Original Article

Chocolate Consumption Does Not Reduce the Risk of Cardiovascular Events and Increases the Risk of Gastrointestinal Bleeding One Year After the First Myocardial Infarction

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Abstract

Background: **Coronary artery disease is the leading cause of death worldwide, with high social and financial costs. Although previous studies have demonstrated the potential of chocolate to reduce coronary events, data on its effects in patients who have suffered an acute myocardial infarction (AMI) are lacking.**

Objective: **To evaluate the impact of chocolate consumption on the incidence of events in patients with AMI followed for one year.**

Methods: **A subanalysis of the Catarina Heart study, which evaluated patients hospitalized with a diagnosis of the first AMI, was conducted. During hospitalization, patients were asked about their chocolate consumption before the event. The incidence of events was compared between consumers and non-consumers of chocolate before the AMI. The analyzed outcomes included major adverse cardiovascular events (MACE), all-cause mortality, cardiovascular mortality, reinfarction, stroke, in-stent restenosis, acute stent thrombosis, gastrointestinal bleeding, and bleeding requiring transfusion. Cox regression models were applied, and $p < 0.05$ was considered statistically significant.**

Results: **A total of 1404 patients were analyzed, of whom 490 (34.9%) consumed chocolate. Chocolate consumption neither reduced the risk of MACE (hazard ratio [HR] = 0.88 [0.57 - 1.37], p = 0.569) nor showed benefits in other outcomes, such as cardiovascular mortality, reinfarction, or stroke. However, its consumption was significantly associated with an increased risk of gastrointestinal bleeding (HR = 2.89 [1.16 - 7.24], p = 0.023) without increasing the risk of bleeding requiring transfusion or acute stent thrombosis.**

Conclusion: **Chocolate consumption before AMI did not reduce major cardiovascular events and was associated with an increased risk of gastrointestinal bleeding.**

Keywords: **Coronary Artery Disease; Infarction; Chocolate; Hemorrhage.**

Introduction

Coronary artery disease is the leading cause of death worldwide and presents a great social and financial burden for healthcare systems.[1] Although the entire process of atherosclerotic plaque formation and progression to myocardial infarction is driven by inflammation, few therapies targeting this mechanism are available (e.g., colchicine).[2,3]

In this context, foods with bioactive properties, such as chocolate, have drawn interest for their potential cardiovascular benefits. Prospective studies and meta-analyses have demonstrated that chocolate consumption may reduce the incidence of coronary events.[4-6] Chocolate composition varies according to cocoa content; for example, dark chocolate is rich in flavonoids (epicatechin, catechin, and procyanidins) and methylxanthines (theobromine and caffeine).[7] Chocolate and cocoa are not interchangeable terms. Cocoa refers to the non-fat component of cocoa liquor (finely ground cocoa beans), which is used in chocolate production or as cocoa powder, typically containing about 12% fat. Cocoa liquor contains approximately 55% cocoa butter, and the remaining part is composed of cocoa solids, often indicated on chocolate packages. In contrast, chocolate is the final solid product resulting from the combination of cocoa, cocoa butter, sugar, and other ingredients.[8]

Cocoa flavonoids have antioxidant properties, improve endothelial function, reduce inflammatory markers, and are considered the main compound responsible for the cardioprotective effects of chocolate.[6] Furthermore, methylxanthines may potentiate the effects of flavonoids on endothelial function.[9] Small clinical trials suggest that chocolate

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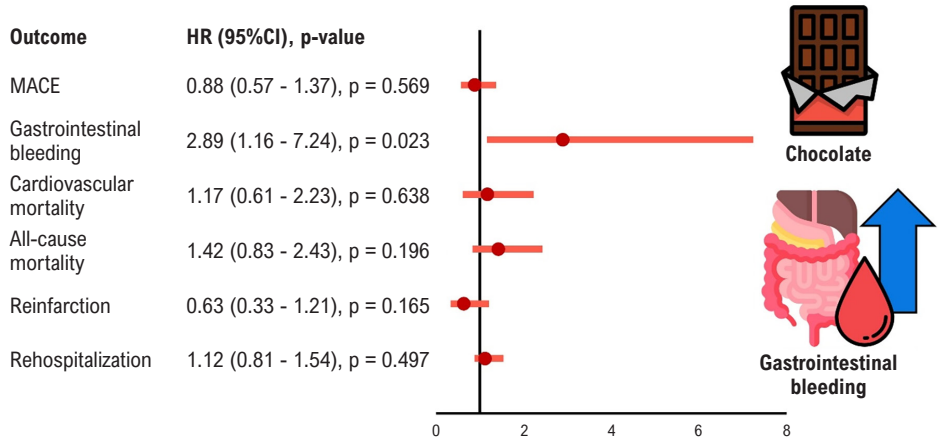
Central Illustration: Chocolate Consumption Does Not Reduce the Risk of Cardiovascular Events and Increases the Risk of Gastrointestinal Bleeding One Year After the First Myocardial Infarction



