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Chocolate Intake and Incidence of Heart Failure

A Population-Based Prospective Study of Middle-Aged and Elderly Women

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Background—Randomized clinical trials have shown that chocolate intake reduces systolic and diastolic blood pressure, and observational studies have found an inverse association between chocolate intake and cardiovascular disease. The aim of this study was to investigate the association between chocolate intake and incidence of heart failure (HF).

Methods and Results—We conducted a prospective cohort study of 31 823 women aged 48 to 83 years without baseline diabetes or a history of HF or myocardial infarction who were participants in the Swedish Mammography Cohort. In addition to answering health and lifestyle questions, participants completed a food-frequency questionnaire. Women were followed from January 1, 1998, through December 31, 2006, for HF hospitalization or death through the Swedish inpatient and cause-of-death registers. Over 9 years of follow-up, 419 women were hospitalized for incident HF (n=379) or died of HF (n=40). Compared with no regular chocolate intake, the multivariable-adjusted rate ratio of HF was 0.74 (95% CI, 0.58 to 0.95) for women consuming 1 to 3 servings of chocolate per month, 0.68 (95% CI, 0.50 to 0.93) for those consuming 1 to 2 servings per week, 1.09 (95% CI, 0.74 to 1.62) for those consuming 3 to 6 servings per week, and 1.23 (95% CI, 0.73 to 2.08) for those consuming ≥1 servings per day (P=0.0005 for quadratic trend).

Conclusions—In this population, moderate habitual chocolate intake was associated with a lower rate of HF hospitalization or death, but the protective association was not observed with intake of ≥1 servings per day. **(*Circ Heart Fail*. 2010;3:612-616.)**

Key Words: diet ■ epidemiology ■ heart failure

Although heart failure (HF) shares many risk factors with other cardiovascular diseases, such as hyperlipidemia, obesity, and increasing age, elevated blood pressure is a particularly strong risk factor for HF.[1] Seventy-five percent of HF cases have antecedent hypertension, and the lifetime risk for persons with a blood pressure >160/90 mm Hg is double the risk compared with those with a blood pressure <140/90 mm Hg.[2]

Clinical Perspective on p 616

Both short-term randomized feeding trials and long-term observational studies indicate that chocolate products may have beneficial effects for cardiovascular health.[3,4] Two metaanalyses of small, relatively short-duration randomized clinical trials suggested that chocolate reduces both systolic and diastolic blood pressure[5,6] and increases flow-mediated dilation after acute and chronic intake,[6] and others have shown that cocoa flavanoids are associated with decreased susceptibility to low-density lipoprotein oxidation[7] and improved endothelial function.[8] Observational studies have shown that chocolate intake is associated with lower blood pressure,[9,10] lower incidence of stroke and myocardial infarction (MI),[9,10] lower incidence of mortality from coronary heart disease,[4,11] and lower cardiac mortality in patients after their first MI.[12] However, despite clinical trials showing the effect of chocolate on blood pressure and the strong relationship between blood pressure and HF, no prior studies have examined the association between chocolate intake and HF incidence. Therefore, we examined whether chocolate intake is associated with the risk of incident HF hospitalization or mortality in a population of middle-aged and elderly Swedish women.

Methods

Study Population

The recruitment process, characteristics, and study methods of the Swedish Mammography Cohort have been described previously.[13,14] In brief, the cohort includes women born between 1914 and 1948 living in the Västmanland and Uppsala counties of central Sweden. In 1997 and 1998, 39 227 women completed a questionnaire that included items on demographic, behavioral, and anthropometric factors and consumption of foods and beverages. Participants who did not provide or provided incorrect national identification numbers, reported implausible energy intakes (>3 SDs from the natural log-transformed mean), had had cancer (other than nonmelanoma skin cancer), had a history of HF, left more than half of the food and beverage items blank (n=1126), and had missing data on chocolate

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intake (n=3186) were excluded. Additionally, for these analyses, participants who had a history of MI or diabetes at baseline were excluded (n=3092) because persons who develop these diseases receive dietary counseling and may change both their diet and their reporting of diet. Thus, there were 31 823 women with data available for use in this study. History of HF and MI were determined through linkage to the inpatient register; history of diabetes was assessed using self-report and linkage to the inpatient register. The study was approved by the Regional Ethical Review Board at Karolinska Institute (Stockholm, Sweden). Completion and return of the self-administered questionnaire was taken to imply consent.

