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Adipose tissue palmitoleic acid is inversely associated with nonfatal acute myocardial infarction in Costa Rican adults

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Abstract

Background and Aims—Animal models have shown that adipose-derived palmitoleic acid may act as a lipokine by conferring resistance to diet-induced obesity; however, human epidemiologic studies investigating this relationship thus far have not provided data in support of this hypothesis. Because metabolic syndrome and cardiovascular disease are intricately linked with the former being a major risk factor for the latter, we hypothesized that adipose-derived palmitoleic acid may be inversely associated with myocardial infarction. We examined whether adipose tissue palmitoleic acid was associated with nonfatal acute myocardial infarction in a representative population of Costa Rican adults.

Methods and Results—Odds ratios of nonfatal acute myocardial infarction by quintiles of adipose tissue palmitoleic acid were calculated using conditional logistic regression in a case-control study of 1,828 cases and 1,828 controls matched by age, sex, and area of residence. We observed an inverse relationship between nonfatal acute myocardial infarction and adipose tissue palmitoleic acid (OR for highest quintile compared to lowest quintile of palmitoleic acid: 0.55; 95% CI: 0.41, 0.75; *P* for trend: <0.0001). We additionally observed a significant positive association between adipose tissue palmitoleic acid and high-density lipoprotein cholesterol.

Conclusion—These data demonstrate an inverse association between adipose tissue palmitoleic acid and nonfatal acute myocardial infarction; however, further research is required in order to better understand the opposing associations between palmitoleic acid and high-density lipoprotein cholesterol and systolic blood pressure.

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Keywords

Costa Rican adults; nonfatal acute myocardial infarction; adipose tissue palmitoleic acid; metabolic syndrome; HDL cholesterol; case-control study

INTRODUCTION

Cardiovascular disease (CVD) has become one of the leading causes of early mortality among adults over the past few decades. In 2012, CVD accounted for approximately 46.2% of mortality from non-communicable diseases or 17 million deaths, globally [1]. With the global burden of CVD projected to rise to more than 23.6 million deaths by the year 2030, recent research has focused on identifying mechanisms and understanding risk factors for CVD in an effort to design more effective interventions for its treatment [2]. In particular, investigations into the associations between fatty acids and CVD have become increasingly common for a variety of reasons, one of which being a direct translation to intervention [3–6]. In the past decade, research has increasingly focused on palmitoleic acid, a minor monounsaturated fatty acid; in 2008, Cao *et al.* identified a potential role of palmitoleic acid as a lipokine, a role which they identified via systemic lipid profiling of mice deficient in adipose tissue lipid chaperones aP2 and mal1 [7]. Cao *et al.* demonstrated the ability of adipose tissue palmitoleic acid to improve muscle insulin signaling and suppress hepatosteatosis, thereby reversing two hallmarks of metabolic syndrome. A protective effect on metabolic syndrome may translate to a similarly protective effect on CVD due to the former being a risk factor for the latter [8]. However, despite these data in mice, evidence in human epidemiologic studies is sparse and controversial. With regards to metabolic syndrome, most data do not support the role of palmitoleic acid as a lipokine [9–11]. For CVD, the data are even less conclusive [12–14]. This research study aims to investigate the relationship between adipose tissue palmitoleic acid and nonfatal acute myocardial infarction (MI) in a large population-based case-control study of Costa Rican adults. This study also aims to evaluate effect modification by sex and assess potential mediators in the relationship between adipose tissue palmitoleic acid and MI.

METHODS

Study population

The subjects in this study were cases of nonfatal acute MI identified in Costa Rica between 1994 and 2004. The catchment area of the study, the Central Valley of Costa Rica, included 34 counties and covered a full range of lifestyles and socioeconomic characteristics. Full details of the study design are provided elsewhere [15]. Briefly, cases were adults who were diagnosed as survivors of a first acute MI by independent examinations of two cardiologists at any of the six recruiting hospitals in the catchment area. All cases met the World Health Organization (WHO) criteria for MI, which includes typical symptoms as well as either elevation in cardiac enzyme concentrations or diagnostic changes in the electrocardiogram [16]. For each eligible case, one population-based control was randomly identified from the underlying source population using data from the National Census and Statistics Bureau of Costa Rica. Controls were matched to cases by age (± 5 years), sex, and area of residence

(county). All subjects provided written informed consent to participate in the study. This study was approved by the Ethics Committee of the Harvard School of Public Health and the National Institute of Health Research at the University of Costa Rica.