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MACE: major adverse cardiovascular events; HR: hazard ratio; CI : confidence interval.

may have antiplatelet and anticoagulant properties; thus, contributing to its protective role.[10,11]

Despite evidence supporting the potential role of chocolate in preventing coronary events, significant gaps remain in data regarding its benefits or risks in patients with a history of major coronary events. Moreover, current guidelines for the management of patients with acute myocardial infarction (AMI) or atherosclerosis prevention do not include specific recommendations for chocolate consumption.[12-14] Therefore, this study aimed to assess the potential effects of chocolate consumption on the incidence of events in patients who have experienced a first AMI, with a one-year follow-up.

Methods

This is an exploratory subanalysis of the Catarina Heart study, a prospective cohort that investigated patients diagnosed with first AMI according to the Third Universal Definition of Myocardial Infarction (in effect at the time of the study).[15,16] Data were collected consecutively and by convenience using individual interviews with patients diagnosed with their first AMI. Data were recorded in a structured questionnaire and supplemented with information obtained from electronic medical records.

Inclusion criteria were age over 18 years, chest pain suggestive of AMI associated with an electrocardiogram (new ST-segment ≥ 0.1 mV at the J point in two contiguous leads except V2-V3, in which the thresholds were ≥ 0.2 mV for men older than 40 years, ≥ 0.25 mV for men younger than 40 years, and ≥ 0.15 mV for women), or chest pain suggestive of AMI associated with elevated troponin I or CK-MB above the 99th percentile of the upper reference limit. Exclusion criteria were a previous history of AMI and refusal or inability to sign the informed consent form.

The primary outcome of the study was the comparison of the incidence of major adverse cardiovascular events (MACE) (i.e., cardiovascular mortality, reinfarction, or stroke) after the first year in patients with or without chocolate consumption before the first event. Secondary outcomes included the comparison between patients who did or did not consume chocolate before the first AMI: all-cause mortality, cardiovascular mortality, reinfarction, stroke, intrastent restenosis, acute stent thrombosis, gastrointestinal bleeding, and bleeding requiring transfusion.

Epidemiological data and information regarding chocolate consumption were collected using a specific questionnaire applied by a trained researcher. Patients hospitalized with a diagnosis of first AMI were asked about their consumption of dark chocolate in the weeks preceding hospitalization, excluding white chocolate, which does not contain cocoa. The cocoa content of the chocolate consumed was not assessed. Participants reported the intake in "bars per week", with each bar averaging 43 g. Although the quantity consumed was recorded, this study evaluated only the presence or absence of chocolate consumption. Outcomes were assessed by reviewing medical records after one year of follow-up; if necessary, patients without outpatient follow-up were contacted by phone.

A sample size of 944 patients was calculated to be sufficient to detect an absolute risk reduction of 3.9% (90% power and alpha of 0.05) when comparing consumers and non-consumers of chocolate.

This study was approved by the institutional research ethics committee following resolution 466/12 of December 12, 2012, of the Brazilian Health Council, based on the principles of beneficence, non-maleficence, justice, and autonomy.

Statistical analysis

Data were tabulated and analyzed using the Statistical Package for Social Sciences software, version 13.0 (IBM Corp, Illinois, USA). Categorical variables were presented as absolute and relative frequencies, whereas continuous variables were expressed as mean ± standard deviation. Normality was assessed using the Kolmogorov-Smirnov test. Continuous and categorical variables were compared using the unpaired t-test and chi-square test, respectively. Cox regression models included chocolate consumption, body mass index, age, and variables associated with chocolate consumption in the univariate analysis (alcohol use, diabetes mellitus, and family history). A p-value < 0.05 was considered statistically significant, and confidence intervals were set at 95%.

Results

A total of 1404 patients with a first AMI were assessed between July 2016 and July 2024; of these, 1099 patients were followed up after one year. ST-segment elevation myocardial infarction was the reason for hospitalization in 662 (47.4%) cases, and 490 patients (34.9%) reported chocolate consumption (Table 1).

