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ORIGINAL COMMUNICATION

# Individual saturated fatty acids and nonfatal acute myocardial infarction in Costa Rica

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**Background:** Epidemiological studies on the effect of individual saturated fatty acids (SFAs) on cardiovascular disease, especially in developing countries with different dietary patterns, are scarce.
**Objective:** To determine the risk of nonfatal acute myocardial infarction (MI) associated with consumption of individual SFAs and their food sources in Costa Rica.
**Design:** The cases ($n = 485$) were survivors of a first acute MI and were matched by age, sex and area of residence to population controls ($n = 508$). Data on anthropometrical measurements, lifestyle and diet were collected using interviewer-administered questionnaires.
**Results:** In analyses adjusted for confounders, consumption of total and individual SFAs was associated with an increased risk of MI. The odds ratio (OR) (95% confidence intervals) for 1% increase in energy from total saturated fat was 1.12 (1.03–1.21) while it was 1.51 (1.03–2.22) for lauric acid + myristic acid, 1.14 (1.01–1.30) for palmitic acid and 2.00 (1.34–3.00) for stearic acid. Although lauric and myristic acids were associated with increased risk of MI, they were consumed in small amounts and most of the saturated fat (87%) came from palmitic and stearic acids, which derived mainly from red meat and fried foods. Consumption of cheese (1–2 *vs* 0 servings/day) was associated with increased risk of MI (OR = 3.07; 95% confidence interval: 1.74–5.39; $P$ for trend $< 0.0001$), while consumption of low-fat milk was not.
**Conclusion:** Increased consumption of total and individual SFAs is associated with increased risk of MI. Lauric, myristic and stearic acids were more potent than palmitic acid.
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**Keywords:** diet; fatty acids; coronary disease; risk factors; epidemiology

## Introduction

Increased saturated fat intake is a risk factor for cardiovascular disease (CVD) (Hu *et al*, 1999, 2001), the leading cause of death in many Western and Latin American countries (Anon, 2002; Reddy & Yusuf, 1998). Although the effect of saturated fat on CVD risk has been mainly attributed to its ability to raise total and low-density lipoprotein (LDL) cholesterol (Kris-Etherton & Yu, 1997), it could be due, in part, to low-fiber intake among consumers of high-fat diets (Ascherio *et al*, 1996). Studies in Nigeria suggest that the effects of saturated fat on serum cholesterol depend on the subject's physical activity level, total fat and total energy intakes (Kesteloot *et al*, 1989; Glew *et al*, 2001). Most studies on saturated fat have been experimental and compared individual saturated fatty acids (SFAs) to carbohydrates and/or oleic acid with regard to changes in serum lipid profiles (Katan *et al*, 1995; Kris-Etherton & Yu, 1997). Most of these studies showed that lauric, myristic and palmitic acids were hypercholesterolemic and that myristic acid was the most potent (Denke & Grundy, 1992; Zock *et al*, 1994; Katan *et al*, 1995) while stearic acid and the short-chain SFAs were considered to be neutral (Grundy & Denke, 1990; Yu *et al*, 1995; Kris-Etherton & Yu, 1997; Judd *et al*, 2002).

Epidemiological studies on saturated fat and CVD end points are few (Garcia-Palmieri *et al*, 1980; Shekelle *et al*, 1981; McGee *et al*, 1984; Kushi *et al*, 1985; Kromhout *et al*, 1995; Ascherio *et al*, 1996; Pietinen *et al*, 1997; Hu *et al*, 1999; Suh *et al*, 2001); most were conducted in industrialized countries and did not investigate individual SFAs (Garcia-Palmieri *et al*, 1980; Shekelle *et al*, 1981; McGee *et al*, 1984; Kushi *et al*, 1985; Ascherio *et al*, 1996; Pietinen *et al*, 1997). A large prospective cohort (Hu *et al*, 1999) of mainly US

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Caucasian women showed that individual SFAs were associated with increased risk of coronary heart disease. Data from the seven-country study showed similar results (Kromhout *et al*, 1995). Since dietary patterns, reporting of food intakes, physical activity levels and lifestyles in developing countries are different from those found in industrialized ones, it is important to investigate the relation between individual SFAs and CVD in populations living in developing countries. For instance, most of the saturated fat in the US comes from dairy and meat products (Hu *et al*, 1999). In contrast, in developing countries, such as Nigeria, saturated fat derives mainly from palm oil, which is low in lauric and myristic acid but contains a large amount of palmitic acid (Kesteloot *et al*, 1989). Intake of dietary fiber also varies in different countries and fiber is known to be hypocholesterolemic (Nicolosi *et al*, 2001), and was found to protect against CVD morbidity and mortality in epidemiological studies (Pietinen *et al*, 1996; Liu *et al*, 2002). However, intake of dietary fiber tends to be inversely related to saturated fat intake (Ascherio *et al*, 1996; Hu *et al*, 1999; Monge-Rojas, 2001) and may confound associations between saturated fat and CVD (Ascherio *et al*, 1996), especially in populations with low-fiber intakes. We investigated the effects of total and individual SFAs and their food sources on the risk of myocardial infarction (MI) in a Costa Rican population.

