# **ORIGINAL ARTICLE**

# Dietary Fat Intake and its Association with Adiposity and Inflammatory Markers in Individuals at Cardiometabolic Risk

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# **Abstract**

Background: Fatty acids are important components of diet that may influence the development of CVD.

**Objective:** To verify the relationship of dietary fatty acids with cardiometabolic markers in individuals at the cardiometabolic risk.

**Methods:** This cross-sectional study involved 282 subjects (116 M/166 F, 42 ± 16 years) attended the Cardiovascular Health Care Program, *Universidade Federal de Viçosa* (Brazil). Anthropometric and body composition measurements as well as metabolic and inflammatory markers were assessed by standard procedures. Demographic and lifestyle variables were obtained by semi-structured questionnaire. Food consumption was evaluated by 24h recall. Student's t-test or Mann-Whitney-U test and chi-square test were used, considering the statistical significance level of 5% probability.

**Results:** Individuals who eaten fat, fatty acids saturated and fatty acids polyunsaturated above recommendation (> 35, 7%, and 10% of caloric intake) were more likely to be overweight (p < 0.05). Those individuals with higher intake of medium-chain fatty saturated acids ( $\geq$  1.05 g/d) had lower values (p < 0.05) of body mass index, waist circumference, waist-hip ratio and waist-height ratio and higher values (p < 0.05) of total leukocytes, C-reactive protein and total cholesterol, and LDL. Subjects with higher of palmitoleic acid intake ( $\geq$  0.94 g/d) presented higher values of BMI, fat percentage and HOMA-IR (p < 0.05).

**Conclusion:** This cross-sectional study found different associations of dietary fat and cardiometabolic risk related to adiposity and inflammatory markers, according with chain-size and saturation, indicating the need the more detailed on the dietary assessment of obese patients to identify risk factors and established best strategies to control. (Int J Cardiovasc Sci. 2020; [online].ahead print, PP.0-0)

**Keywords:** Cardiovascular Diseases, Risk Factors; Metabolic, Syndrome; Obesity/prevention and control; Fatty, Acids; Biomarkers.

#### Introduction

The prevalence of overweight and obesity has grown at an alarming rate1, and sedentary lifestyle and inadequate dietary patterns, with high fat and sugar intake contribute to the positive energy balance.<sup>1,2</sup> In addition, excessive fat accumulation, mainly in the abdominal region, has been implicated in the development of other chronic noncommunicable diseases (CNCD), such as diabetes

(DM), dyslipidemias, systemic arterial hypertension and cardiovascular diseases (CVD).<sup>3</sup>

In this context, fatty acids are important components of diet that may influence the development of CVD, since fatty acids participate in important biological functions, such as energy substrate, regulation of metabolic pathways and inflammatory processes, hormone production, and participate in complex systems of intracellular signaling. Derivatives of fatty acids also

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act on the synthesis of prostaglandins, leukotrienes and thromboxanes,<sup>4,5</sup> being dietary fat important modulator of inflammatory status and cardiovascular risk.<sup>6</sup>

The medium chain fatty acids are absorbed in the non-esterified form and transported to the liver, bound to albumin, where they are rapidly metabolized. In turn, long-chain fatty acids undergo a process of esterification, forming triglycerides, which can remain in the bloodstream, carried by chylomicrons, or released into the tissues, acting as a form of fat storage in the body. Thus, excessive deposition of these lipids may lead to an increase in CVD. However, little is known about the relationship between the consumption of medium and long chain fatty acids and cardiovascular risk parameters.

Dietary fatty acids can also be classified as saturated (SFA), monounsaturated (MUFA), and polyunsaturated (PUFA), according to saturation level. In this sense, high MUFA diet causes reduction in serum levels of total cholesterol, low density lipoprotein (LDL-c), triglycerides and increase in high density lipoprotein (HDL-c).<sup>8,9</sup> The PUFAs, especially those of the omega 3 series, are recognized by cardioprotective activity. However, SFAs are associated with proven deleterious effects, since they increase triglyceridemia and cholesterolemia, and have a proinflammatory action.<sup>10</sup> Regarding inflammation modulation by fat, Studies have found strong association of saturated fat intake with the synthesis of inflammatory biomarkers compared to polyunsaturated fatty acids.<sup>11,12</sup>

In this sense, the objective of the present study was to verify the relationship between dietary fatty acids and cardiometabolic markers in individuals at cardiometabolic risk treated at the Cardiovascular Assistance Program of the Federal University of Viçosa (PROCARDIO-UFV).

