

## ORIGINAL ARTICLE

## Association Between Chocolate Consumption and Severity of First Infarction

Heloyse Martins Duarte,<sup>1</sup> Milena Christy Rocha de Oliveira,<sup>1</sup> Ramona Jung,<sup>1</sup> Roberto Léo da Silva,<sup>2</sup> Tammuz Fatah,<sup>2</sup> Daniel Medeiros Moreira<sup>1,2</sup>

Universidade do Sul de Santa Catarina (Unisul) - Unidade Pedra Branca,<sup>1</sup> Palhoça, SC - Brazil  
 Instituto de Cardiologia de Santa Catarina (ICSC)<sup>2</sup> - São José, SC - Brazil

## Abstract

**Background:** Cardiovascular diseases, such as acute myocardial infarction, are the main causes of death in the world. The flavonoids present in chocolate can have benefits for people who have risk factors to the development of cardiovascular diseases and have a coadjuvant effect on known therapies.

**Objective:** To analyze the association between chocolate consumption, severity of coronary lesions, risk factors and severity of the first infarction in patients attended at the Cardiology Institute of Santa Catarina and other hospitals in the State of Santa Catarina.

**Methods:** Subanalysis of the Catarina Heart Study cohort, evaluated 350 patients with first myocardial infarction. We evaluated clinical, echocardiographic, hemodynamic laboratorial variables. We used chi square test to evaluate qualitative variables, t student test in the case of parametric variables and U Mann Whitney test in non-parametric variables. We considered significant  $p < 0,05$ .

**Results:** Lower prevalence of hypertension (43.2% vs. 62.3%  $p = 0.003$ ), diabetes mellitus (13.5% vs. 25.7%,  $p = 0.027$ ) and smoking (24.3% vs. 37.7%,  $p = 0.032$ ) among those who consume chocolate. Higher use of alcohol (40.5% vs. 26.4%,  $p = 0.018$ ) and drugs (9.5% vs. 3.3%,  $p = 0.023$ ) among those who consumed chocolate. Among the patients who consumed chocolate, there was a negative correlation between amount consumed and Syntax ( $r = -0.296$ ,  $p = 0.019$ ).

**Conclusion:** There was association between chocolate consumption and lower prevalence of hypertension, diabetes and smoking. There was no association between amount of chocolate consumed and post-infarction ventricular function and TIMI frame count. Higher prevalence of alcohol and drug use among those who consume chocolate. Negative correlation between Syntax and the amount of chocolate consumed. (Int J Cardiovasc Sci. 2019; [online]. ahead print, PP.0-0)

**Keywords:** Cardiovascular Diseases/mortality; Myocardial Infarction/physiopathology; Flavonoids; Polyphenols; Cacao.

## Introduction

Cardiovascular diseases (CVD) are the leading cause of death worldwide.<sup>1</sup> These include acute myocardial infarction (AMI) which, from 2008 to 2017, accounted for 813,982 hospital admissions in Brazil.<sup>2</sup>

There is evidence of the link between reduction of risks of cardiovascular events and chocolate consumption in larger amounts, as chocolate contains flavonoids.<sup>3,4</sup>

Studies indicate that flavonoids present in cocoa or cocoa products have the potential to benefit people with risk factors for the development of CVD through different mechanisms, such as anti-inflammatory action.<sup>5-8</sup> This is of great importance, as AMI is also characterized as an inflammatory disease.<sup>9</sup>

However, aspirin and statins are the only medications that fight inflammation and are used in AMI.<sup>9</sup> The inclusion of a relatively high amount of high-flavonoid

## Mailing Address: Heloyse Martins Duarte

Rua das Cerejeiras, 235, Pedra Branca. Postal Code: 88137-250. Palhoça, SC - Brazil.  
 E-mail: heloysem@hotmail.com

cocoa in the daily diet could reduce cardiovascular outcomes, make them less severe and improving the prognosis of patients after an AMI episode.

Chocolate, whose composition is rich in flavonoids, may have an adjuvant effect to ischemic disease therapies, mainly due to the anti-inflammatory action.<sup>5-7</sup> However, although there are indications that chocolate may decrease the occurrence of AMI events, there is no evidence that it may be associated with lower complexity of coronary lesions in patients with AMI or that AMI may be less severe. This study analyzes the association between chocolate consumption and the complexity of coronary lesions, as well as the risk factors for cardiovascular outcomes and the severity of first infarction.