## Subjects and methods

### Study population

All subjects were Hispanic Americans of Mestizo background who lived in Costa Rica between 1995 and 1998 (Campos & Siles, 2000). The catchment area for this study was the 18 counties that compose the metropolitan area of San José, Costa Rica. Eligible case subjects were men and women who were diagnosed as survivors of a first acute MI by two independent cardiologists at any of the three recruiting hospitals in the catchment area (San Juan de Dios Hospital, Calderón Guardia Hospital, and México Hospital) between 1994 and 1998 (Campos & Siles, 2000). In order to achieve 100% ascertainment, fieldworkers carried out daily visits to the three hospitals. All cases met the World Health Organization criteria for MI, which require typical symptoms plus either elevations in cardiac enzyme levels or diagnostic changes in the electrocardiogram (Tunstall-Pedoe *et al*, 1994). Cases were ineligible if they (a) died during hospitalization, (b) were 75 y or older on the day of their first MI, or (c) were physically or mentally unable to answer the questionnaire and (d) had a previous hospital admission related to CVD. Enrollment was carried out while cases were in the hospital's stepdown unit.

Cases ($n=530$) were matched by age ($\pm 5$ y), sex and area of residence to population controls ($n=531$) randomly identified with the aid of data from the National Census and Statistics Bureau of Costa Rica. As a result of the comprehensive social services provided in Costa Rica, all persons living in the catchment area had access to medical care without regard to income. Therefore, control subjects come from the source population that gave rise to the cases and are not likely to have been having CVD that was not diagnosed because of poor access to medical care. Control subjects were ineligible if they had ever had an MI or if they were physically or mentally unable to answer the questionnaires. All cases and controls were visited at their homes for the collection of dietary and health information, anthropometric measurements and biological specimens. Data collection was completed $26\pm10$ (mean $\pm$ s.d.) days after the MI in cases, and $31\pm15$ days after recruitment in the matched controls. Participation was 97% for cases and 90% for controls. All subjects gave informed consent on documents approved by the Human Subjects Committee of the Harvard School of Public Health and the University of Costa Rica.

### Data collection

Trained personnel visited all study participants at their homes. Sociodemographic characteristics, smoking, socioeconomic status, physical activity and medical history data were collected during an interview using a questionnaire with close-ended questions. Self-reported diabetes and hypertension were validated using the recommended definitions by the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus (Anon, 1998b), and the Third Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNCIII) (Anon, 1997). We computed sensitivities, specificities, and positive and negative predictive values from the questionnaire data and measurements of blood pressure and blood sugar. These parameters showed that self-reported assessments of diabetes and hypertension are reliable in this population (Campos & Siles, 2000).

### Dietary assessment

We collected dietary data using a food-frequency questionnaire (FFQ) that has been developed and validated specifically to assess energy and nutrient intake among the Costa Rican population (El-Sohemy *et al*, 2001, 2002; Kabagambe *et al*, 2001; Baylin *et al*, 2002). The FFQ asked subjects to specify the principal type of oil used for cooking and frying at home. This was confirmed by visual inspection of the oil containers at the time of the house visit. Soybean oil (50%), palm oil (available as shortening) (36%) and corn oil (10%) were used most by this study population; canola oil, olive oil and sunflower oil were used by only 4% of the population (El-Sohemy *et al*, 2001). To estimate the amount of each oil used for cooking and frying at home, we complemented the FFQ data by asking each study subject about his/her recipes for staple dishes (rice and beans) and fried foods and incorporated them into the FFQ. The fatty acid compositions of the most widely used oils and margarines in Costa Rica were analyzed by gas–liquid chromatography and incorpo-

rated into the food composition database. The protocol for this analysis has been described previously (Baylin *et al*, 2002). Briefly, the fatty acids in the oil were extracted using hexane:isopropanol (3:2) mixture and esterified with methanol and acetyl chloride. After esterification, the methanol and acetyl chloride were evaporated, and the fatty acid methyl esters were redissolved in isooctane. The methyl esters were quantitated by gas–liquid chromatography. Peak retention times and area percentages of total fatty acids were identified by injecting known standards (NuCheck Prep, Elysium, MN, USA), and analyzed with the Agilent Technologies ChemStation A.08.03 software.