# Methodology

#### **Subjects**

Participated in this cross-sectional study 282 patients included in PROCARDIO-UFV and had their first consultation until July/2016. PROCARDIO-UFV is a program that performs nutritional intervention to promote cardiovascular health in the academic community of UFV, registered in the Brazilian Clinical Trials Registry (ReBEC, number RBR-5n4y2g7).<sup>13</sup> The inclusion criteria in the program are: men and women; patients ≥ 20 years of age; students, workers and workers' dependents UFV; cardiovascular disease or occurrence

of at least one cardiometabolic risk factor: overweight or obesity (Body Mass Index (BMI)  $\geq 25$  or 27 Kg/m²)¹⁴,¹⁵ or/and dyslipidemia (Triglycerides (TG)  $\geq 150$  mg/dL or/and Total cholesterol (TC)  $\geq 200$  mg/dL or/and HDL-c < 40 or < 50 mg/dL for men and women)¹⁰,¹⁶ or/and blood pressure  $\geq 130/\geq 85$  mmHg¹⁶ or diagnosed hypertension or/and fasting glucose  $\geq 110$  mg/dL¹⁶ or diagnosed diabetes mellitus.

The study did not include individuals who were not associated with the UFV, who did not present cardiometabolic risk or CVD, pregnant women, children and adolescents.

The study was approved by the Human Research Ethics Committees of the UFV (n° 066/2012/CEPH), in accordance to the Resolution 466/2012 of the National Health Council (CNS/Ministry of Health, Brazil) and to principles of the Declaration of Helsinki. All participants of the study read and signed the written informed consent form.

The data used were related to the first consultation. Of the 417 program users, 282 were selected for having complete data fatty acid intake.

#### **Dietary Assessment**

The volunteers responded to a 24-hour recall, reporting all food and drink consumed the day before (weekend or weekday) the consultation, as well as their quantities. In the present study, the daily intake of calories and total lipids (SFA, MUFA, and PUFA) were assessed using software, DietPRO, version 5.0i.

The determination of the intake of caprylic (C8: 0), capric (C10: 0), lauric (C12: 0), myristic (C14: 0), palmitic (C16: 0), stearic (C18: 1), SFA and oleic MUFA (C18: 1), linoleic (C18: 2, LA, family  $\omega$ -6) and  $\alpha$ -linolenic PUFA (C18: 3, LNA, family  $\omega$  -3) and trans fatty acids were performed using the National Nutrient Database for Standard Reference (USDA) table.<sup>17</sup> The foods present in the recall and not listed in the USDA table had their composition estimated considering foods that presented nutritional composition and similar cooking methods. 17 In addition, the preparations were dismembered in their constituent ingredients and, in the case of not having the option of the composition for the cooked food, the raw food composition was used. The intake of each fatty acid was performed using a standard spreadsheet (Microsoft Excel®), developed specially for this aim.

Medium chain fatty acids were the sum of C8: 0 (caprylic acid), C10: 0 (capric acid) and C12: 0 (lauric acid).

3

And as long chain fatty acids the sum of myristic (C14: 0), palmitic (C16: 0) and stearic (C18: 0), monounsaturated fatty acids palmiticleic (C16: 1) and oleic (C18: 1) fatty acids (C18: 2, LA, family  $\omega$ -6) and  $\alpha$ -linolenic acid (C18: 3, LNA,  $\omega$ -3 family). Adequate consumption of total fat, SFA, MUFA, PUFA and linoleic fatty acid was considered when the ingestion was between 25 and 35%;  $\leq$  7%;  $\leq$  20%; ≤10% of the daily energy value and between 1.1 and 1.6 g/day, respectively. 10 To assess the possible association of palmitoleic acid consumption and other variables of interest, the present study sample was categorized according to the median palmitoleic acid consumption (0.94g/day), medium chain fatty acids consumption (1.05 g/day) and long-chain fatty acids (LCFA) (18.92 g/day). The use of the median as a cutoff point has been used 18,19 based on the premise of the creation of risk groups in epidemiological studies.20

### **Anthropometry and Body Composition**

Body weight and height were measured using a standardized protocol<sup>21</sup>

The Waist circumference was measured on the umbilical scar and hip ratio and waist-to height ratio were calculated. Waist circumference (WC) was measured from the umbilical scar in the horizontal plane.<sup>22</sup>

Abdominal obesity was considered WC greather than or equal to 80 and 90cm for women and men respectively.<sup>23</sup> Waist-to-height ratio (WH+R) and waist-to—hip ratio (WHR) were also calculated. WH+R and classified as high risk for (CVD) when ≥ 0,5 (both sexes); 0,85 (women) and 1.00 (men), respectively.<sup>24,25</sup> Total body fat (BF%) was assessed by tetrapolar electrical bioimpedance analysis, performed with standard protocol.<sup>26</sup> Obesity was diagnosed according to cut-off points proposed by Bray et al.;<sup>27</sup>: > 33 and 25% for women and men, respectively.