Diet Assessment

The details of the food-frequency questionnaire have been described previously.[15] Self-administered food-frequency items in questionnaires asked participants to report usual consumption frequency of 96 foods and beverages over the previous year. For foods such as milk, coffee, cheese, and bread, which are commonly eaten in Sweden, participants reported their consumption in servings per day or per week in the past year. For chocolate and other foods, there were 8 predefined responses, ranging from never to ≥3 times per day (no regular intake, 1 to 3 servings per month, 1 to 2 servings per week, 3 to 4 servings per week, 5 to 6 servings per week, 1 serving per day, 2 servings per day, and 3 servings per day). In the 1990s, approximately 90% of chocolate consumption in Sweden was milk chocolate, and it contained approximately 30% cocoa solids.[12] A study comparing our questionnaire to 7-day diet records indicated that among Swedish women aged ≤61 years, the average portion of chocolate was 30 g and 19 g in women aged ≥62 years. In contrast, the standard portion size in the United States is 20 g.[16] Nutrient intake was calculated by multiplying nutrient composition data from the Swedish National Food Administration by age-specific portion sizes determined using weighted diet records and the frequency of consumption. Using the residuals method,[17] nutrient values were adjusted to 1700 kcal per day, the mean energy intake from diet records of women from central Sweden.

Assessment of Other Covariates

History of MI at baseline and incident MI during follow-up were assessed through the Swedish inpatient register. We considered participants to have diabetes if they self-reported diabetes on the questionnaire or had been given any diagnosis of diabetes as recorded in the inpatient register. Total physical activity (metabolic equivalent in hours per day) was estimated using information collected on the study questionnaires regarding occupational physical activity, exercise, and sedentary behavior.[18] Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). The questionnaire included items on education (less than high school, high school, university), cigarette smoking (current, past, never), alcohol consumption (frequency of consumption of beer, wine, and spirits), family history of MI before age 60 (yes, no), history of hypertension (yes, no), history of high cholesterol (yes, no), and postmenopausal hormone use (yes, no).

Follow-Up and Ascertainment of HF

Participants contributed follow-up time from January 1, 1998, until the earliest of the following: December 31, 2006, date of death of causes other than HF, or HF hospitalization or mortality. Participants were followed through record linkage to the Swedish inpatient and cause-of-death registers. The inpatient register captures >99% of inpatient care.[19] Hospitalization for or death of HF was identified by *International Classification of Diseases, Ninth Edition*, code 428 or *International Classification of Diseases, 10th Edition*, I50 or I11.0. Ingelsson and colleagues[20] found that 95% of persons given these codes as a primary diagnosis in the inpatient register had HF on medical record review using European Society of Cardiology criteria. We only included hospitalizations or deaths with HF listed as the primary diagnosis and only the first HF event recorded in the registers for each individual. Incident MI during follow-up also was assessed through the inpatient register.

Statistical Analysis

Chocolate intake was categorized as no regular chocolate intake, 1 to 3 servings of chocolate per month, 1 to 2 servings per week, 3 to 6 servings per week, and ≥1 servings per day. Because some of the participants were missing data on BMI (1.3%) and physical activity (19.7%), we used Markov chain Monte Carlo multiple imputation to simulate 5 complete data sets, as previously described.[14,21] All statistical analyses described were performed in each data set separately. The results were averaged, and CIs and *P* values were calculated, accounting for the uncertainty in the imputed estimates.[21]

We reported baseline characteristics stratified by category of chocolate intake as mean±SD or as counts with proportions, as appropriate, and the corresponding *P* value for the ANOVA or χ^2 test. We used Cox proportional hazards models to compute multivariable-adjusted rate ratios with corresponding 95% CIs, with participants in the lowest category of chocolate intake as the reference group. For the Cox proportional hazards models, we chose covariates a priori that we considered potential confounders on the basis of their association with both chocolate intake and development of HF. We accounted for the effect of age by allowing the baseline rate to vary with age and adjusted for total energy intake (linear term). A second model was additionally adjusted for education (less than high school, high school, university), BMI (linear term), physical activity (linear term), cigarette smoking (current, past, never), living alone (yes, no), postmenopausal hormone use (yes, no), alcohol consumption (linear term), family history of MI before age 60 (yes, no), self-reported history of hypertension (yes, no), and self-reported history of high cholesterol (yes, no). To examine whether the inverse association between chocolate intake and HF was mediated through blood pressure, the rate ratios for chocolate intake in the multivariable-adjusted model were contrasted with the estimates for chocolate intake when an indicator variable for hypertension was removed from the model.