It should be noted that the soybean oil used in Costa Rica at the time of the study was partially hydrogenated. Compared to this oil, palm oil shortening is lower not only in total unsaturated fatty acids, especially the polyunsaturated ones, but also in total tocopherol content. The proportions of saturated, monounsaturated, polyunsaturated and *trans*-fatty acids in palm oil were 49.7, 39.0, 9.6 and 1.7%, respectively, while soybean oil had 15.4, 26.0, 32.7 and 26.0%, respectively. The amounts of $\alpha$- and $\gamma$-tocopherol in 100 g of palm oil were 2132 and 213 μg, respectively, while they were 1385 and 5539 μg in 100 g of soybean oil, respectively (Kabagambe *et al*, 2002).

### Statistical analysis

Data were analyzed with the SAS software (SAS Institute, Cary, NC, USA). Subjects who were missing values for major confounders or the type of oil used for cooking ($n=45$ for cases and $n=23$ for controls) were excluded leaving 485 cases and 508 matched controls for the final analysis. Individual nutrients were correlated with total energy intake and were adjusted for total energy intake as described (Kabagambe *et al*, 2001; Willett, 1998). Nutrients contributing to energy intake (fatty acids, protein, carbohydrate and alcohol) were also expressed and analyzed as a percentage of total energy. We used the following formula to compute Keys score, an estimate of projected changes in serum cholesterol (mg/dl): Keys score $=1.26(2S-P)+1.5$ $(\sqrt{C})$, where $S$ and $P$ are the percentages of energy from saturated fat and polyunsaturated fat intake, respectively, and $C$ is the daily intake of cholesterol in mg/1000 kcal (Keys & Parlin, 1966; Hu *et al*, 1997). We used the *t*-test, for continuous variables, and the $\chi^2$ test, for categorical variables to test differences in means or distributions of lifestyle and dietary variables in the cases and the controls. We assessed variables for confounding by distributing them across quintiles of percent energy from saturated fat and by investigating the change in point estimates when a given variable was entered into the conditional logistic regression model. Correlations among potential confounders were assessed. We observed that the intake of folate is highly correlated with that of dietary fiber ($r=0.78$), and because dietary fiber has previously been identified as a confounder in studies on saturated fat (Ascherio *et al*, 1996), we chose fiber instead of folate as a covariate in all the models. Adjusting for folate instead of fiber gave the same results. In an attempt to identify independent effects of SFAs, we individually regressed percent energy from stearic acid and from lauric plus myristic acid on percent energy from palmitic acid using the methods described for energy adjustment (Willett, 1998; Kabagambe *et al*, 2001). Percent energy from palmitic acid and the residuals of stearic acid and of lauric plus myristic acid were entered into the multivariate model simultaneously.

We examined the associations between fatty acids, their food sources and MI by distributing the study subjects into quintiles of intake and comparing the top four quintiles to the lowest quintile using multivariate conditional logistic regression. In another analysis, we compared the potencies of individual SFAs by estimating the risk of MI associated with 1% increase in energy from the intake of each one of them. Since individual SFAs were highly correlated, and lauric and myristic acids were consumed in very small amounts, we first analyzed each SFA individually and later combined lauric and myristic acids. We also estimated the risk of MI associated with 1% increase in intake of energy from total fat.

To determine the main food sources of saturated fat in Costa Rica, we identified foods in the FFQ that contributed $\geq 1\%$ of total and each individual SFA. The identified foods were grouped as follows: fried foods, dairy (cheese, milk, other), chicken, red meat (beef and pork products) and other foods. For each subject, the foods in each category were summed up to give the total contribution by a given food group. Each of the top five food groups was distributed into quintiles. Dummy variables comparing the top quintiles to the lowest quintile of each food group were simultaneously entered into a conditional logistic regression model to estimate the risk of MI associated with each food source of saturated fat. We then adjusted the odds ratios (OR) for established CVD risk factors and dietary confounders. We tested for linear trends by assigning the median intake of each quintile to each subject in the same quintile.

## Results

Lifestyle and dietary characteristics of the MI case and control subjects in Costa Rica are presented in Table 1. Compared to controls, the cases had significantly higher ($P<0.05$) intakes of total fat, animal fat, total saturated fat, individual SFAs, cholesterol and total energy. Lauric (12:0) and myristic (14:0) acids were consumed in small amounts ($<1\%$ of energy) while palmitic (16:0) and stearic (18:0) acids were the most abundant and contributed 66 and 21% of the total saturated fat intake, respectively. Total consumption of saturated fat was moderately high at 36% of total fat and 12% of total energy. Average consumption of dietary fiber was high ($\geq 24$ g/day) in both cases and controls. There