A comparative analysis of risk factors revealed that consumers had a lower prevalence of diabetes mellitus (23.9%) than non-consumers of chocolate (29.5%; p = 0.027). In contrast, the prevalence of alcohol use was higher in consumers (36.5%) than in non-consumers (29.3%; p = 0.006). Additional comparisons are detailed in Table 2.

Table 1 – Baseline characteristics of patients*

Characteristic	All patients	Patients with a 1-year follow-up
Age (years)	60.9 ± 11.6	61.0 ± 11.5
LVEF (%)	51.5 ± 12.5	51.0 ± 12.5
BMI (kg/m^2)	27.8 ± 5.1	27.7 ± 5.2
Female – n (%)	459 (32.7)	366 (33.3)
SAH – n (%)	826 (59.0)	651 (59.3)
Diabetes mellitus – n (%)	385 (27.5)	296 (27.0)
Dyslipidemia – n (%)	463 (33.1)	359 (32.8)
Family history – n (%)	652 (46.5)	483 (44.0)
Smoking – n (%)	442 (32.0)	345 (31.8)
Alcohol use – n (%)	446 (31.8)	334 (30.4)
Physical inactivity – n (%)	874 (62.4)	689 (62.8)
STEMI – n (%)	662 (47.4)	533 (48.8)
Chocolate – n (%)	490 (34.9)	362 (32.9)

**Values expressed as mean ± standard deviation. LVEF: left ventricular ejection fraction after infarction; BMI: body mass index; SAH: systemic arterial hypertension; STEMI: acute ST-segment elevation myocardial infarction.*

No reduction in MACE hazard ratio (HR) was found in patients who consumed chocolate before the first infarction (HR = 0.88 [0.57 - 1.37]; p = 0.569). No reduction was observed in HR for secondary outcomes; however, HR increased for gastrointestinal bleeding in those who consumed chocolate (HR = 2.89 [1.16 - 7.24]; p = 0.023) (Table 3 and Figure 1).

Discussion

This study was one of the first to assess chocolate consumption among patients who experienced the first AMI and evaluate its potential association with outcomes at one-year follow-up. In addition to reducing outcomes, the study found that patients who consumed chocolate before the first AMI had an increased risk of gastrointestinal bleeding (Central Illustration).

Several studies have demonstrated that chocolate consumption may help reduce coronary events in healthy individuals,[4,5] mainly because of the antioxidant and anti-inflammatory properties of chocolate. Flavonoids found in chocolate (e.g., epicatechin) reduce intracellular inflammatory reactivity in response to acute psychosocial stress by decreasing DNA-binding activity of the pro-inflammatory transcription factor NF-κB and mRNA levels of pro-inflammatory cytokines IL-1β and IL-6, while increasing mRNA expression of the anti-inflammatory cytokine IL-10.[17] Moreover, the consumption of cocoa-based products reduces the expression of adhesion molecules in monocytes and serum concentrations of adhesion molecules derived from endothelium, such as P-selectin and ICAM-1. In contrast, these products increase the bioavailability of nitric oxide, improve endothelial function, and reduce lipid peroxidation of Low-density lipoprotein cholesterol (LDL), which are crucial for preventing atherogenesis.[18,19]

Among patients with arterial disease, although evidence is limited about the additional benefits of chocolate, data suggest that its effects on nitric oxide bioavailability may persist after an infarction. A clinical trial evaluating the acute effects of chocolate consumption in patients after an acute coronary syndrome episode showed a significant improvement in flow-mediated vasodilation, indicating a positive impact on endothelial function.[20] Furthermore, patients who consumed higher quantities of chocolate and experienced AMI presented less complex coronary lesions, as assessed by the Syntax score.[21]

The present study found a lower prevalence of diabetes mellitus among consumers of chocolate, which may be attributed to reverse causality, as patients with diabetes tend to avoid sweets due to dietary restrictions. Additionally, the increased prevalence of alcohol use among consumers of chocolate suggests specific behavioral or lifestyle patterns, including dietary indulgence and social drinking. These factors may independently act as potential confounders in the observed results. Alcohol use is a risk factor for gastrointestinal bleeding due to its effects on the gastric mucosa and coagulation. However, the multivariate analysis performed in this study included alcohol use and diabetes as covariates and observed that the increased risk of gastrointestinal bleeding associated with chocolate consumption is independent of these factors.

