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Habitual Chocolate Intake and Vascular Disease: A Prospective Study of Clinical Outcomes in Older Women

Cocoa, the principal ingredient of chocolate, is a rich source of flavonoids. Higher flavonoid intakes are associated with a lower risk of cardiovascular disease, and flavonoid-rich cocoa and chocolate can reduce blood pressure and improve endothelial function.¹ Interest in the potential of cocoa and chocolate to prevent cardiovascular disease has been stimulated by recent prospective cohort studies in which consuming more than 2.25 g/d of cocoa (average, 4.2 g/d)

was associated with a 50% lower risk of cardiovascular mortality.^{2,3} Our objective was to investigate the relationship between chocolate consumption and atherosclerotic vascular disease (ASVD) events in a prospective study of older women followed up for 9.5 years. In formulating our prespecified analytical protocol, we hypothesized that the greatest benefit on ASVD risk would likely be for women with daily exposure to the cocoa flavonoids because, to date, much of the reported benefits of cocoa flavonoids on nitric oxide metabolism and endothelial function are short term.⁴

Methods. The participants were recruited in 1998 to a 5-year randomized controlled trial of calcium supplements as described previously.⁵ At baseline, information on food and beverage consumption frequency, medical history and current medications as verified by their general practitioner, physical activity, and socioeconomic status were collected from 1216 women using previously validated questionnaires. The frequency of chocolate consumption was collapsed into the following 3 categories: less than 1 serving/wk (rarely), 1 to 6 servings/wk (weekly), and 7 or more servings/wk (daily). A serving of chocolate weighing 25 to 50 g containing 5% to 15% cocoa by weight is equivalent to a cocoa intake among frequent chocolate consumers of approximately 1 to 5 g/d. The presence of carotid focal plaques and common carotid artery intima-media thickness (CCA-IMT) were assessed once during the study by B-mode carotid ultrasonography. Plaque was defined as a clearly identified area of focal increased thickness (≥ 1 mm) of the intima-media layer. The Western Australian Data Linkage System (WADLS) was used to assess clinical outcomes. This provides a validated record of every hospitalization (from the coded discharge record) and cause of death (from the death certificate) for residents of Western Australia. The use of this data system allows complete ascertainment of verified ASVD events independently of patient report, with the associated problems of loss to follow-up and inaccurate reporting.⁶ Atherosclerotic vascular disease events were defined using diagnosis codes from the *International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Australian Modification (ICD-10-AM)*.⁷ The primary outcome was ASVD events causing either death or hospitalization retrieved from WADLS for each of the study participants from 1998 until 2008.

Results. Of the 1216 participants, 579 (47.6%) had less than 1 serving of chocolate weekly (rarely), 435 (35.8%) had between 1 and 6 servings/wk (weekly), and 202 (16.6%) had at least 7 servings/wk (daily). There were 158 ASVD events (27.3%) in the group that rarely consumed chocolate, compared with 90 events (20.7%) in the group that consumed chocolate weekly, and 42 events (20.8%) in the group that consumed chocolate daily. Because the demographic and outcomes data in the weekly and daily group were similar and because grouping them together to produce a "frequently" group split the cohort at the median frequency of chocolate ingestion, a comparison of the rarely (< 1 serving/wk) and frequently (≥ 1 serving/wk) groups was undertaken.

Table. Atherosclerotic Vascular Disease (ASVD) Hospitalization and Mortality Events Over 9.5 Years According to Frequency of Chocolate Consumption

Event	Chocolate, Servings/wk		P Value
	<1	≥1	
Total No. of women	579	637	
ASVD events			
Events per 1000 person-years	33.2	24.3	
Event, No. (%)	158 (27.3)	132 (20.7)	.01
Age-adjusted HR (95% CI)	1 [Reference]	0.74 (0.59-0.94)	.01
Multivariable-adjusted HR (95% CI) ^a	1 [Reference]	0.76 (0.60-0.97)	.03
Ischemic heart disease events			
Event, No. (%)	88 (15.2)	65 (10.2)	.01
Age-adjusted OR (95% CI)	1 [Reference]	0.65 (0.46-0.92)	.01
Multivariable-adjusted OR (95% CI) ^a	1 [Reference]	0.65 (0.46-0.94)	.02
Heart failure events			
Event, No. (%)	35 (6.0)	18 (2.8)	.01
Age-adjusted OR (95% CI)	1 [Reference]	0.46 (0.26-0.83)	.01
Multivariable-adjusted OR (95% CI) ^a	1 [Reference]	0.41 (0.22-0.76)	.01
Carotid ultrasonography	(n=516)	(n=574)	
Carotid atherosclerotic plaques			
Event, No. (%)	271 (52.5)	263 (45.8)	.03
Age-adjusted OR (95% CI)	1 [Reference]	0.77 (0.61-0.98)	.03
Multivariable-adjusted OR (95% CI) ^a	1 [Reference]	0.77 (0.60-0.98)	.04

Abbreviations: CI, confidence interval; HR, hazard ratio; OR, odds ratio.
^a Multivariable-adjusted for age, body mass index, socioeconomic status, and energy intake at baseline.

Results from ASVD event analyses showed that hospitalization or death was less common in participants who consumed chocolate frequently (**Table**). Compared with women who rarely consumed chocolate, those who consumed chocolate frequently had a significantly lower risk of hospitalization for or death from ischemic heart disease and heart failure in both age and multivariable-adjusted analyses (Table). Women who frequently consumed chocolate also had a significantly lower prevalence of carotid atherosclerotic plaques compared with women who consumed chocolate rarely, but there was no effect on the mean CCA-IMT by age or multivariable-adjusted analysis of variance.

Comment. The data from this prospective cohort study of elderly women are the first, to our knowledge, to show an association between chocolate consumption and carotid atherosclerotic plaque prevalence and provide further evidence that chocolate intake may be protective against atherosclerotic vascular disease events. These data also suggest that weekly chocolate consumption may be as effective as daily consumption to obtain the cardiovascular benefit, since we found similar risk reductions of 24% among daily and weekly chocolate consumers. Furthermore, the association between atherosclerotic plaque prevalence but not CCA-IMT suggests that the effect of habitual chocolate consumption may be primarily on ischemic heart disease risk rather than cerebrovascular disease risk, which is more strongly associated with CCA-IMT.⁸ The observed association between chocolate consumption and atherosclerotic vascular disease is from a prospective study and as such cannot prove causality. However, given the size of the observed risk reduction associated with frequent chocolate consumption for atherosclerotic plaques and atherosclerotic cardiovascular disease, it would be possible to mount a well-designed randomized controlled trial

to determine if indeed cocoa or chocolate would be a safe, acceptable method of reducing atherosclerotic cardiovascular disease in addition to current approaches to the treatment and prevention of atherosclerotic vascular disease.

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