Chocolate Intake and Incidence of Heart Failure: A Population-Based, Prospective Study of Middle-Aged and Elderly Women

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Abstract

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 48–83 years old without baseline diabetes or a history of HF or myocardial infarction who were participants in the Swedish Mammography Cohort. In addition to 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 to no regular chocolate intake, the multivariate-adjusted rate ratio of HF was 0.74 (95%CI 0.58–0.95) for those consuming 1–3 servings of chocolate per month, 0.68 (95%CI 0.50–0.93) for those consuming 1–2 servings per week, 1.09 (95%CI .74–1.62) for those consuming 3–6 servings per week and 1.23 (95%CI 0.73–2.08) for those consuming one or more servings per day (p for quadratic trend = 0.0005).

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 one or more servings per day.

Keywords

diet; epidemiology; heart failure

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INTRODUCTION

While 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 heart failure[1]. Seventy-five percent of HF cases have antecedent hypertension, and the lifetime risk for people with a blood pressure >160/90 mm Hg is double the risk compared to those with a blood pressure <140/90 mm Hg[2].

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 meta analyses of small, relatively short-duration randomized clinical trials suggest that chocolate reduces both systolic and diastolic blood pressure[5, 6] and increases flow-mediated dilation (FMD) after acute and chronic intake[6] and others have shown that cocoa flavanoids are associated with decreased susceptibility to LDL 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 (CHD)[4, 11] and lower cardiac mortality in patients surviving 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 previously described[13, 14]. In brief, the cohort includes women born between 1914 and 1948 living in Västmanland and Uppsala counties in 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, who reported implausible energy intakes (>3 standard deviations from the natural logarithm-transformed mean), who had a previous diagnosis of cancer (other than non-melanoma skin cancer), who had a history of HF or who left more than half of the food and beverage items blank (n = 1,126) and participants with missing data on chocolate intake (n = 3,186) were excluded. Additionally for these analyses, participants who had a history of myocardial infarction (MI) or diabetes at baseline were excluded (n = 3,092) because people 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 frequency of consumption of 96 foods and beverages over the previous year. For foods such as milk, coffee, cheese, and bread that 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/day (no regular intake, 1–3/servings per month, 1–2 servings per week, 3–4 servings per week, 5–6 servings per week, 1 serving per day, 2 servings per day, and 3 servings per day). In the 1990's, 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 61 years of age or younger, the average portion of chocolate was 30 grams and 19 grams in women 62 years of age and older. In contrast, the standard portion size in the US is 20 grams[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 1,700 kcal/d, the mean energy intake from diet records of women from central Sweden.

Assessment of Other Covariates

History of myocardial infarction (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 any diagnosis of diabetes 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 (kilogram) divided by height squared (square meter). The questionnaire included questions 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 from 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 more than 99% of inpatient care[19]. Hospitalization for or death from HF was identified by codes 428 (International Classification of Disease-9), I50, or I11.0 (International Classification of Disease-10). Ingelsson and colleagues found that 95% of people with these codes as primary diagnosis in the inpatient register had HF on medical record review using European Society of Cardiology criteria[20]. 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 was also assessed through the inpatient register.

Statistical Analysis

Chocolate intake was categorized as no regular chocolate intake, 1–3 servings of chocolate per month, 1–2 servings per week, 3–6 servings per week and one or more servings per day. Because some of the participants were missing data on body mass index (1.3%) and physical activity (19.7%), we used Markov chain Monte Carlo multiple imputation to simulate five complete datasets, as previously described[14, 21]. All statistical analyses described were performed in each of the datasets separately. The results were averaged, and confidence intervals (CI) 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 ± standard deviation or as counts with proportions, as appropriate and the corresponding p-value for the ANOVA or chi-square test. We used Cox proportional hazards models to

compute multivariable-adjusted rate ratios with corresponding 95% confidence intervals with subjects in the lowest category of chocolate intake as the reference group. For the Cox models, we chose covariates *a priori* that we considered potential confounders based on 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 intake (linear term), family history of MI before 60 years (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. In order to examine the possibility that subjects reporting lower intake of chocolate had undiagnosed risk factors placing them at immediate HF risk, we conducted a sensitivity analysis excluding individuals with a follow up time of less than 2 years.

Since milk consumption may inhibit the intestinal absorption of flavanoids, which may be responsible for the cardio-protective 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/d) 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/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 (Cary, NC). Two-sided p-value < 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 they were more likely to use postmenopausal hormone therapy and to have completed university (Table 1). However, these associations are likely to be mutually confounded.