Data collection

Information on sociodemographic characteristics and medical histories were collected by trained personnel at the homes of each subject via a questionnaire with closed-ended questions. Anthropometric measurements were collected of subjects in light clothing and without shoes. All measurements were performed in duplicate, with the average of the two measurements used in data analyses. A bathroom scale (Detecto, Webb City, MO) or a Seca Alpha Model 770 digital scale (Seca, Hanover, MD) accurate to 50 g and a steel anthropometer were used to measure weight and height, respectively. The scales were calibrated biweekly. Self-reported dietary intake was collected via a food-frequency questionnaire developed and validated to reflect fatty acid intake in the Costa Rican population [17]. Biological samples were collected in the subject's home in the morning after an overnight fast. A subcutaneous adipose tissue biopsy was also collected from the upper buttock with a 16-gauge needle and disposable syringe, based on protocols established elsewhere [18]. The tissue specimens were stored in liquid nitrogen tanks at -80°C for subsequent fatty acid analysis.

Fatty acid analysis

Fatty acids from adipose tissue biopsy specimens were quantified by gas-liquid chromatography as previously described [19]. Peak retention times and area percentages of total fatty acids were identified by injecting known standards (NuChek Prep; Nuchek, Elysian, MN) and analyzed with Agilent Technologies ChemStationA.08.03 software (Agilent Technologies, Santa Clara, CA). Twelve duplicate samples, which were indistinguishable from the others, were analyzed throughout the study. The CV for palmitoleic acid was 5.7%.

Data analysis

The original sample consisted of 4,547 subjects, of whom 2,274 were controls and 2,273 were cases. After removing subjects with missing information on adipose tissue palmitoleic acid concentrations ($n = 732$) or confounding variables ($n = 34$) included in the fully adjusted model (with the exception of income, which was handled via multiple imputation), and subjects who could not be rematched after the aforementioned exclusions ($n = 125$), 3,656 subjects remained, with 1,828 cases and 1,828 controls matched by age, sex, and area of residence. McNemar's tests were used to assess differences in baseline characteristics between cases and controls for binary variables. Paired t -tests and Wilcoxon signed rank tests were used to assess differences between cases and controls for normally distributed and non-normally distributed continuous variables, respectively. Multiple imputations were performed on missing data for monthly household income ($n = 258$; 7.1% of the entire sample), using a multiple Markov chain Monte Carlo method assuming missing at random. Variables used to predict missing income data included palmitoleic acid concentration, current smoking status, histories of diabetes and hypertension, and adipose tissue oleic, linoleic, arachidonic, and alpha-linolenic fatty acid concentrations. Conditional logistic

regression models were fit to estimate odds ratios (ORs) and 95% confidence intervals (95% CI) of nonfatal acute MI across quintiles of adipose tissue palmitoleic acid concentrations. Quintiles were used in order to examine non-linear dose-response relationships and threshold effects in the association between exposure and outcome. The first model was conditioned on the matching factors (age, sex, and area of residence), while the second model was adjusted for several demographic characteristics, including monthly household income (continuous), smoking status (yes or no), history of diabetes (yes or no), and history of hypertension (yes or no). The fully adjusted model additionally was adjusted for several adipose tissue fatty acids, including oleic acid, linoleic acid, arachidonic acid, and alpha-linolenic acid. The decisions regarding confounder adjustments were based on *a priori* knowledge of risk factors for CVD and supplemented by the associations between confounders and exposure in our study population. Fatty acid confounders were selected based on previous studies demonstrating their associations with CVD [4–6]. Additional adjustment for total energy intake, daily energy expenditure, and waist-to-hip ratio did not appreciably change the measures of association (data not shown). Thus, those variables were not included as covariates in the final models. Tests for trend were performed by fitting conditional logistic regression models, treating the median values of the quintiles of palmitoleic acid as a continuous variable. To evaluate potential effect modification by sex, conditional logistic regression models were fit and tests for trend conducted in men and women separately. Linear models adjusted for the same covariates in the fully adjusted conditional logistic regression model were fit to estimate least-squares means of cardiometabolic risk factors for MI, including total cholesterol, high, low, and very low-density lipoprotein cholesterol, systolic and diastolic blood pressure, triglycerides, waist-to-hip ratio, and C-reactive protein, across quartiles of palmitoleic acid. All analyses were performed with SAS software (version 9.4; SAS Institute, Cary, NC).