**Table 1** Characteristics of MI case and control subjects, Costa Rica, 1995–1998

| *Variable* | *Controls (n=508) Mean±s.d.* | *Cases (n=485) Mean±s.d.* |
|---|---|---|
| Age (y) | 58±11 | 57±10 |
| Females in the population (%) | 27 | 25 |
| Area of residence (%) | | |
| Rural | 15 | 15 |
| Suburban | 29 | 30 |
| Urban | 56 | 55 |
| Smoking status (%)[a] | | |
| Never smoked | 35 | 30 |
| Past smokers | 37 | 27 |
| Current smokers (<10 cigs/day) | 13 | 12 |
| Current smokers (≥10 cigs/day) | 15 | 31 |
| History of diabetes (%)[a] | 11 | 24 |
| History of hypertension (%)[a] | 27 | 43 |
| History of angina (%)[a] | 5 | 12 |
| Weight (kg) | 69±13 | 69±10 |
| Height (m) | 1.63±0.09 | 1.63±0.09 |
| Body mass index (kg/m$^2$) | 26±4 | 26±4 |
| Waist-to-hip ratio[a] | 0.93±0.07 | 0.95±0.07 |
| Physical activity (METS)[a] | 1.85±0.98 | 1.72±0.94 |
| Socioeconomic status index[a,b] | 9.4±3.6 | 8.5±3.4 |
| Years at current address since age 18 y | 27±11 | 26±12 |
| Total dietary fat (% of energy)[a] | 33±6 | 34±6 |
| Total vegetable fat (% of energy)[a] | 20.4±5.5 | 19.5±5.5 |
| Total animal fat (% of energy)[a] | 12.9 ±5.1 | 14.7±5.5 |
| Total saturated fatty acids (% of energy)[a] | 11.7±2.8 | 12.4±2.8 |
| Lauric acid (% of energy)[a] | 0.19±0.15 | 0.21±0.14 |
| Myristic acid (% of energy)[a] | 0.71±0.36 | 0.80±0.34 |
| Palmitic acid (% of energy)[a] | 7.8±1.8 | 8.1±1.8 |
| Stearic acid (% of energy)[a] | 2.4±0.6 | 2.6±0.6 |
| Monounsaturated fat (% energy) | 12.4±3.4 | 12.7±3.5 |
| Polyunsaturated fat (% energy) | 5.6±1.5 | 5.5±1.6 |
| Cholesterol (mg/1000 kcal)[a] | 125±65 | 135±66 |
| Total energy intake (Kcal/day)[a] | 2330±706 | 2516±854 |
| Dietary fiber (g/day) | 25±7 | 24±6 |
| Folic acid (μg/day)[a] | 360±86 | 376±137 |
| Total vitamin E (mg/day) | 23±8 | 23±8 |
| Total carotenoid intake (IU/day) | 8108±5708 | 7859±5331 |
| Alcohol among users only (g/day) | 16±21 | 18±27 |
| Cheese (servings/day)[a,c] | 0.60 | 0.79 |
| Ice cream, sour cream and butter[a,c,d] | 0.38 | 0.48 |
| Milk (servings/day)[c,e] | 0.69 | 0.75 |
| Meat and pork (servings/day)[a,c] | 1.14 | 1.44 |
| Fried foods (servings/day)[a] | 6.79 | 7.11 |
| Keys score[a,f,g] | 39±10 | 41±10 |

[a]Cases significantly different from controls ($P<0.05$).
[b]Includes education, occupation, income, and household possessions.
[c]Serving size: 28 g for cheese (one slice); 72 g for ice cream (1/2 cup); 72 g for sour cream (1/2 cup); 5 g for butter (one pat); 244 ml for milk (one glass); 53 g for red meat (one small patty).
[d]Butter includes *lactocrema*, a mixture of butter and margarine.
[e]Mostly 1 and 2% fat milk.
[f]High values indicate potential deleterious plasma lipid profiles.
[g]Keys score=1.26(2S−*P*)+1.5 (C), where *S* and *P* are the percentages of energy from saturated fat and polyunsaturated fat intake, respectively, and *C* is the daily intake of cholesterol in mg/1000 kcal (Keys & Parlin, 1966; Hu et al, 1997).

were 38% of cases and 46% of controls who reported alcohol use. The relation between saturated fat intake and potential confounders is shown in Table 2. A higher intake of saturated fat was associated with increased consumption of palm oil, dairy products, cholesterol and red meat. Intake of dietary fiber, folic acid, vitamin E, carotenoids and alcohol tended to be lower among subjects with higher saturated fat intakes. Increased saturated fat intake was also correlated with lower socioeconomic status and higher prevalence of diabetes and angina. People in the lower quintiles of saturated fat intake tended to be taller than those in the highest quintile.