## Methods

This study is a subanalysis of the Catarina Heart Study<sup>10</sup> — a prospective cohort study that began in July 2016 that is intended to evaluate 1,426 patients by the year 2020 and proposes a follow-up of thirty days and one year. The patients selected were diagnosed as having the first AMI and were assisted at the Cardiology Institute of Santa Catarina and other hospitals in the State of Santa Catarina. Once the patients' consent was taken, they answered a questionnaire that included different clinical, laboratory, electrocardiographic, echocardiographic and angiographic variables from July 2016 to July 2018.

Inclusion criteria were minimum 18 years of age, presence of precordial pain suggestive of AMI associated with electrocardiogram with new ST-segment elevation at point J in two contiguous leads with  $\geq 0.1$  mv limits on all leads, in addition to the V2-V3 leads in which the following limits apply:  $\geq 0.2$  mv in men  $\geq 40$  years of age;  $\geq 0.25$  mv in men  $< 40$  years of age, or  $\geq 0.15$  mV in women or the presence of precordial pain suggestive of AMI associated with elevation of troponin I or CK-MB above the 99<sup>th</sup> percentile of the upper reference limit. Exclusion criterion was the presence of previous AMI.

The primary endpoint of this study evaluated the association between chocolate consumption with severity, complexity and AMI complications. Secondary outcomes assessed the association between chocolate consumption and prevalence of classic cardiovascular risk factors and the correlation between chocolate consumption and variables associated with the complexity of coronary lesions and severity of infarction in patients who ate chocolate.

Measurement of chocolate consumption was done by asking the patients whether they had chocolate or not and the number of chocolate bites eaten per week. 43 grams were used as standard for each bite eaten, and the total consumption per week was divided by the days in order to evaluate the average consumption in grams per day.

To assess the severity and complexity of AMI, three variables were used: Syntax, Thrombolysis in Myocardial Infarction (TIMI) frame count and Left Ventricular Ejection Fraction (LVEF). The first variable is a score that considers the location, quantity and the respective repercussion of the lesions in the functioning of the coronary arteries, and the higher the Syntax index, the greater the complexity of coronary lesions.<sup>11</sup> The TIMI frame count evaluates the number of film frames from the beginning of the contrast injection to the range of the coronary artery end. It is an estimate of arterial perfusion performed after therapeutic management.<sup>12</sup> This variable was only applied for patients with AMI with ST-segment elevation. LVEF was estimated by transthoracic echocardiography within 72 hours after AMI.

Hypertension, diabetes mellitus and dyslipidemia were self-reported at the time of the study. Chocolate consumption was considered positive in those who ate it regularly, at least once a week. Patients with a positive family history were considered those who had first-degree relatives with coronary artery disease, women  $\leq 65$  years old and men  $\leq 55$  years old. Regarding the use of drugs and alcohol, any consumption of these substances was considered positive. As for relevant smoking, consumption of any tobacco at the time of the interview.

## Statistical analysis

The current study sample was calculated as 158 patients with a power of 90% and alpha = 0.05 for a correlation of 0.35 between the consumption of chocolate per day in grams. Data were organized into a table and analyzed by the software SPSS 13.0. The qualitative variables were expressed using absolute and percentage numbers and evaluated using the chi-square test. Quantitative variables with normal distribution were presented as mean  $\pm$  standard deviation and were evaluated using Student's *t*-test for independent samples, while quantitative variables with non-normal distribution were presented as median and interquartile range and were evaluated using Mann-Whitney's *U* test. Normality was evaluated using the Kolmogorov-Smirnov test. Among patients who consumed chocolate, the amount in grams

per day was correlated with the variables of AMI severity using Spearman's correlation. In this study,  $p < 0.05$  was considered statistically significant.

The Catarina Heart Study was submitted to the Research Ethics Committee of *Instituto de Cardiologia de Santa Catarina* pursuant to Resolution 466/12, under the protocol 55450816.0.1001.0113. The patients were informed about the secrecy of the information collected in the questionnaire, and signed a consent form before applying the questionnaire.