RESULTS

Table 1 shows the baseline characteristics of 1,828 cases of nonfatal myocardial infarction and 1,828 controls matched on age, sex, and area of residence. Cases were more likely to be smokers and have histories of diabetes and hypertension compared to controls. In contrast, controls had higher monthly incomes and were more physically active. Levels of dietary variables and adipose tissue fatty acid compositions were comparable between cases and controls.

Table 2 presents the baseline characteristics of study controls across quintiles of adipose tissue palmitoleic acid. Among controls, percentages of women and concentrations of adipose tissue monounsaturated fatty acids and arachidonic acid increased across quintiles of palmitoleic acid. In contrast, monthly income and concentrations of adipose tissue alpha-linolenic and linoleic acids decreased.

The associations between adipose tissue palmitoleic acid concentrations and MI were investigated by conditional logistic regression and described in Table 3. In the unadjusted model, the OR of MI in the highest compared to the lowest quintile of palmitoleic acid was 0.90 (95% CI: 0.72, 1.13; *P* for trend: 0.4263). While a clear relationship was not evident in the unadjusted model, a decreasing trend of ORs emerged after adjusting for covariates. In

the final multivariate model adjusted for matching factors, lifestyle characteristics, and adipose tissue fatty acid concentrations, the inverse association between adipose tissue palmitoleic acid concentrations and MI became pronounced and significant. The OR in the highest compared to the lowest quintile of palmitoleic acid in the fully adjusted model was 0.55 (95% CI: 0.41, 0.75; *P* for trend: <0.0001). The models were stratified by sex to examine potential effect modification by sex. Quintiles of the exposure derived from the total study population were applied individually to males and females. Although male and female controls exhibited similar trends in covariates across palmitoleic acid quintiles (data not shown), the inverse association between palmitoleic acid and MI was more pronounced among females (*n* = 972) than among males (*n* = 2,684). The OR in the highest compared to the lowest quintile of palmitoleic acid was 0.47 (95% CI: 0.25, 0.89; *P* for trend: 0.0101) and 0.57 (95% CI: 0.40, 0.81; *P* for trend: 0.0013) for females and males, respectively. However, the interaction between palmitoleic acid and sex was not significant by likelihood ratio test.

To further investigate the association between palmitoleic acid and MI described in Table 3, the associations between palmitoleic acid and cardiometabolic risk factors for MI, including total cholesterol, high, low, and very low-density lipoprotein cholesterol, systolic and diastolic blood pressure, triglycerides, waist-to-hip ratio, and C-reactive protein, were examined among controls with linear regression models. As has been previously reported, increased levels of palmitoleic acid were significantly associated with increased least-squares means of systolic blood pressure (Figure 1A; *P* for trend: 0.0006) [20]. Between the lowest and highest quartiles of palmitoleic acid, the least-squares means of systolic blood pressure increased 2.09%. This increase in systolic blood pressure was accompanied by a significant elevation in the least-squares means of high-density lipoprotein cholesterol (HDL-C) across quartiles of palmitoleic acid (Figure 1B; *P* for trend: 0.0033). Between the lowest and highest quartiles of palmitoleic acid, the least-squares means of HDL-C increased 13.0%. Remaining relationships between risk factors and quintiles of palmitoleic acid are presented in Supplementary Table 1. Similar observations were made in sex-stratified analyses (data not shown).

DISCUSSION

In a large population-based case-control study conducted in Costa Rica, we identified a strong, inverse association between adipose tissue palmitoleic acid and nonfatal acute MI. This association was also present in sex-stratified analyses. These results were consistent with the observed association between adipose tissue palmitoleic acid and higher HDL-C in the current study.

In our study, and based on our previous results [21], we hypothesized that adipose tissue palmitoleic acid would be inversely associated with CVD. Results from our study support this hypothesis. In contrast, a study in a cohort of 853 Swedish men did not find an association between adipose tissue palmitoleic acid and cardiovascular mortality after adjustment for CVD risk factors [14].