#### **Metabolic Biomarkers**

Fasting serum glucose, triglycerides, total cholesterol HDL, ferritin, uric acid and ultra-sensitive C-reactive protein (CRP-us) total leukocytes, were determined at the Laboratory of Clinical Analysis of the Health Division of the UFV, according to standardized protocol of this Laboratory.

Insulin resistance was estimated by the homeostasisinsulin resistance (HOMA-IR) model, which was calculated as follows: HOMA-IR = [fasting glucose (mmol/L)] fasting insulin (μUI/ml)]/ 22.5 and by the index triglycerides/glycemia (TyG), which was calculated as follows: Ln [fasted triglycerides (mg/dl) × fasting blood glucose (mg / dl)/2].<sup>28</sup>

#### **Demographic and Lifestyle Variables**

The variables age, sex, schooling, income, smoking, regular practice of physical activity and alcohol consumption were collected through interview of the participants.

#### Statistical Analyzes

The results were presented in absolute and relative frequencies, mean ± standard deviation and, or median (p25-p75). The normality of each variable was assessed by the Kolmogorov-Smirnov test. All dietary intake variables were adjusted by total caloric intake using the residual method, as proposed by WILLETT & STAMPFER.<sup>29</sup>

Non-paired Student-t and Mann-Whitney-U tests were used for comparison of two groups, where appropriate. Pearson's chi-square test was used to verify associations between socio-demographic variables, lipid consumption and nutritional status. All statistical analyzes were performed using the SSPS 21.0® program. We considered the level of statistical significance of 5% probability.

#### **Results**

Of the 282 subjects, 58.9% were female; 81.9% adults; 53.4% individuals reported practicing physical activity (self report) and 17.4% had diabetes. Of the overweight individuals, 76.6% were dyslipidemic (p = 0.028) (Table 1).

Table 2 shows dietary fat intake according to weightstatus. Among the overweight individuals, 45.7% presented fat intake within the recommendation, but 79.7% of individuals consumed above recommendation to SFA.

The individuals (normal-weight and overweight) with higher consumption of medium chain fatty acids had lower values (p < 0.05) for BMI, perimeters of the waist, hip waist ratios, waist height ratios, ferritin, glycemia and uric acid. On the other hand, they had higher values (p < 0.05) of total leukocytes, total cholesterol, low density lipoprotein (LDL), HDL and CRP (Table 3). However, for long-chain fatty acids, only the total leukocyte count was significant (p = 0.038) for those with higher consumption ( $\geq$  18.92 g/day) (data not shown). Individuals with higher intakes of palmitoleic

Variables n (%)	Total (n = 282)	Normal-weight (n = 85)	Overweight (n = 197)	p-value	
Sex					
Male	116 (41.1)	33 (38.8)	83 (42.1)	0.604	
Female	166 (58.9)	52 (61.2)	114 (57.9)		
Age					
Adults	231 (81.9)	64 (75.3)	167 (84.8)		
Seniors	51 (18.1)	21 (24.7)	30 (15.2)	0.058	
Schooling (n = 265)					
Illiterate incomplete/high school	62 (23.4)	17 (21.5)	45 (24.2)		
Complete high school	46 (17.4)	11 (13.9)	35 (18.8)	0.479	
Graduated/incomplete graduated	157 (59.2)	51 (64.6)	106 (57.0)		
Income					
Did not inform	30 (10.6)	12 (14.1)	18 (9.1)	0.399	
Up to 2 wages	66 (23.4)	19 (22.4)	47 (23.9)		
2 to 4 salaries	103 (36.5)	25 (29.4)	78 (39.6)		
4 to 10 salaries	71 (25.2)	25 (29.4)	46 (23.4)		
More than 10 wages	12 (4.3)	4 (4.7)	8 (4.1)		
Smoking (n = 281)					
Never smoked	189 (67.3)	65 (77.4)	124 (62.9)		
Have you smoked	80 (28.5)	14 (16.7)	66 (33.5)	0.014	
Smokes currently	12 (4.2)	5 (6)	7 (3.6)		
Physical activity (n = 281)					
No	131 (46.6)	42 (49.4)	89 (45.4)	0.527	
Yes	150 (53.4)	43 (50.6)	107 (54.6)	0.537	
Alcohol drink (n = 277)					
Never drinks	114 (41.2)	34 (41)	80 (41.2)		
Eventually	156 (56.3)	48 (57.8)	108 (55.7)	0.648	
Daily	7 (2.5)	1 (1.2)	6 (3.1)		
Hypertension (n = 281)					
No	173 (61.6)	67 (79.8)	106 (53.8)	-0.004	
Yes	108 (38.4)	17 (20.2)	91 (46.2)	< 0.001	
Diabetes (n = 281)					
No	232 (82.6)	67 (79.8)	165 (83.8)	0.410	
Yes	49 (17.4)	17 (20.2)	32 (16.2)	0.419	
Dyslipidemia (n = 281)					
No	56 (19.9)	10 (11.9)	46 (23.4)	0.000	
Yes	225 (80.1)	74 (88.1)	151 (76.6)	0.028	