## Results

From July 2016 to July 2018, 350 patients aged  $59.0 \pm 11.0$  years were evaluated. Most patients were males (64.0%) and hypertensive (58.3%). Regarding chocolate, 21.1% of the patients consumed it regularly, while Syntax presented a median value of 12.0 (6.0 — 19.0). The prevalence of diabetes mellitus in the interviewed population was 23.1% and the diagnosis of infarction with ST-segment elevation was delivered in 169 patients (48.0%). Median chocolate consumption among those who had chocolate was 21.5 grams per day. The other variables are presented in Table 1.

The study showed an association between chocolate consumption and the absence of systemic arterial hypertension: 43.2% of the patients who consumed chocolate were hypertensive, while 62.3% of those who did not eat the food had hypertension ( $p = 0.003$ ). Likewise, there is a significant association between absence of diabetes mellitus and consumption of chocolate: 13.5% of patients who consume chocolate have the disease, while 25.7% of those who do not eat chocolate have diabetes, with  $p = 0.027$ . There was a higher prevalence of smokers among patients who did not consume chocolate (37.7%) compared to those who consumed chocolate (24.3%), with  $p = 0.032$ .

In addition, there was greater consumption of alcoholic beverages among those who consume chocolate (40.5%) compared to those who do not consume chocolate (26.4%), with  $p = 0.018$ . The group that used drugs was bigger among those who consumed chocolate (9.5%), compared to those who do not consume chocolate (3.3%), with  $p = 0.023$ . Dyslipidemia and family history of cardiovascular diseases were not associated with chocolate consumption. (Table 2).

**Table 1 - Demographic, clinical and lifestyle characteristics of the study population**

Variables	
Male sex - N (%)	224 (64.0)
Hypertension - N (%)	204 (58.3)
Diabetes mellitus - N (%)	81 (23.1)
Dyslipidemia - N (%)	120 (34.4)
Family history - N (%)	153 (43.7)
Smoking - N (%)	122 (34.9)
Alcohol - N (%)	103 (29.4)
Chocolate consumption - N (%)	74 (21.1)
ST-segment elevation infarction - N (%)	39 (50.6)
Age*	$59.0 \pm 11.0$
Body mass index*	$27.6 \pm 5.0$
Waist*	$95.5 \pm 13.8$
Weight - median (AIQ)	74.0 (65.0 – 83.0)
Chocolate† - median (AIQ)	21.5 (6.1 – 56.8)
Syntax - median (AIQ)	12.0 (6.0 – 19.0)
TIMI frame - median (AIQ)	22.0 (14.0 – 34.0)

\* = Mean  $\pm$  standard deviation, † = Chocolate grams per day, only among those who consume chocolate.

**Table 2 - Association between chocolate consumption and risk factors**

Variables	Chocolate consumption		p value
	Yes	No	
	n (%)	n (%)	
Hypertension	32 (43.2)	172 (62.3)	0.003
Diabetes mellitus	10 (13.5)	71 (25.7)	0.027
Dyslipidemia	23 (31.1)	97 (35.3)	0.500
Family history	39 (52.7)	114 (41.3)	0.079
Smoking	18 (24.3)	104 (37.7)	0.032
Alcohol	30 (40.5)	73 (26.4)	0.018
Drugs	7 (9.5)	9 (3.3)	0.023

The mean LVEF among those who consumed chocolate ( $48.7 \pm 15.3$ ) did not present any significant difference to those who did not consume chocolate ( $51.2 \pm 13.0$ ), with  $p = 0.228$ . The other variables are presented in Table 3.

Among the patients who consumed chocolate, there was a negative correlation between the amount consumed and Syntax ( $r = -0.296$ ,  $p = 0.019$ ), characterizing a lower complexity of coronary lesions in patients consuming more chocolate. (Table 4).

## Discussion

This study analyzed the complexity of coronary lesions and the severity of the first infarction with chocolate consumption. The data showed that, among patients who consume chocolate, there is a negative correlation between Syntax and the amount consumed, characterizing lower

severity of coronary lesion in patients who had chocolate in larger amounts. In addition, there was a lower prevalence of hypertension, diabetes and smoking among those who consumed chocolate.