Our finding that HDL-C levels increase concomitantly with adipose tissue palmitoleic acid concentrations in this population of Costa Rican adults may provide a partial explanation for the inverse association between adipose-derived palmitoleic acid and nonfatal acute MI. The cardioprotective effects of HDL have been explained by its role in reverse cholesterol transport, as well as its role in the production of atheroprotective signaling molecules and its antithrombotic properties [22]. Recent mendelian randomization studies have cast doubt on the causal association between HDL-C and CVD [23]. However, HDL-C is a complex family of particles with many diverse functions. In particular, a recent study demonstrated differential associations between HDL-C and CVD based on the presence or absence of apolipoprotein C (apoC)-III [24]. On the other hand, our data showed that higher levels of adipose tissue palmitoleic acid were also associated with higher systolic blood pressure, a well-known risk factor for CVD [25]. It is possible that the potential benefits of elevated HDL-C levels may offset the potential consequences of elevated systolic blood pressure. Since HDL-C levels are generally lower among Costa Ricans than Caucasians [26], small increases in HDL-C levels could have a stronger impact when the overall levels in the population are low. However, these hypotheses require further research to substantiate. Finally, levels of palmitoleic acid may not be causally associated with CHD, but may instead represent other phenomena such as *de novo* lipogenesis (DNL). For example, in a randomized-controlled trial of high-carbohydrate feeding, researchers found that SCD1, the rate-limiting enzyme in the synthesis of palmitoleic acid from palmitic acid, activity and DNL were simultaneously activated [27].

Findings from epidemiological studies in other populations using circulating biomarkers of palmitoleic acid rather than adipose tissue have been mixed. An ancillary study of the Physicians' Health Study found that erythrocyte membrane palmitoleic acid was positively associated with CHD [12]. In contrast, a study of 25,639 individuals from the European Prospective Investigation into Cancer (EPIC)-Norfolk study that assessed palmitoleic acid in plasma did not find an association [13]. It is known that the fatty acid composition of adipose tissue, erythrocyte membrane, and plasma varies substantially. For example, in a recent meta-analysis, palmitoleic acid comprised 7.2, 0.7, and 2.8 mole percent of total fatty acids in adipose tissue, erythrocyte membrane, and plasma, respectively [28]. In addition, in our study population, correlations between adipose tissue palmitoleic acid and palmitoleic acid in plasma and whole blood were 0.55 and 0.47, respectively (unpublished data). It is likely that the levels of fatty acids in these pools represent differences in their metabolism and their effects on CVD. Furthermore, stearoyl-CoA desaturase 1 (SCD1) exhibits tissue-specific expression, thus also potentially impacting the association between palmitoleic acid and CVD [29]. In humans, SCD1 is predominantly expressed in adipose tissue and the liver and is largely responsible for the presence of palmitoleic acid in adipose tissue.

In sex-stratified analyses, we observed that the inverse association between adipose tissue palmitoleic acid and MI was stronger among women than among men. This may be explained by the fact that the median concentration of palmitoleic acid is higher among women than among men, as evidenced by a larger proportion of women than men occupying the highest quintile of palmitoleic acid (Table 3). This sexual dimorphism in palmitoleic acid concentrations has been noted before [30]. However, this hypothesis requires further research to substantiate.

The strengths of our current study include a large sample size and a population-based design that minimized the possibility of selection bias because controls were selected directly and randomly from the source population that gave rise to cases. The Central Valley of Costa Rica included people with diverse lifestyle and socioeconomic characteristics; as such, the results are also likely to be generalizable to the entire Costa Rican population. Our study also has some limitations. Due to the observational design, despite our best attempts at adjusting for potential confounders, residual confounding could not be ruled out. In addition, we want to draw caution to the interpretation of data from biomarker studies. At their very core, biomarker studies are conducted when the true object of interest is very difficult or impossible to ascertain. We selected adipose tissue as our fatty acid depot as opposed to other tissues because of its slow turnover and lack of response to acute disease; thus, fatty acids measured in adipose tissue are more reflective of pre-disease fatty acid levels than those measured in other depots [19]. However, we still have to be cautious concluding that they represent what we are interested in measuring. Future research is required to evaluate if the cardioprotective associations exerted by adipose tissue palmitoleic acid are present in other populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors' responsibilities were as follows—DL: conducted data analyses and wrote the manuscript; DQ: proofread and edited the manuscript; HC: designed the research project, contributed to the interpretation of the data and proofread and edited the manuscript; AB: designed the research project, supervised data analyses and main aspects of data interpretation, proofread and edited the manuscript, and has primary responsibility for final content. This work was supported by the National Institutes of Health [HL49086, HL60692], USA.