 $Variables\ expressed\ as\ absolute\ and\ relative\ frequency.\ P\ values\ in\ bold\ refer\ to\ statistical\ significance\ (p<0.05)\ using\ the\ Pearson\ chi-square\ test.$  \* $Variables\ self$ -reported\ by\ participants.

225 (80.1)

74 (88.1)

151 (76.6)

5

Table 2 - Lipid intake of PROCARDIO-UFV participants, according to body fat status

Fat intake	Normal- weight (n = 85)	Overweight (n = 197)	p-values	
Total fat				
< 25 % CI (n = 93)	37 (43.5)	57 (28.9)		
25% -35% CI (n = 127)	38 (44.7)	90 (45.7)	0.011	
> 35% CI (n = 60)	10 (11.8)	50 (25.4)		
Saturated fatty acid				
$\leq$ 7% CI (n = 68)	29 (34.1)	40 (20.3)	0.012	
> 7% CI (n = 212)	56 (65.9)	157 (79.7)	0.013	
Polyunsaturated fatty acid				
≤ 10% CI (n = 252)	82 (96.5)	172 (87.3)	0.018	
> 10% CI (n = 28)	3 (3.5)	25 (12.7)		
Monounsaturated fatty acid				
≤ 20% CI (n = 275)	84 (98.8)	193 (98.0)	0.710	
> 20% CI (n = 5)	1 (1.2)	4 (2.0)	0.618	

Variables expressed as absolute and relative frequency. p values in bold refer to statistical significance (p < 0.05) using the Pearson chi-square test. CI: caloric intake.

acid presented higher values for BMI, body fat (%) and HOMA-IR (Figure 1).

In relation to PUFA intake, 91.8% of study participants (n = 259) consume less than 0.6% of the total calories in  $\alpha$ -linolenic acid, and 60.3% (n = 170) consume less than 5% of total calories in linoleic fatty acid. No significant relation was found between the recommended intake of  $\alpha$ -linolenic acid (0.6-1.2% of total calories) and linoleic acid (5-10% of total calories) and cardiometabolic markers, neither there is significant result regarding the consumption of trans fatty acids (data not show).

# Discussion

In this study, 45.7% and 87.3% of the individuals with overweight had consumption within the total fat and PUFA recommendations, respectively, and 79.7% above the recommendation for saturated fatty acids. This result shows the importance of dietary fat assessment

regarding to its quality, since dietary fatty acid is more important determinant of cardiovascular risk than its total amount.<sup>30,31</sup>

In previous study, with adults aged 20 to 59 years and overweight prevalence of 76.79%, SFA intake remained within the established values. However, there was an inadequacy of the PUFA consumption being below the recommended level.<sup>32</sup> This difference in results can be explained by the fact that the authors used the recommendations of up to 7% of total calories in SFA and up to 10% of total calories in PUFA, in the study cited, 10% of total calories and 6 to 10%, respectively.