Similarities were found in the literature regarding the profile of the interviewed population, with a higher prevalence of males in patients affected by AMI.<sup>13-17</sup> In addition, it was found that most of these patients had hypertension as a risk factor for the cardiovascular event<sup>13-16</sup>. Regarding smoking, less than half of the population interviewed had this addiction, as also found in other publications.<sup>14,15,17</sup>

There was a lower prevalence of hypertension among those who consumed chocolate. This relationship has also been found in several other studies, which have shown reduced blood pressure with consumption of flavonoids, which are present in foods such as chocolate.<sup>4,8,18,19</sup> This association can be justified by the fact that flavonoids would improve endothelial function, since endothelial dysfunction is associated with hypertrophy and arterial wall stiffening.<sup>18,20,21</sup> One of the mechanisms of endothelial function improvement is the increased bioavailability of nitric oxide from the consumption of flavonoids, which results in a vasodilator effect and increases blood flow in the vessels, with consequent reduction in blood pressure levels.<sup>22,23</sup> Another important route of the benefits of flavonoids in reducing blood pressure is the inhibition of the angiotensin converting enzyme activity, as the formation of angiotensin II results in vasoconstriction and increased blood pressure, which increases the risk of cardiovascular outcomes.<sup>23,24</sup>

An association was also found between the use of alcohol and drugs with chocolate consumption, and a higher prevalence of consumption of these substances among patients have drink chocolate on a weekly basis. Some studies justify this relationship by the addictive characteristics of chocolate, which has compounds that can cause addiction, as in other substances, such as alcohol and other drugs.<sup>25,26</sup> Moreover, chocolate addiction also includes the typical stages of alcoholism and other drug addictions, such as relapse. At this stage, the individual goes back to having chocolate compulsively, without thinking about the adverse effects of exaggerated consumption, which further corroborates the additive effect of chocolate, which may prevail in those who are prone to addictive behaviors.<sup>27</sup> Another relevant point is that drugs, such as marijuana, are appetite stimulants, so they can increase the consumption of foods, including chocolate.<sup>28,29</sup>

**Table 3 - Association between chocolate consumption and quantitative variables**

Variables	Chocolate consumption		p value
	Yes	No	
Age*	58.5 ± 11.6	59.2 ± 10.9	0.639
BMI*	27.9 ± 4.7	27.6 ± 5.1	0.624
Waist*	97.4 ± 14.8	95.0 ± 13.5	0.202
LVEF*	48.7 ± 15.3	51.2 ± 13.0	0.228
Weight†	74 (64.0–86.0)	74 (65.0 - 82.0)	0.386
Syntax†	14 (6.8 - 18.6)	11 (6.0 - 19.0)	0.778
TIMI frame†	28 (12.0 - 48.0)	20 (14.0 - 32.5)	0.360

\* = Mean ± standard deviation, † = Median (Interquartile range); BMI: Body mass index; FEVE: Left ventricular ejection fraction.

**Table 4 - Correlation between chocolate consumption and variables associated with coronary complexity and severity of infarction in patients who had chocolate**

Variables	r	p value
LVEF*	-0.070	0.613
TIMI frame	0.131	0.499
Syntax	-0.296	0.019

\* = Left ventricular ejection fraction.

There was also an association between chocolate consumption and lower prevalence of smoking, but this finding only seems to be coincidental.

An association between chocolate consumption and diabetes mellitus was also found. Studies suggest an inverse relationship between the prevalence of diabetes mellitus and chocolate intake.<sup>8,30-33</sup> Research studies have found that one of the mechanisms of this inverse relationship between chocolate and diabetes mellitus is the increased sensitivity to insulin caused by flavonoids, which helps to reduce blood glucose in the stream and can delay the onset of the disease.<sup>34,35</sup> An important point, reported in one of the studies analyzed, is that flavonoid consumption as a protective effect of diabetes mellitus should be recommended with caution. This is relevant because the study argues that large amounts of sugars and calories can be found in a number of cocoa products rather than high flavonoid content, which can generate a rebound effect, worsening the glycemic control of patients with type 2 diabetes mellitus.<sup>36</sup> Some authors believe that the beneficial effect of flavonoids also occurs in patients who already have established diabetes mellitus, reducing the risk of cardiovascular outcomes in these individuals, such as AMI.<sup>19,20</sup> However, it is relevant to express that patients who already have diabetes mellitus are advised not to consume sugars and, in this study, the patients interviewed already had the disease and, therefore, should eat less chocolate.

