (0.66–0.99)	0.01
Cerebral infarction					
Cases, n	737	145	231	87	
Age-adjusted	1.00	0.99 (0.80–1.23)	0.92 (0.79–1.08)	0.82 (0.65–1.03)	0.02
Multivariable model‡	1.00	1.01 (0.81–1.26)	0.95 (0.81–1.11)	0.83 (0.66–1.04)	0.04
Hemorrhagic stroke§					
Cases, n	116	42	49	17	
Age-adjusted	1.00	0.96 (0.63–1.46)	0.85 (0.59–1.21)	0.66 (0.39–1.12)	0.09
Multivariable model‡	1.00	0.95 (0.62–1.45)	0.83 (0.57–1.20)	0.58 (0.34–1.00)	0.04

*Median values in parenthesis. †Test for trend was performed by modeling chocolate consumption as a continuous variable. ‡Adjusted for age, education (less than high school, high school, or university), smoking status and pack-years of smoking (never; past <20, 20 to 39, or ≥40 pack-years; or current <20, 20 to 39, or ≥40 pack-years), body mass index (<20, 20 to 24.9, 25 to 29.9, or ≥30 kg/m^2), total physical activity (metabolic equivalent of energy expenditure hours/day, quartiles), aspirin use (never, 1 to 6, ≥7 tablets/week), self-reported history of hypertension (yes or no), diagnosis of atrial fibrillation (yes or no), family history of myocardial infarction before 60 years of age (yes or no), and intakes of total energy (kcal/day), alcohol (nondrinkers or <3.4, 3.4 to 9.9, or ≥10.0 g/day), coffee (<1, 1 to 2, 3 to 4, or ≥5 cups/day), tea (0, <1, 1 to 1.9, 2 to 3.9, ≥4 cups/day), and quartiles (g/day) of fresh red meat, processed red meat, fish, fruits, and vegetables. §Including 148 intracerebral hemorrhages and 76 subarachnoid hemorrhages.

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REFERENCES

1. Desch S, Schmidt J, Kobler D, et al. Effect of cocoa products on blood pressure: systematic review and meta-analysis. Am J Hypertens 2010; 23:97–103.
2. Corti R, Flammer AJ, Hollenberg NK, Luscher TF. Cocoa and cardiovascular health. Circulation 2009;119:1433–41.
3. Engler MB, Engler MM. The emerging role of flavonoid-rich cocoa and chocolate in cardiovascular health and disease. Nutr Rev 2006;64: 109–18.
4. Larsson SC, Virtamo J, Wolk A. Coffee consumption and risk of stroke in women. Stroke 2011;42:908–12.
5. Janszky I, Mukamal KJ, Ljung R, Ahnve S, Ahlbom A, Hallqvist J. Chocolate consumption and mortality following a first acute myocardial infarction: the Stockholm Heart Epidemiology Program. J Intern Med 2009;266:248–57.
6. Buijsse B, Feskens EJ, Kok FJ, Kromhout D. Cocoa intake, blood pressure, and cardiovascular mortality: the Zutphen Elderly Study. Arch Intern Med 2006;166:411–7.
7. Mink PJ, Scrafford CG, Barraj LM, et al. Flavonoid intake and cardiovascular disease mortality: a prospective study in postmenopausal women. Am J Clin Nutr 2007;85:895–909.

Letters to the Editor

The Early Repolarization Pattern: What's in the Name?

I have read with interest the report by Noseworthy et al. (1) on the prevalence and heritability of the early repolarization pattern (ERP) in the general population. The ERP has for a long time been considered a benign electrocardiographic finding, but recent studies have challenged this view by reporting a significant association with ventricular tachyarrhythmias and sudden cardiac death (2–5). Thus, knowledge of its prevalence and determinants in the general population is relevant for putting ERP in the right clinical perspective. There are 2 major points in Noseworthy et al.'s study, however, that, in my opinion, deserve comment.

The ERP in this study was defined as "J-point elevation of ≥0.1 mV in ≥2 leads in the inferior or lateral territory, or both" (1), a definition similar to that applied in recent studies (2–5). However, how the J point was identified on the electrocardiogram was not specified in any of these studies. I think this issue is relevant, because identification of the J wave cannot be taken for granted. A careful reading of previous studies, indeed, leaves doubts regarding how the J point was located, in particular in the presence of prominent notched or slurred J waves (2–5), and inevitably, a similar concern holds true for the present study (1). Moreover, the definition of the ERP given in this and in recent studies does not fit with what clinical cardiologists usually diagnose as the ERP in their routine clinical practice. In the classic definition of the ERP, the presence of typical up-sloping ST-segment elevation is specifically required (6,7), but this is not taken into any account in the definition adopted in this and in previous studies (1–5).

A second questionable point of the study by Noseworthy et al. (1) is the conclusion that the ERP "has a heritable basis." Indeed,