We conducted a test for the quadratic component of trend by assigning an ordinal score (0, 1, 2, 3, or 4) for each level of chocolate intake and determined the statistical significance of its squared value in the multivariable model. To examine the possibility that participants reporting lower intake of chocolate had undiagnosed risk factors placing them at immediate HF risk, we conducted a sensitivity analysis that excluded individuals with a follow-up time of <2 years.

Because milk consumption may inhibit the intestinal absorption of flavanoids, which may be responsible for the cardioprotective effects of chocolate,[22] we examined the association between chocolate intake and HF above and below the median milk consumption. We performed formal tests of interaction by conducting a likelihood ratio test of nested models with and without all interaction terms of the product of indicator variables for chocolate intake and milk consumption above or below the median. We also examined whether the association varied by regular physical activity, an indicator of general health, by performing a similar test of interaction. We calculated the product of indicator variables for chocolate intake and for physical activity (metabolic equivalent of task×hours per day) above or below the median and tested the significance of this term in the multivariable model using a likelihood ratio test.

Finally, we tested whether intake of other snack foods is associated with HF risk by creating a variable for total servings per day of biscuits, pastries, candy, ice cream, and chips and popcorn. We tested the proportional hazards assumption by including product terms of the predictors and the log of survival time, and we found no significant violations. Statistical analyses were performed using SAS version 9.2. Two-sided $P<0.05$ was considered statistically significant.

Results

Over 9 years of follow-up, 419 of 31 823 women were hospitalized for HF for the first time (n=379) or died of HF (n=40), corresponding to a rate of 15.1 cases per 10 000 person-years. Women with higher levels of chocolate intake had higher levels of total calorie intake and were more likely to use postmenopausal hormone therapy and to have com-

Table 1. Baseline Characteristics of 31 823 Respondents by Chocolate Intake

Characteristic	No Intake (n=4705)	1–3 Servings/mo (n=16 912)	1–2 Servings/wk (n=7648)	3–6 Servings/wk (n=2046)	≥1 Servings/d (n=512)	*P*
Age, y	62.1±9.0	60.4±8.6	60.0±8.6	60.4±8.9	64.7±9.9	<0.0001
Physical activity, MET h/d	42.6±5.0	42.5±4.7	42.3±4.6	41.8±4.6	41.7±5.1	<0.0001
BMI, kg/m^2	25.2±4.2	25.0±3.9	24.7±3.7	24.3±3.9	23.9±3.8	<0.0001
Cigarette smoking*						0.0002
Never	2437 (51.8)	8819 (52.2)	3954 (51.7)	990 (48.4)	263 (51.4)	
Past	1135 (24.1)	4055 (24.0)	1793 (23.4)	458 (22.4)	110 (21.5)	
Current	1076 (22.9)	3788 (22.4)	1778 (23.3)	561 (27.4)	127 (24.8)	
Living alone	3361 (71.4)	13 057 (77.2)	5899 (77.0)	1495 (73.1)	332 (64.8)	<0.0001
Postmenopausal hormone therapy	2217 (47.1)	8511 (50.3)	3865 (50.5)	1129 (55.2)	245 (47.9)	<0.0001
Education†						<0.0001
Less than high school	3624 (77.0)	12 216 (72.2)	5163 (67.5)	1286 (62.9)	355 (69.3)	
High school	362 (7.7)	1396 (8.3)	719 (9.4)	197 (9.6)	43 (8.4)	
University	695 (14.8)	3263 (19.3)	1757 (23.0)	557 (27.2)	113 (22.1)	
Family history of MI before age 60	716 (15.2)	2360 (14.0)	944 (12.3)	238 (11.6)	57 (11.1)	<0.0001
History of hypertension	1048 (22.3)	3203 (18.9)	1321 (17.3)	368 (18.0)	92 (18.0)	<0.0001
History of high cholesterol	433 (9.2)	1323 (7.8)	535 (7.0)	158 (7.7)	30 (5.9)	0.0002
Energy intake, kcal/d	1644.3±524.2	1721.6±490.1	1842.5±500.7	1966.9±517.1	2202.0±681.0	<0.0001
Alcohol consumption, g/d	3.7±5.8	4.3±5.1	4.9±5.1	5.6±5.8	5.0±6.7	<0.0001