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Highlights

- Adipose palmitoleate is inversely associated with heart attacks among Costa Ricans.
- This effect is accompanied by a concomitant increase in HDL cholesterol.
- This inverse association was stronger among women than men.

Figure 1.

Least-squares means of systolic blood pressure (**A**) and high-density lipoprotein cholesterol (**B**), obtained by linear models comparing nonfatal acute MI across quartiles of adipose tissue palmitoleic acid. Linear models were conditioned on matching factors and adjusted for monthly household income, smoking status, history of diabetes, history of hypertension, and adipose tissue oleic, linoleic, arachidonic, and alpha-linolenic fatty acids.

Table 1Characteristics of men and women with a nonfatal myocardial infarction event and controls¹

Variables	Cases(n = 1828)	Controls (n = 1828)	P
Age (y)	58.5 ± 10.9 ²	58.2 ± 11.1	
Female (%)	26.6	26.6	
Urban residence (%)	39.1	39.1	
Income (\$/mo) ³	506 ± 393	579 ± 425	<0.0001
Waist-to-hip ratio ⁴	0.97 ± 0.07	0.95 ± 0.07	<0.0001
Current smoker (%)	39.4	20.9	<0.0001
Current drinker (%)	47.1	52.8	0.0002
Diabetes history (%)	24.6	14.6	<0.0001
Hypertension history (%)	39.1	30.3	<0.0001
EE on daily activity (METs/d)	34.1 ± 15.7	35.3 ± 15.2	0.0003
Dietary variables ⁵			
Total energy intake (kcal/d)	2689 ± 938	2438 ± 751	<0.0001
Total fat (% of energy)	32.4 ± 5.88	31.8 ± 5.82	0.0008
Saturated fat (% of energy)	11.1 ± 2.90	10.4 ± 2.68	<0.0001
Monounsaturated fat (% of energy)	11.9 ± 3.52	11.8 ± 3.82	0.1864
Palmitoleic acid (16:1n-7) (% of energy)	0.50 ± 0.18	0.47 ± 0.17	<0.0001
Polyunsaturated fat (% of energy)	5.97 ± 2.01	6.23 ± 2.04	<0.0001
trans Fat (% of energy)	1.29 ± 0.60	1.26 ± 0.59	0.0502
Carbohydrate (% of energy)	54.3 ± 7.54	55.4 ± 7.37	<0.0001
Protein (% of energy)	13.2 ± 2.21	13.0 ± 2.11	0.0015
Fatty acids in adipose tissue: (g/100 g total fatty acids)			
Saturated fat	26.2 ± 3.70	26.0 ± 3.58	0.0799
Monounsaturated fat	51.9 ± 4.63	51.6 ± 4.62	0.0446
Polyunsaturated fat	17.5 ± 4.04	17.9 ± 4.04	0.0020
Stearic acid (18:0)	2.77 ± 0.94	2.77 ± 1.00	0.3323
Oleic acid (18:1n-9)	42.4 ± 3.21	42.1 ± 3.11	<0.0001
Palmitic acid (16:0)	21.6 ± 2.94	21.3 ± 2.75	0.0062
Palmitoleic acid (16:1n-7)	6.55 ± 2.24	6.60 ± 2.22	0.4765
α-Linolenic acid (18:3n-3)	0.62 ± 0.21	0.65 ± 0.21	<0.0001
Eicosapentaenoic acid (20:5n-3) ⁶	0.04 ± 0.02	0.04 ± 0.02	0.8579
Docosahexaenoic acid (22:6n-3) ⁷	0.15 ± 0.06	0.14 ± 0.05	0.1411
Linoleic acid (18:2n-6)	15.2 ± 3.81	15.5 ± 3.83	0.0005
Arachidonic acid (20:4n-6)	0.50 ± 0.14	0.47 ± 0.14	<0.0001
SCD1 activity (18:1/18:0)	17.2 ± 6.54	17.2 ± 6.57	0.9749
SCD1 activity (16:1/16:0)	0.31 ± 0.13	0.32 ± 0.12	0.1764

¹EE, energy expenditure; METs, metabolic equivalent tasks. The McNemar's test was used for binary variables, and the paired *t* test and the Wilcoxon signed rank test were used for normally distributed and not normally distributed continuous variables, respectively

²Average ± SD (all such values)