Compared to no regular chocolate intake, the multivariate-adjusted rate ratio of HF was 26% lower among those who consumed 1–3 servings of chocolate per month and 32% lower among those who consumed 1–2 servings of chocolate per week, but the rate of HF was similar among women with no regular chocolate intake and those who consumed chocolate

3–6 servings per week (HR=1.09, 95%CI 0.74–1.62) and those who consumed one or more servings per day (HR=1.23, 95%CI 0.73–2.08). Though 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 for quadratic trend = 0.0005; Table 2). Results were not materially different when we did not adjust for self-reported hypertension and when we restricted the analysis to subjects with follow-up times greater than 2 years.

We found that the association between chocolate intake and HF was similar in the high and low dairy groups (p-value for interaction=0.34) and the association between chocolate intake and HF did not differ between subjects with a high and low level of physical activity (p-value for interaction =0.70). Finally, the consumption of biscuits, pastries, candy, ice cream and chips/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 three or more servings per week. Results were similar when we did not adjust for self-reported hypertension and when we restricted the analysis to subjects with follow-up times greater than 2 years. Furthermore, consumption of snacks were all 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 reduced systolic and diastolic blood pressure, possibly by acting as an angiotensin I converting enzyme inhibitor[27, 28]. Flavanoids may protect against LDL oxidation[8, 29, 30] through increased antioxidant capacity and diminished production of oxidative products in plasma[7]. The increased production of nitric oxide 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 HDL[39] and reduced inflammation[40, 41]. Dark chocolate has also 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 myocardial infarction (MI)[9, 10], lower incidence of mortality from coronary heart disease (CHD)[4, 11] and lower cardiac mortality in patients surviving their first MI[12]. Furthermore, a recent meta-analysis reported that flavanoid intake is associated with decreased cardiovascular mortality[4].

There are several aspects 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 four 7-day open-ended diet records to the food-frequency questionnaire[15] and indicates that the reporting of 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 impacted a participant's risk of incident heart failure.

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 heart failure of 15.1 cases per 10,000 woman-years is similar to the reported incidence rate among women in the national Swedish registers discharged in 2000 (17.1 cases per 10,000 woman-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 vs. 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 and the prospective nature of our study reduces the potential for bias caused by differential recall of chocolate intake by cases and non-cases 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 one or more servings per day. Further studies are needed to confirm or refute these findings and to determine the optimal dose and type of chocolate and to clarify the mechanisms involved.

Acknowledgments

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Table 1

Baseline characteristics of 31,823 respondents by chocolate intake; Mean ±standard deviation or n(%)

	None (n=4705)	1–3 servings / month (n=16912)	1–2 servings / week (n=7648)	3–6 servings / week (n=2046)	≥1 servings / day (n=512)	P-Value*
Age (y)	62.1±9.0	60.4±8.6	60.0±8.6	60.4±8.9	64.7±9.9	<.0001
Physical activity (MET hr/d)*	42.6±5.0	42.5±4.7	42.3±4.6	41.8±4.6	41.7±5.1	<.0001
Body mass index (kg/m²)	25.2±4.2	25.0±3.9	24.7±3.7	24.3±3.9	23.9±3.8	<.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)	13057 (77.2)	5899 (77.0)	1495 (73.1)	332 (64.8)	<.0001
Postmenopausal hormone therapy (%)	2217 (47.1)	8511 (50.3)	3865 (50.5)	1129 (55.2)	245 (47.9)	<.0001
Education (%) ***						<.0001
Less than high school	3624 (77.0)	12216 (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 60 (%)	716 (15.2)	2360 (14.0)	944 (12.3)	238 (11.6)	57 (11.1)	<.0001
History of hypertension (%)	1048 (22.3)	3203 (18.9)	1321 (17.3)	368 (18.0)	92 (18.0)	<.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	<.0001
Alcohol (g/d)	3.7±5.8	4.3±5.1	4.9±5.1	5.6±5.8	5.0±6.7	<.0001

*
MET= Metabolic Equivalent of Task

**
479 with no data on smoking history

***
23 with no data on education level

Table 2

Rate ratios and 95% confidence intervals comparing different levels of chocolate intake to those reporting no chocolate intake

Chocolate Intake	Cases	Person Years	Model 1[*]	Model 2[†]
None	93	40497.61	1.00 (reference)	1.00 (reference)
1–3 servings per month	194	147768.51	0.71 (0.56–0.91)	0.74 (0.58–0.95)
1–2 servings per week	78	66935.77	0.66 (0.48–0.89)	0.68 (0.50–0.93)
3–6 servings per week	36	17791.75	1.02 (0.69–1.51)	1.09 (0.74–1.62)
≥1 servings per day	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), body mass index (linear term), physical activity (linear term), cigarette smoking (current, past, never), living alone (yes, no), postmenopausal hormone use (yes, no), alcohol intake (linear term), family history of myocardial infarction before 60 years (yes, no), self-reported history of hypertension (yes, no), and self-reported history of high cholesterol (yes, no).