**Table 2** Distribution of potential confounders by quintiles of energy from saturated fat in 508 controls, Costa Rica, 1995–1998

| | *Quintiles of energy from saturated fat (median intake)* | | | | |
|---|---|---|---|---|---|
| *Variable* | *1 (8.8%)* | *2 (10.5%)* | *3 (11.7%)* | *4 (13.2%)* | *5 (15.7%)* |
| Smoking status (%) | | | | | |
| Never smoked | 32 | 38 | 31 | 38 | 38 |
| Past smokers | 41 | 36 | 45 | 31 | 31 |
| Current smokers (<10 cigs/day) | 14 | 12 | 10 | 14 | 16 |
| Current smokers (≥10 cigs/day) | 13 | 14 | 14 | 18 | 16 |
| History of diabetes (%) | 10 | 8 | 13 | 13 | 14 |
| History of hypertension (%) | 27 | 18 | 29 | 35 | 27 |
| History of angina (%) | 2 | 5 | 5 | 2 | 10 |
| Height (m) | 1.64 | 1.64 | 1.63 | 1.62 | 1.62 |
| Body mass index (kg/m$^2$) | 26 | 25 | 26 | 26 | 26 |
| Waist-to-hip ratio | 0.95 | 0.93 | 0.94 | 0.92 | 0.93 |
| Physical activity (METS) | 1.81 | 1.88 | 1.71 | 1.81 | 2.07 |
| Socioeconomic status index[b] | 9.7 | 9.7 | 9.1 | 9.1 | 9.1 |
| Monounsaturated fat (% energy) | 10 | 12 | 13 | 14 | 15 |
| Polyunsaturated fat (% energy) | 5.7 | 5.9 | 5.6 | 5.4 | 5.3 |
| Cholesterol (mg/1000 kcal) | 91 | 112 | 122 | 141 | 175 |
| Total energy intake (Kcal/day) | 2488 | 2469 | 2249 | 2248 | 2104 |
| Dietary fiber (g/day) | 27 | 25 | 25 | 24 | 21 |
| Folic acid (μg/day)[a] | 382 | 372 | 372 | 348 | 316 |
| Total vitamin E (mg/day)[a] | 24 | 26 | 24 | 23 | 20 |
| Total carotenoid intake (IU/day)[a] | 8689 | 7799 | 8789 | 8049 | 6986 |
| Alcohol among users only (g/day) | 23 | 16 | 12 | 10 | 11 |
| Cheese (servings/day)[c] | 0.22 | 0.43 | 0.43 | 0.57 | 0.51 |
| Ice cream, sour cream and butter[c,d] | 0.08 | 0.14 | 0.16 | 0.22 | 0.43 |
| Milk (servings/day)[c,e] | 0.14 | 0.43 | 0.43 | 0.43 | 0.43 |
| Meat and pork (servings/day)[c] | 0.69 | 1.09 | 1.13 | 1.16 | 1.43 |
| Fried foods (servings/day) | 6.86 | 6.73 | 6.36 | 6.57 | 6.83 |
| Major type of cooking oil (%) | | | | | |
| Palm oil | 13 | 21 | 39 | 53 | 72 |
| Soybean oil | 68 | 65 | 46 | 38 | 18 |
| Other oil[f] | 20 | 15 | 16 | 9 | 10 |

[a]Excluding intake from vitamin supplements.
[b]Includes education, occupation, income, and household possessions.
[c]Serving size: 28 g for cheese (one slice); 72 g for ice cream (1/2 cup); 72 g for sour cream (1/2 cup); 5 g for butter (one pat); 244 ml for milk (one glass); 53 g for red meat (one small patty).
[d]Butter includes *lactocrema*, a mixture of butter and margarine.
[e]Mostly 1 and 2% fat milk.
[f]Mostly corn (73%) and olive (8%) oil.

Table 3 shows the risk of nonfatal acute MI associated with the consumption of total and individual SFAs in Costa Rica. The risk of nonfatal acute MI estimated from the Keys score, a relative measure of predicted changes in total serum cholesterol for given intakes of saturated fat, polyunsaturated fat and cholesterol, is also given. In the multivariate models adjusted for established CVD risk factors and dietary confounders, subjects in the highest compared to the lowest quintile of intake of each saturated fatty acid were associated with a two- to four-fold increase in risk of MI. The same magnitude of risk of MI was observed for subjects in the highest compared to the lowest quintiles of total saturated fat intake and the Keys score **(**Table 3**)**. In all the above multivariate models, the *P* for trend was ≤0.04. In these models dietary *trans*-fat was also associated with increased risk of nonfatal acute MI. In a secondary multivariate analysis including intake of total saturated fat (other covariates as in Table 3), *trans*-fat (in quintiles) and cholesterol (in quintiles), subjects in the highest quintile (2.5% of energy) of dietary *trans*-fat intake were 1.83 times (95% CI: 1.04–3.25) more likely to have nonfatal acute MI than those in the lowest quintile (0.6% of energy). The corresponding OR (95% CI) for the top (576 mg) *vs* the lowest quintile (132 mg) of dietary cholesterol was 0.95 (0.43–2.08).