^{3,4,6,7} 258, 11, 629, and 1 missing observations, respectively

⁵ 4 missing observations each

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Characteristics of controls according to quintiles of palmitoleic acid concentrations (n = 1828)¹

	Quintiles of palmitoleic acid (16:1n-7) in adipose tissue				
	1 (n = 365)	2 (n = 366)	3 (n = 366)	4 (n = 366)	5 (n = 365)
Adipose tissue palmitoleic acid	3.65 ± 0.74 ²	5.33 ± 0.36	6.44 ± 0.31	7.69 ± 0.41	9.86 ± 1.24
Age (y)	57.7 ± 10.8	57.0 ± 10.8	58.1 ± 11.3	58.4 ± 11.1	60.0 ± 11.6
Female (%)	11.8	19.7	26.2	31.7	43.6
Urban residence (%)	43.3	42.1	38.8	35.8	35.3
Income (\$/mo) ³	665 ± 463	612 ± 423	587 ± 425	528 ± 399	498 ± 391
Waist-to-hip ratio ⁴	0.95 ± 0.07	0.95 ± 0.07	0.95 ± 0.08	0.95 ± 0.08	0.95 ± 0.08
Current smoker (%)	17.5	21.0	21.0	24.9	20.0
Current drinker (%)	54.0	58.5	55.5	51.4	44.9
Diabetes history (%)	16.4	10.9	12.8	14.8	17.8
Hypertension history (%)	24.4	27.6	32.2	29.5	37.5
EE on daily activity (METs/d)	35.3 ± 14.4	36.0 ± 15.9	35.8 ± 15.7	35.3 ± 15.4	34.3 ± 14.8
Dietary variables ⁵					
Total energy intake (kcal/d)	2460 ± 686	2457 ± 724	2447 ± 790	2404 ± 765	2420 ± 787
Total fat (% of energy)	32.5 ± 6.06	32.6 ± 5.88	32.0 ± 5.80	31.3 ± 5.51	30.4 ± 5.55
Saturated fat (% of energy)	10.1 ± 2.70	10.3 ± 2.54	10.4 ± 2.67	10.6 ± 2.70	10.5 ± 2.78
Monounsaturated fat (% of energy)	12.0 ± 4.01	12.2 ± 4.28	11.9 ± 3.88	11.5 ± 3.35	11.2 ± 3.43
Palmitoleic acid (16:1n-7) (% of energy)	0.48 ± 0.18	0.49 ± 0.17	0.48 ± 0.17	0.47 ± 0.15	0.44 ± 0.18
Polyunsaturated fat (% of energy)	6.80 ± 1.90	6.61 ± 2.16	6.18 ± 1.89	6.00 ± 1.99	5.58 ± 2.05
<i>trans</i> Fat (% of energy)	1.41 ± 0.67	1.29 ± 0.60	1.24 ± 0.58	1.23 ± 0.56	1.14 ± 0.52
Carbohydrate (% of energy)	54.9 ± 7.32	54.8 ± 7.20	55.3 ± 7.42	55.5 ± 7.44	56.7 ± 7.35
Protein (% of energy)	13.1 ± 2.17	13.0 ± 2.03	13.0 ± 2.08	13.0 ± 2.21	12.8 ± 2.06
Fatty acids in adipose tissue: (g/100 g total fatty acids)					
Saturated fat	27.7 ± 4.08	26.7 ± 3.31	26.3 ± 3.33	25.5 ± 3.02	23.9 ± 2.89
Monounsaturated fat	47.3 ± 4.01	49.7 ± 3.23	51.5 ± 3.38	53.3 ± 3.09	56.3 ± 3.50
Polyunsaturated fat	20.0 ± 4.18	18.9 ± 4.00	17.8 ± 3.83	16.9 ± 3.33	15.7 ± 3.33
Stearic acid (18:0)	3.98 ± 0.98	3.08 ± 0.69	2.70 ± 0.59	2.31 ± 0.51	1.77 ± 0.47