Data are presented as mean±SD or no. (%). MET indicates metabolic equivalent of task.
*479 with no data on smoking history.
†23 with no data on education level.

pleted university-level education (Table 1). However, these associations are likely to be mutually confounded.

Compared with no regular chocolate intake, the multivariable-adjusted rate ratio of HF was 26% lower among women who consumed 1 to 3 servings of chocolate per month and 32% lower among those who consumed 1 to 2 servings of chocolate per week, but the rate of HF was similar among women with no regular chocolate intake and those who consumed 3 to 6 servings per week (hazard ratio, 1.09; 95% CI, 0.74 to 1.62) and those who consumed ≥1 servings per day (hazard ratio, 1.23; 95% CI, 0.73 to 2.08). Although not all of these estimates were statistically significant, there was a statistically significant quadratic trend, suggesting a J-shaped relationship between chocolate intake and HF (P=0.0005 for quadratic trend) (Table 2). Results were not materially different when we did not adjust for self-reported hypertension and when we restricted the analysis to participants with follow-up times >2 years.

We found that the association between chocolate intake and HF was similar in the high and low dairy intake groups (P=0.34 for interaction), and the association between chocolate intake and HF did not differ between women with a high and low level of physical activity (P=0.70 for interaction). Finally, the consumption of biscuits, pastries, candy, ice cream, and chips and popcorn, which were all strongly related to chocolate intake, was not associated with HF (P=0.84).

Discussion

In this prospective study, we found that moderate habitual chocolate intake was associated with a lower rate of HF hospitalization or death, but the protective association was not observed with intake of ≥3 servings per week. Results

Table 2. Rate Ratios and 95% CIs Comparing Different Levels of Chocolate Intake to Those Reporting No Chocolate Intake

Chocolate Intake	Cases	Person-Years	Model 1*	Model 2†
None	93	40 497.61	1.00 (reference)	1.00 (reference)
1–3 servings/mo	194	147 768.51	0.71 (0.56–0.91)	0.74 (0.58–0.95)
1–2 servings/wk	78	66 935.77	0.66 (0.48–0.89)	0.68 (0.50–0.93)
3–6 servings/wk	36	17 791.75	1.02 (0.69–1.51)	1.09 (0.74–1.62)
≥1 servings/d	18	4285.00	1.14 (0.68–1.90)	1.23 (0.73–2.08)
P for quadratic trend			0.0003	0.0005

*Cox proportional hazards model adjusted for total energy intake (linear term) and accounting for age.
†Additionally adjusted for education (less than high school, high school, university), BMI (linear term), physical activity (linear term), cigarette smoking (current, past, never), living alone (yes, no), postmenopausal hormone use (yes, no), alcohol consumption (linear term), family history of MI before age 60 (yes, no), self-reported history of hypertension (yes, no), and self-reported history of high cholesterol (yes, no).

were similar when we did not adjust for self-reported hypertension and when we restricted the analysis to participants with follow-up times >2 years. Furthermore, consumption of snacks all were strongly related to chocolate intake but was not associated with HF, suggesting a specific association between chocolate and HF incidence.