Since in this and other populations the proportions of individual SFAs in the diet vary greatly, being very low for lauric acid and highest for palmitic acid, we computed the risk associated with 1% change in intake of energy from each one of them and used the risk to compare their individual potencies **(**Table 4**)**. In this analysis, lauric acid, myristic acid and stearic acid were the most potent while palmitic acid was the least. In the analysis combining lauric and myristic acid, we estimated that a change of 1% energy from these two

**Table 3** Risk of nonfatal acute MI across quintiles of energy from saturated fat in 485 cases and 508 controls, Costa Rica, 1995–1998

| | *Odds ratios and 95% CI by quintiles of dietary intake* | | | | | |
|---|---|---|---|---|---|---|
| *Variable* | *1* | *2* | *3* | *4* | *5* | P *for trend* |
| Lauric acid (12:0) | | | | | | |
| Median[a] | 0.07 | 0.12 | 0.16 | 0.23 | 0.38 | |
| Basic model[b] | 1.0 | 1.50 (1.00–2.25) | 1.44 (0.97–2.14) | 2.04 (1.37–3.04) | 1.79 (1.21–2.67) | 0.004 |
| Multivariate[c] | 1.0 | 2.25 (1.31–3.88) | 1.67 (0.99–2.82) | 2.19 (1.27–3.78) | 2.20 (1.27–3.83) | 0.04 |
| Myristic acid (14:0) | | | | | | |
| Median[a] | 0.35 | 0.54 | 0.70 | 0.88 | 1.22 | |
| Basic model[b] | 1.0 | 1.24 (0.82–1.87) | 1.35 (0.91–1.99) | 1.69 (1.11–2.55) | 2.22 (1.49–3.30) | <0.0001 |
| Multivariate[c] | 1.0 | 1.49 (0.87–2.53) | 1.33 (0.78–2.45) | 1.91 (1.08–3.36) | 2.54 (1.39–4.63) | 0.002 |
| Lauric+myristic | | | | | | |
| Median[a] | 0.42 | 0.66 | 0.86 | 1.13 | 1.68 | |
| Basic model[b] | 1.0 | 1.31 (0.87–1.98) | 1.33 (0.90–1.95) | 1.56 (1.03–2.34) | 2.33 (1.56–3.49) | <0.0001 |
| Multivariate[c] | 1.0 | 1.72 (1.01–2.96) | 1.40 (0.84–2.34) | 1.74 (0.98–3.09) | 2.84 (1.57–5.15) | 0.002 |
| Palmitic acid (16:0) | | | | | | |
| Median[a] | 5.8 | 6.9 | 7.8 | 8.7 | 10.2 | |
| Basic model[b] | 1.0 | 1.93 (1.27–2.94) | 1.75 (1.15–2.67) | 1.96 (1.28–3.02) | 1.86 (1.23–2.81) | 0.02 |
| Multivariate[c] | 1.0 | 2.23 (1.31–3.79) | 1.90 (1.09–3.31) | 2.41 (1.28–4.54) | 2.76 (1.39–5.47) | 0.01 |
| Stearic acid (18:0) | | | | | | |
| Median[a] | 1.74 | 2.14 | 2.40 | 2.74 | 3.30 | |
| Basic model[b] | 1.0 | 1.28 (0.86–1.92) | 1.54 (1.01–2.35) | 1.87 (1.24–2.82) | 2.68 (1.79–4.01) | <0.0001 |
| Multivariate[c] | 1.0 | 1.20 (0.70–2.05) | 1.64 (0.90–2.96) | 2.48 (1.33–4.60) | 3.96 (1.95–8.01) | <0.0001 |
| Total saturated fat | | | | | | |
| Median[a] | 8.9 | 10.5 | 11.8 | 13.3 | 15.6 | |
| Basic model[b] | 1.0 | 1.61 (1.07–2.44) | 1.94 (1.28–2.94) | 2.35 (1.54–3.58) | 2.04 (1.37–3.05) | 0.0003 |
| Multivariate[c] | 1.0 | 1.64 (0.95–2.82) | 2.40 (1.37–4.19) | 2.74 (1.51–4.99) | 3.00 (1.54–5.84) | 0.001 |
| Keys score[d] | | | | | | |
| Median[e] | 28.0 | 34.5 | 39.3 | 45.1 | 52.3 | |
| Basic model[b] | 1.0 | 1.39 (0.92–2.12) | 1.61 (1.07–2.44) | 1.97 (1.30–2.97) | 2.02 (1.34–3.04) | 0.0002 |
| Multivariate[f] | 1.0 | 1.22 (0.71–2.07) | 1.46 (0.87–2.45) | 1.64 (0.98–2.74) | 2.23 (1.29–3.85) | 0.002 |