Table 2 – Comparison of characteristics between consumers and non-consumers of chocolate*

Characteristic	Consumers	Non-consumers	p-value
Age (years)	60.1 ± 12.0	61.3 ± 11.3	0.058
LVEF (%)	51.6 ± 12.9	51.5 ± 12.2	0.895
BMI (kg/m^2)	27.9 ± 5.2	27.7 ± 5.0	0.512
Female – n (%)	154 (31.4)	305 (33.4)	0.460
SAH – n (%)	281 (57.3)	545 (59.8)	0.369
Diabetes mellitus – n (%)	117 (23.9)	268 (29.5)	0.027
Dyslipidemia – n (%)	148 (30.3)	315 (34.6)	0.099
Family history – n (%)	248 (50.6)	404 (44.3)	0.025
Smoking – n (%)	147 (30.6)	295 (32.7)	0.438
Alcohol use – n (%)	179 (36.5)	267 (29.3)	0.006
Physical inactivity – n (%)	296 (60.7)	578 (63.3)	0.329
STEMI – n (%)	246 (50.7)	416 (45.6)	0.066

**Values expressed as mean ± standard deviation. LVEF: left ventricular ejection fraction after infarction; BMI: body mass index; SAH: systemic arterial hypertension; STEMI: acute ST-segment elevation myocardial infarction.*

Table 3 – Association between chocolate consumption and cardiovascular outcomes

Outcome	HR (Confidence interval)	p-value
MACE	0.88 (0.57 - 1.37)	0.569
Gastrointestinal bleeding	2.89 (1.16 - 7.24)	0.023
Bleeding requiring transfusion	1.27 (0.64 - 2.53)	0.497
Cardiovascular mortality	1.17 (0.61 - 2.23)	0.638
All-cause mortality	1.42 (0.83 - 2.43)	0.196
Reinfarction	0.63 (0.33 - 1.21)	0.165
Stroke	1.12 (0.42 - 3.00)	0.817
Acute stent thrombosis	0.54 (0.15 - 1.99)	0.354
Stent restenosis	0.89 (0.22 - 3.64)	0.876
Readmission	1.12 (0.81 - 1.54)	0.497

MACE: major adverse cardiovascular events; HR:Hazard Ratio.

Despite evidence supporting the cardiovascular benefits of chocolate among patients with coronary disease, this study did not demonstrate a reduction in MACE or other outcomes (e.g., cardiovascular mortality and reinfarction) in patients who consumed chocolate before the AMI. These findings contrast with the Stockholm Heart Epidemiology Program study, which assessed 1169 patients without diabetes. The study found an inverse association between chocolate consumption and cardiovascular mortality, with a significant 63% risk reduction in patients who consumed chocolate twice or more times per week compared with non-consumers.[22] One possible explanation for the contrast between the Catarina Heart study and the Stockholm study is that chocolate consumption may serve as an indicator of access to healthcare. Patients with greater financial resources are more likely to afford "superfluous" food items, which may reflect higher socioeconomic status and, consequently, better access to healthcare. A satirical analysis suggested that chocolate consumption was correlated with cognitive performance and, consequently, more Nobel laureates per country.[23] Unlike the Swedish study, which included data from 10 emergency healthcare services, the Catarina Heart study included patients from only two public healthcare centers, which may have influenced the findings.

The nearly threefold increase in the risk of gastrointestinal bleeding may be surprising, but it can be explained by the "positive" effects of flavonoids, which modulate platelet aggregation. Flavonoids found in dark chocolate may increase the closure time in platelet function analyzer (PFA-100)