Chocolate is one of the most concentrated sources of flavanoids,[23] a subclass of polyphenols. Short-term randomized feeding trials suggest that the flavanoids in chocolate may be responsible for the improvement in cardiovascular risk factors.[3,4] Some[5,6,24] but not all[25,26] feeding trials have indicated that chocolate intake significantly reduces systolic and diastolic blood pressure, possibly by acting as an angiotensin-I-converting enzyme inhibitor.[27,28] Flavanoids may protect against low-density lipoprotein oxidation[8,29,30] through increased antioxidant capacity and diminished production of oxidative products in plasma.[7] The increased production of NO also causes increased vasodilation and inhibits platelet aggregation.[8] Cocoa and chocolate intake is associated with lower platelet activation after a single dose,[31–34] improved endothelial function,[35–38] increased high-density lipoprotein cholesterol,[39] and reduced inflammation.[40,41] Dark chocolate also has been shown to influence metabolic function. Daily intake of 100 g of dark chocolate for 2 weeks reduced fasting insulin and glucose levels and decreased glucose and insulin responses after an oral glucose load.[42,43]

Although the association between chocolate intake and HF is not known, there have been observational studies documenting its association with lower blood pressure,[9,10] lower incidence of stroke and MI,[9,10] lower incidence of mortality from coronary heart disease,[4,11] and lower cardiac mortality in patients after their first MI.[12] Furthermore, a recent metaanalysis reported that flavanoid intake is associated with decreased cardiovascular mortality.[4]

There are several limitations of this study that warrant discussion. Although we had extensive data on lifestyle, diet, and comorbid conditions, we cannot rule out residual or unmeasured confounding. However, our results are robust after using multivariable analyses that adjust for age, socioeconomic status, smoking status, and other potential confounders.[17] Our food-frequency questionnaire was validated in a study comparing 4 7-day open-ended diet records to the food-frequency questionnaire[15] and indicates that intake of sweets was well reported (Spearman correlation, 0.6). Furthermore, if the misclassification of chocolate was unrelated to HF incidence, the results would likely be an underestimate of the protective effect of chocolate. Chocolate consumption and risk factors were only measured at baseline, so we have no information on how changes in chocolate consumption may have affected a participant's risk of incident HF.

In the European Union, dark chocolate must consist of at least 35% cocoa solids, and in the United States, the minimum is set at 15%.[12] Despite the fact that most of the chocolate consumed in our sample probably contained relatively low concentrations of the potentially protective ingredients (approximately 30% cocoa solids[12]), we still saw a statistically significant trend, suggesting that our findings may underestimate the protective effects of dark chocolate.

Our observed incidence rate of HF of 15.1 cases per 10 000 person-years is similar to the reported incidence rate among women in the national Swedish registers discharged in 2000 (17.1 cases per 10 000 person-years).[44] Although the accuracy of the diagnosis of HF in the Swedish registers was shown to be high,[20] only cases of HF that resulted in hospitalization or death were recorded. In addition, the registers do not contain information on HF etiology or subtype (systolic versus diastolic). Our assessment of hypertension and high cholesterol was based on self-report, which is inherently less reliable than clinical measurement.

On the other hand, this study has many strengths, including a large sample size and long duration of follow-up. Further, the prospective nature of our study reduces the potential for bias caused by differential recall of chocolate intake by cases and noncases of HF.

In conclusion, in this population of middle-aged and elderly Swedish women, moderate habitual chocolate intake was associated with a lower rate of HF hospitalization or death, but the protective association was not observed with intake of ≥1 servings per day. Further studies are needed to confirm or refute these findings, determine the optimal dose and type of chocolate, and clarify the mechanisms involved.

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Disclosures

None.

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CLINICAL PERSPECTIVE

Although the association between chocolate intake and heart failure (HF) is not known, there have been observational studies documenting its association with lower incidence of hypertension and cardiovascular and overall mortality. Therefore, we evaluated the association between chocolate consumption and incidence of HF using data from the Swedish Mammography Cohort. The study population included 31 823 women aged 48 to 83 years without baseline diabetes or a history of HF or myocardial infarction. Compared with no regular chocolate intake, the multivariable-adjusted rate ratio of HF was 0.74 (95% CI, 0.58 to 0.95) for women consuming 1 to 3 servings of chocolate per month, 0.68 (95% CI, 0.50 to 0.93) for those consuming 1 to 2 servings per week, 1.09 (95% CI, 74 to 1.62) for those consuming 3 to 6 servings per week, and 1.23 (95% CI, 0.73 to 2.08) for those consuming ≥1 servings per day (P=0.0005 for quadratic trend). On the basis of these results, moderate chocolate consumption appears to be protective against HF incidence among women in the Swedish Mammography Cohort. Definitive proof would require a large-scale randomized clinical trial, which is unlikely to occur in the near future.