[a]Median percent energy from saturated fat in each quintile.
[b]Odds ratios (OR) adjusted for age, gender and county of residence through matching.
[c]Adjusted for smoking (never, past, <10 and ≥10 cigarettes/day), alcohol intake (never, past, three tertiles of current drinkers), history of diabetes, history of hypertension, history of angina, waist-to-hip ratio (in quintiles), physical activity (in quintiles), socioeconomic status (in tertiles), years living at current residence since age 18, and intake of dietary fiber (in quintiles), total energy (in quintiles), cholesterol (in mg/1000 kcal) and percent energy from protein, monounsaturated fat, polyunsaturated fat and *trans*-fat.
[d]Keys score computed as in Table 1.
[e]Median Keys score in each quintile.
[f]Adjusted for variables in the multivariate models above except protein, cholesterol, monounsaturated and polyunsaturated fat.

fatty acids is associated with a 1.5-fold increase in the risk of nonfatal acute MI. In an attempt to identify independent effects of SFAs, we adjusted stearic acid and lauric plus myristic acid for the variation that may be attributable to palmitic acid. In this analysis, the ORs (95% CI) for 1% change in energy from lauric plus myristic acid, palmitic acid and stearic acid were 1.08 (0.65–1.81), 1.16 (1.01–1.32) and 1.98 (1.08–3.65), respectively. A 1% change in energy from total saturated fat, which is mainly palmitic acid, was also associated with an increased risk of MI (OR = 1.12; 95% CI: 1.03–1.21). Adjusting this association for body mass index instead of waist-to-hip ratio did not change the result (OR = 1.09; 95% CI: 1.02–1.17). For comparison with total saturated fat, we investigated the effect of a 1% increase in energy from total fat (Table 4). In this analysis, the increase in risk of MI was only marginal (OR = 1.03; 95% CI: 0.99–1.06).

Next, we investigated the main food sources of saturated fat and estimated the risk of MI associated with consumption of each food source. As shown in Table 5, most of the lauric acid and myristic acid are derived from dairy products, mainly cheese, ice cream, sour cream and butter (includes *lactocrema*, a mixture of butter and margarine). Palmitic acid and stearic acid are derived mainly from red meat and fried

**Table 4** Risk of nonfatal acute MI associated with a 1% increase in energy intake from total and individual SFAs in 485 cases and 508 controls, Costa Rica, 1995–1998

| *Variable* | *OR (95% CI)* | P |
|---|---|---|
| Lauric acid (12:0)[a,b] | | |
| Basic model[c] | 2.39 (1.01–5.68) | 0.05 |
| Multivariate[d] | 3.24 (1.17–8.98) | 0.02 |
| Multivariate[e] | 1.92 (0.63–5.85) | 0.25 |
| Myristic acid (14:0)[a] | | |
| Basic model[c] | 1.98 (1.37–2.86) | 0.0003 |
| Multivariate[d] | 2.23 (1.45–3.45) | 0.0003 |
| Multivariate[e] | 1.95 (1.13–3.36) | 0.02 |
| Lauric+Myristic[a] | | |
| Basic model[c] | 1.57 (1.20–2.06) | 0.001 |
| Multivariate[d] | 1.73 (1.26–2.37) | 0.001 |
| Multivariate[e] | 1.51 (1.03–2.22) | 0.04 |
| Palmitic acid (16:0)[a] | | |
| Basic model[c] | 1.09 (1.01–1.17) | 0.02 |
| Multivariate[d] | 1.08 (0.99–1.18) | 0.08 |
| Multivariate[e] | 1.14 (1.01–1.30) | 0.04 |
| Stearic acid (18:0)[a] | | |
| Basic model[c] | 1.67 (1.39–2.33) | $<0.0001$ |
| Multivariate[d] | 1.80 (1.38–2.31) | $<0.0001$ |
| Multivariate[e] | 2.00 (1.34–3.00) | 0.001 |
| Total saturated fat[a] | | |
| Basic model[c] | 1.09 (1.04–1.14) | 0.0004 |
| Multivariate[d] | 1.09 (1.03–1.16) | 0.002 |
| Multivariate[e] | 1.12 (1.03–1.21) | 0.01 |
| Total fat[a] | | |
| Basic model[c] | 1.03 (1.00–1.05) | 0.02 |
| Multivariate[d] | 1.04 (1.01–1.07) | 0.01 |
| Multivariate[f] | 1.03 (0.99–1.06) | 0.11 |