	Quintiles of palmitoleic acid (16:1n-7) in adipose tissue				
	1 (n = 365)	2 (n = 366)	3 (n = 366)	4 (n = 366)	5 (n = 365)
Oleic acid (18:1n-9)	41.1 ± 3.56	41.7 ± 2.96	42.3 ± 3.05	42.5 ± 2.74	42.9 ± 2.84
Palmitic acid (16:0)	21.9 ± 3.16	21.7 ± 2.71	21.6 ± 2.67	21.2 ± 2.46	20.2 ± 2.36
α-Linolenic acid (18:3n-3)	0.74 ± 0.25	0.69 ± 0.21	0.66 ± 0.20	0.61 ± 0.18	0.56 ± 0.17
Eicosapentaenoic acid (20:5n-3) ⁶	0.04 ± 0.02	0.04 ± 0.02	0.04 ± 0.02	0.04 ± 0.02	0.05 ± 0.02
Docosahexaenoic acid (22:6n-3)	0.14 ± 0.06	0.14 ± 0.05	0.14 ± 0.05	0.14 ± 0.05	0.14 ± 0.05
Linoleic acid (18:2n-6)	17.7 ± 3.99	16.6 ± 3.75	15.4 ± 3.59	14.6 ± 3.11	13.4 ± 3.11
Arachidonic acid (20:4n-6)	0.40 ± 0.12	0.44 ± 0.13	0.47 ± 0.13	0.51 ± 0.14	0.55 ± 0.14
SCD1 activity (18:1/18:0)	10.8 ± 2.48	14.1 ± 2.83	16.3 ± 3.44	19.2 ± 4.15	25.7 ± 6.72
SCD1 activity (16:1/16:0)	0.17 ± 0.04	0.25 ± 0.04	0.30 ± 0.04	0.37 ± 0.05	0.50 ± 0.09

¹ EE, energy expenditure; METs, metabolic equivalent tasks.

² Mean ± SD (all such values)

^{3,4,6} 132, 3, and 333 missing observations, respectively

⁵ 2 missing observations each

Table 3

Odds ratios for myocardial infarction according to quintiles of palmitoleic acid concentrations in adipose tissue of Costa Rican adults (n = 3656)

	Quintiles					P for trend
	1	2	3	4	5	
Palmitoleic acid levels in adipose tissue	3.65 ± 0.73 ¹	5.28 ± 0.35	6.41 ± 0.33	7.64 ± 0.39	9.87 ± 1.30	
Unadjusted model ²	1.0	1.00 (0.81, 1.24)	0.87 (0.71, 1.07)	1.01 (0.81, 1.24)	0.90 (0.72, 1.13)	0.4263
Adjusted model ³	1.0	1.00 (0.80, 1.26)	0.86 (0.69, 1.08)	0.91 (0.72, 1.15)	0.81 (0.63, 1.04)	0.0612
Adjusted model ⁴	1.0	0.90 (0.71, 1.14)	0.71 (0.56, 0.91)	0.68 (0.52, 0.89)	0.55 (0.41, 0.75)	<0.0001
Palmitoleic acid levels among men (n = 2684)	635	581	548	515	405	
Unadjusted model ²	1.0	1.01 (0.80, 1.27)	0.92 (0.73, 1.16)	1.10 (0.87, 1.40)	0.90 (0.69, 1.18)	0.7181
Adjusted model ³	1.0	1.00 (0.79, 1.30)	0.88 (0.69, 1.13)	0.98 (0.76, 1.27)	0.79 (0.59, 1.05)	0.1202
Adjusted model ⁴	1.0	0.91 (0.70, 1.18)	0.76 (0.58, 0.99)	0.77 (0.57, 1.04)	0.57 (0.40, 0.81)	0.0013
Palmitoleic acid levels among women (n = 972)	95	151	183	217	326	
Unadjusted model ²	1.0	0.83 (0.49, 1.42)	0.63 (0.37, 1.05)	0.69 (0.42, 1.15)	0.74 (0.44, 1.22)	0.3336
Adjusted model ³	1.0	0.91 (0.50, 1.67)	0.76 (0.42, 1.37)	0.72 (0.41, 1.29)	0.78 (0.44, 1.38)	0.3593
Adjusted model ⁴	1.0	0.83 (0.45, 1.54)	0.58 (0.31, 1.08)	0.50 (0.27, 0.94)	0.47 (0.25, 0.89)	0.0101

¹ Mean ± SD (all such values)² Conditioned on age, sex, and area of residence³ Adjusted for age, sex, area of residence, income, smoking status, history of diabetes, and history of hypertension⁴ Adjusted for age, sex, area of residence, income, smoking status, history of diabetes, history of hypertension, adipose tissue oleic acid, adipose tissue linoleic acid, adipose tissue arachidonic acid, and adipose tissue alpha-linolenic acid