In the last decades, there have been medical and nutritional recommendations for the reduction of the consumption of SFA due to the action of these in the increase of the LDL-c in the increase of the risk of cardiovascular disease.<sup>33</sup> However, different SFA may have different effects on the lipid profile and cardiovascular risk factors.<sup>34</sup>

When compared to carbohydrates, lauric fatty acid (C12: 0) is what increases the LDL-c and consequently TC.<sup>35</sup> This may explain the fact that the individuals in the present study had a higher intake of saturated medium chain fatty acids (SCMA), among them lauric acid, with higher values of TC and LDL. Considering the high prevalence of dyslipidemic in this population (80.1%, n = 225), this finding may contribute to the prescription of diets, restricting foods containing higher amounts of these fatty acids, such as whole milk and its derivatives, coconut and their derivatives.

Lower values in the adiposity indexes (BMI, perimeters of the waist, hip waist ratios, waist height ratios) of the participants with the highest consumption of SCMA can be explained by the metabolism of the medium chain triglycerides. These are absorbed, mainly as free fatty acids, directly from the portal vein, thus reaching the liver faster than the long chain fatty acids. In the liver, oxidation is rapid because it does not need to be activated by coenzyme A, making it a good ketogenic substrate.<sup>36,37</sup> In clinical trials with men and women fed a diet containing medium chain triglycerides, mainly lauric acid, they achieved a reduction in body mass and abdominal fat, since these components are not easily incorporated into adipose tissue triglycerides.<sup>38-40</sup>

Inflammation is a prominent feature of many chronic diseases, high-fat and carbohydrate meals contribute to increased oxidative stress and inflammation.<sup>41</sup> A high-

Table 3 - Indicators of adiposity and cardiometabolic markers, according to the intake of medium chain fatty acids (n = 282)

Variável	Lower intake (< 1,05g/day)	Higher intake (≥ 1,05 g/day)	p
BMI (kg/m²)	29.48 (5.1)	28.20 (5.7)	0.049
Waist circumference (cm)	99.51(13.6)	94.09 (14.9)	0.002
Waist-hip ratio	0.96 (0.09)	0.91 (0.09)	< 0.001
Waist-height ratio	0.60 (0.09)	0.58 (0.10)	0.026
Total body fat (%)	30.30 (6.7)	31.66 (9.1)	0.222
Leukocytes (mil/mm³)	6,000 (5,120 - 7,035)	6,500 (5,425 - 7,750)	0.035
Ferritin (µg/L)	113.2 (54.9 - 237.7)	66.95 (30.5 - 153.0)	0.012
Uric acid (mg/dL)	4.5 (3.7 - 6.0)	3.9 (3.1 - 4.7)	0.002
Glycemia (mg/dL)	96.0 (87.0 - 108.0)	88.0 (80.8 - 97.0)	< 0.001
HOMA-IR	2.0 (1.2 - 3.4)	2.2 (1.5 - 3.0)	0.900
TyG	4.8 (0.3)	4.8 (0.3)	0.113
Total cholesterol (mg/dL)	195.2 (40.6)	215.6 (42.8)	< 0.001
LDL (mg/dL)	118.4 (37.4)	130.8 (37.6)	0.010
HDL (mg/dL)	44.7 (12.9)	51.4 (15.6)	< 0.001
TC/ HDL	4.64 (1.46)	4.49 (1.43)	0.402
LDL/HDL	2.81 (1.18)	2.75 (1.07)	0.696
Triglycerides (mg/dL)	140.0 (104.0 - 226.0)	146.5 (92.0 - 227.8)	0.597
CRP (mg/dL)	1.3 (0.3 - 3.2)	2.9 (0.8 - 5.8)	0.008

Data presented in mean and standard deviation or median (p25-p75). Values of p by t-test or Mann-Whitney.

fat meal has been suggested to increase inflammation, although there is currently no consensus regarding the specific changes in many of the pro-inflammatory markers that are often evaluated after a high-fat diet.<sup>42</sup>

SFA can cause inflammation of adipose tissue by processes involving, among others, the "toll-like receptor" TLR-4, a sensor that binds to bacterial lipopolysaccharide (LPS).<sup>43</sup> High fat diets, especially those rich in SFA, have been shown to increase LPS uptake in the intestine.<sup>44,45</sup> Evidence suggests that SFA and LPS share the same inflammatory signaling pathway as TLR4, thus promoting the expression of proinflammatory transcription factors such as nuclear kappa B and cyclooxygenase-2.<sup>42</sup>

The subjects with higher intake of medium chain fatty acids had a higher total leukocyte count. It has been demonstrated that CRP-us<sup>46</sup> and leukocyte count<sup>47</sup> can independently predict vascular risk in

apparently healthy men and women, asymptomatic for cardiovascular risk factors.<sup>46</sup>

A study conducted by Raz et al.,<sup>48</sup> with 54 subjects with a BMI of  $25 \pm 0.9$  kg/m², with a mean age of  $41.7 \pm 3.1$  years, demonstrated a significant increase in CRP-us after a high-acid meal (51 g), it did not work when the meal was high in monounsaturated fatty acids.