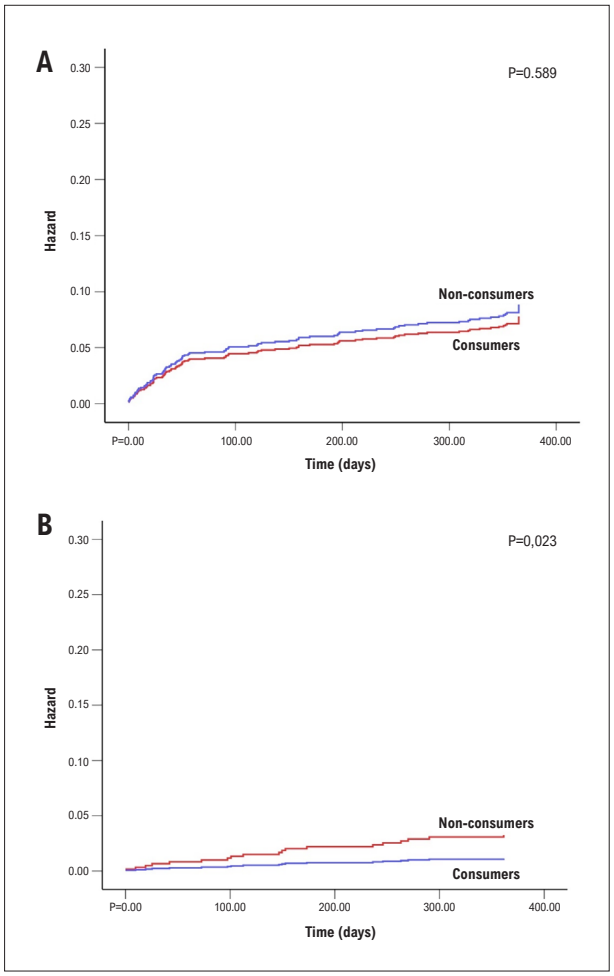

Figure 1 – *One-year events in patients who consumed chocolate before the first infarction: A) MACE; B) gastrointestinal bleeding.*

tests induced by collagen/adenosine diphosphate (ADP), suggesting reduced platelet reactivity.[24] Dark chocolate may also reduce platelet adhesion and the formation of reactive oxygen species, especially among smokers, by the inhibition of NOX2 activation.[25] While the potential antiplatelet effect may benefit patients with greater cardiovascular risk (e.g., smokers), patients from the Catarina Heart study had experienced their first AMI and were expected to receive dual antiplatelet therapy for at least one year.[26] This possible antiplatelet interaction with chocolate may explain the increased HR for gastrointestinal bleeding observed in patients who consumed chocolate. The ECLAIR study demonstrated that consuming 30 g/day of 65% cocoa chocolate for one week increased the inhibitory effects of clopidogrel in patients with stable coronary artery disease without significantly impacting the effect of aspirin.[27] Another non-randomized study found that chocolate might increase the antiplatelet effects of aspirin.[28] Despite the increased risk of gastrointestinal bleeding, no increase in the risk of bleeding events requiring transfusion or reduction in the risk of acute stent thrombosis (expected due to the increased clopidogrel effect) was observed.

This study has limitations that should be acknowledged. First, as a cohort study, chocolate consumption was assessed only upon hospitalization using a questionnaire about dietary habits in the weeks preceding admission. Therefore, in addition to recall bias, it is impossible to confirm if chocolate consumption remained consistent after the infarction. Second, although patients were asked about the consumption of dark chocolate, the lack of information about the cocoa content hindered the calculation of flavonoid or methylxanthine intake. Third, a one-year follow-up period is relatively short and may not be sufficient to observe the long-term impacts or significant changes in dietary habits. Fourth, this was an exploratory analysis, and the findings generate hypotheses rather than establishing causality. Fifth, the findings considered negative may reflect an insufficient statistical power, and the association between chocolate consumption and increased risk of gastrointestinal bleeding may be attributed to a chance finding. Despite these limitations, the findings provide important insights regarding chocolate consumption and raise awareness among patients under antiplatelet therapy. Further studies specifically designed to address this question are needed.

Conclusion

This study found no evidence that chocolate consumption before the first AMI is associated with a reduced risk of major cardiovascular events, including cardiovascular mortality, all-cause mortality, reinfarction, stroke, rehospitalization, acute stent thrombosis, or restenosis. On the other hand, a potential association between chocolate consumption and increased risk of gastrointestinal bleeding was observed, but without a significant impact on bleeding events requiring transfusion.

Given the exploratory nature of the analyses and methodological limitations (e.g., self-reported chocolate consumption and lack of detailed data regarding the type and quantity of consumed chocolate), these findings should be interpreted with caution. Further studies with more robust designs are needed to confirm these associations and explore the underlying mechanisms.

Author Contributions

Conception and design of the research and critical revision of the manuscript for intellectual content: Moreira DM, Silva RL, Fattah T, Joaquim RM; acquisition of data: Moreira DM, Dandolini LM, Silva RL, Fattah T, Joaquim RM; analysis and interpretation of the data, statistical analysis and writing of the manuscript: Moreira DM, Dandolini LM; obtaining financing: Dandolini LM.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Instituto de Cardiologia de Santa Catarina under the protocol number 55450816.0.1001.0113. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

Use of Artificial Intelligence

During the preparation of this work, the author(s) used ChatGPT for spell check. After using this tool/service, the author(s) reviewed and edited the content as needed and take full responsibility for the content of the published article.

Availability of Research Data

The data cannot be made publicly available because the database contains sensitive data that cannot be disclosed (LGPD).

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