Among the patients who consumed chocolate, there was a negative correlation between Syntax and the amount of chocolate consumption. The median chocolate consumption among the patients was 21.5 grams per day. There is evidence that a daily dose of 80 mg could promote beneficial vascular outcomes.<sup>18</sup> There is also data showing an immediate improvement in coronary flow after consumption of 45 grams of chocolate with high cocoa content.<sup>37</sup> The correlation between higher amount of chocolate consumption and lower complexity of coronary lesions may be justified by the anti-inflammatory properties of the flavonoids present in chocolate.<sup>5-7</sup> Another important mechanism is the antioxidant action of flavonoids, which helps reducing free radicals and may result in coronary lesions of lower severity.<sup>7,38</sup> Also, a recent clinical trial has shown that chocolate with high cocoa content improves endothelial function (assessed through flow-mediated vasodilatation of the brachial artery) in patients with established coronary artery disease.<sup>39</sup> In addition to

that, the beneficial effects of chocolate consumption are associated with lower mortality due to cardiovascular outcomes, which suggests lower severity of AMI in those who consume chocolate in higher amounts.<sup>8,40</sup> However, it was not possible to establish the exact amount of recommended consumption in order to reduce the severity of the cardiovascular outcome. It is worth noting that, although there was a negative correlation between the complexity of coronary lesions and the amount of chocolate consumed, there was no association between the amount consumed and other variables associated with severity, such as post-infarction ventricular function (LVEF) and coronary flow after primary angioplasty (TIMI frame count).

Regarding the limitations of this study, the comorbidities of patients and the risk factors for cardiovascular outcomes were evaluated at a single moment, which may compromise the cause-effect relationship. Variables such as alcoholism and smoking were self-reported, which could underestimate their prevalence. Also, some risk factors such as prior coronary artery bypass grafting or kidney disease requiring dialysis were not exclusion criteria and could influence the outcomes: however, the prevalence of these variables was less than 1% (data not shown). Type I error may have occurred in some findings, such as the association between chocolate consumption and lower prevalence of smoking. It was not possible to measure the proportion of cocoa present in the chocolate consumed. Another limitation of the study was the lack of income evaluation, since there could be a bias of contamination, since higher consumers of chocolate could be those with higher incomes and greater access to health services, even though the evaluation was performed exclusively in public hospitals. Besides, most patients interviewed were from a single hospital. These biases, however, do not invalidate the data found: literature data on the subject are still scarce and this evidence justifies new research studies such as clinical trials designed with adequate power to evaluate the association between chocolate consumption in patients with ischemic heart disease and the reduction of outcomes such as mortality.

## Conclusion

There was an inverse association between chocolate consumption and hypertension, diabetes mellitus and smoking. There was also an association between

chocolate consumption and higher prevalence of drug and alcohol use. There was no association between the amount of chocolate consumed and post-infarction ventricular function (LVEF) and coronary flow after TIMI frame count. There was also a negative correlation between Syntax and the amount of chocolate consumed, suggesting lower severity of coronary lesion in patients who consumed chocolate in larger amounts.

### Author contributions

Conception and design of the research: Duarte HM, Moreira DM, Silva RL, Fattah T. Acquisition of data: Duarte HM, Moreira DM, Silva RL, Fattah T. Analysis and interpretation of the data: Duarte HM, Moreira DM, Silva RL, Fattah T. Statistical analysis: Duarte HM, Moreira DM. Writing of the manuscript: Duarte HM, Moreira DM, Oliveira MCR, Jung R. Critical revision of the manuscript for intellectual content: Duarte HM, Moreira DM, Oliveira MCR, Jung R.

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### Potential Conflict of Interest

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

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This article is part of the thesis of work of course conclusion submitted by Heloyse Martins Duarte, from *Universidade do Sul de Santa Catarina (Unisul)*.

### Ethics approval and consent to participate

This study was approved by the Ethics Committee of the *Instituto de Cardiologia de Santa Catarina (ICSC)* under the protocol number 55450816010010113. 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.

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