We also found tha individuals with higher intakes of C16:  $1 (\geq 0.94g/day)$  had higher values for BMI, fat percentage and HOMA-IR. Studies evaluating the palmitoleic MUFA intake and its relation with cardiometabolic markers have not been reported yet. However, some studies have pointed out that higher proportions of palmitoleic acid in blood or adipose tissue are consistently associated with chronic diseases outcomes, such as obesity,  $^{49,50}$  hypertriglyceridemia,  $^{51}$  hyperglycemia,  $^{52}$  inflammation,  $^{53,54}$  metabolic syndrome,  $^{55,56}$  diabetes type 2,  $^{57}$  disease coronary heart disease,  $^{57}$  and heart failure.  $^{58}$  In obese individuals

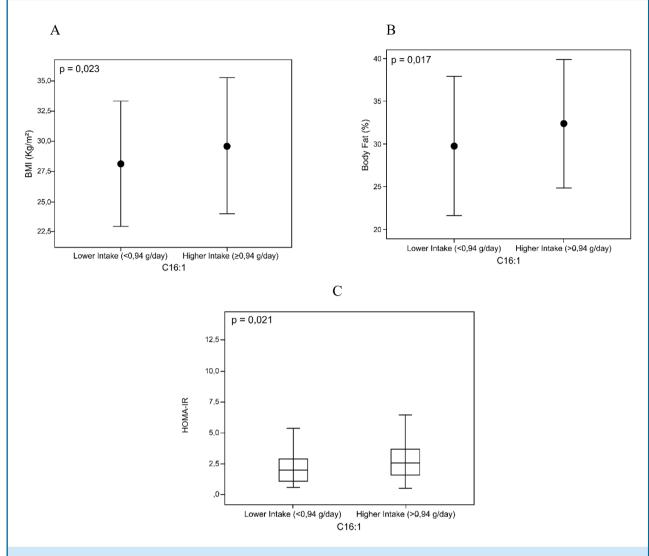


Figure 1 - Values of BMI (A), body fat (B) and HOMA-IR (C), according to intake of C16: 1 (palmitoleic acid). Data are mean and standard deviation or median (p25-p75), according to normality. Values of p by t-test or Mann-Whitney, where appropriate. C16: 1 was adjusted by caloric intake by residual method.

with significant weight loss, high palmitoleic acid in adipose tissue was associated with higher inability to maintain weight loss.<sup>50</sup> Moreover, in 18-week nutrition intervention study, with sixteen metabolic syndrome patients,<sup>59</sup> plasma palmitoleic acid was gradually increasing when participants fed related low-carbohydrate diet to high-carbohydrate diet (47 to 346 g/d).

The study has as its limitation the use of only a 24-hour recall that provides us with current and not habitual diet information, although this food survey has been extensively used in epidemiological studies to investigate food consumption relationship with chronic diseases.<sup>60</sup>

# Conclusion

In this cross-sectional study, individuals with a higher intake of medium-chain SFA had lower values of indicators of adiposity, ferritin, uric acid, and fasting glucose, and higher leukocyte, CRP, CT, LDL, and HDL concentrations. While higher palmitoleic MUFA consumption was related to higher BMI, fat percentage and HOMA-IR values. Our results suggest the relevance of a detailed assessment of the dietary fatty acid profile in the high-risk cardiometabolic population, considering chain size and saturation.

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#### **Author contributions**

Conception and design of the research: Fortes FS, Almeida AP, Silveira BKS, Hermsdorff HHM. Acquisition of data: Fortes FS, Almeida AP, Silveira BKS. Analysis and interpretation of the data: Fortes FS, Almeida AP. Writing of the manuscript: Fortes FS, Almeida AP. Critical revision of the manuscript for intellectual content: Fortes FS, Almeida AP, Rosa COB, Hermsdorff HHM.

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#### **Potential Conflict of Interest**

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

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#### **Study Association**

This article is part of the thesis of master submitted by Nínive de Almeida Reis, from *Universidade Federal* de Viçosa.

#### Ethics approval and consent to participate

This study was approved by the Ethics Committee of the *Universidade Federal de Viçosa* under the protocol number 066/2012/CEPH. 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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