[a]OR for a 1% increase in energy from a specific type of fat.
[b]Average consumption of lauric acid was $<1\%$ of total energy.
[c]OR adjusted for age, gender and county of residence through matching.
[d]Adjusted for smoking (never, past, $<10$ and $\geq 10$ cigarettes/day), alcohol intake (never, past, three tertiles of current drinkers), history of diabetes, history of hypertension and history of angina, waist-to-hip ratio (in quintiles), physical activity (in quintiles), socioeconomic status (in tertiles), and years living at current residence since age 18.
[e]Further adjusted for the intake of dietary fiber, total energy, cholesterol and energy from protein, monounsaturated fat, polyunsaturated fat and *trans*-fat.
[f]Covariates same as in the final multivariate model for total saturated fat except for energy from monounsaturated fat, polyunsaturated fat and *trans*-fat.

foods. Fried foods, red meat, cheese, milk and other dairy products (ice cream, sour cream and butter) were the top five sources of saturated fat in this population.

The risk of nonfatal acute MI associated with each of the five top sources of saturated fat is presented in Table 6. A three-fold increase in risk was found among subjects consuming 1.4 servings of cheese per day (highest quintile) compared to those who did not consume cheese (lowest quintile). Intake of ice cream, sour cream and butter was also associated with increased risk of MI, although the association was not statistically significant. The OR was 1.58 for subjects consuming 1.1 servings per day compared to those who did not consume these products. In contrast, intake of low-fat milk (in Costa Rica most people consume 1–2% fat milk) was not associated with risk of MI. Subjects consuming 2–3 servings/day of meat and pork were also associated with increased risk of MI compared to those whose intake was 2 servings/week ($P$ for trend $= 0.02$). An increase in the frequency of consumption of fried foods from 4.57 to 9.75 servings/day) was not associated with MI. Palm oil, partially hydrogenated soybean oil and corn oil were the major oils used for frying. The proportion of subjects using palm oil, soybean oil and corn oil was 50, 40 and 5% in the top quintile of fried foods, and 27, 43 and 12% in the lowest quintile, respectively. Total animal fat was also independently associated with increased risk of MI (OR of the top *vs* the lowest quintile $= 3.09$; 95% CI: 1.65–5.79). This OR was adjusted for established CVD risk factors and dietary confounders (fiber, total energy and cholesterol), and did not change appreciably (OR $= 3.48$; 95% CI: 1.74–6.98) after adjusting for vegetable fat intake.

## Discussion

We have shown that high consumption of total and individual SFAs is independently associated with increased risk of nonfatal acute MI in Costa Rica. Lauric acid, myristic acid and stearic acid were more potent than palmitic acid. Although lauric and myristic acids were associated with increased risk of MI, they were consumed in small amounts and most of the saturated fat (87%) came from palmitic and stearic acids, which were mainly from red meat and fried foods.

The estimates of risk for individual SFAs in this study support the findings from metabolic ward studies, in that individual SFAs may vary in their mechanisms of action and potency to raise total and LDL cholesterol (Kris-Etherton & Yu, 1997; Connor, 1999). This study emphasizes the importance of not relying exclusively on experimental evidence. For instance, lauric and myristic acids are more potent than palmitic acid in increasing LDL cholesterol (Kris-Etherton & Yu, 1997), but compared to palmitic acid they are consumed in very small amounts and therefore likely to have a less impact on the occurrence of CVD. Stearic acid has not been associated with a major increase in serum cholesterol in metabolic ward studies, which are usually of short duration. However, stearic acid in this study as well as those of others (Kromhout *et al*, 1995; Hu *et al*, 1999) was associated with increased risk of CVD. In addition to hypercholesterolemia, there may be other mechanisms (Connor, 1999) that are relevant to CVD. We found out that substitution of 1% energy from carbohydrate with an equivalent amount of energy from saturated fat was associated with a 12% increase in the risk of nonfatal acute MI while substitution of the same amount of energy with total fat had a marginal effect (3%). This finding supports the hypothesis that replacing

**Table 5** Food sources of saturated fat in Costa Rica, 1995–1998[a]

| *Lauric acid (12:0)* | *Myristic acid (14:0)* | *Palmitic acid (16:0)* | *Stearic acid (18:0)* | *Total saturated fat* |
|---|---|---|---|---|
| Dairy (77%) | Dairy (62%) | Fried foods (40%) | Red meat (28%) | Fried foods (30%) |
| Cheese (23%) | Cheese (24%) | Red meat (18%) | Fried foods (20%) | Dairy (23%) |
| Milk (18%)[b] | Milk (17%) | Dairy (13%) | Dairy (20%) | Cheese (9%) |
| Other (36%)[c] | Other (21%) | Cheese (6%) | Cheese (8%) | Milk (6%) |
| Red meat (4%)[d] | Red meat (18%) | Milk (4%) | Milk (6%) | Other (8%) |
| Fried foods (2%)[e] | Fried foods (6%) | Other (3%) | Other (6%) | Red meat (19%) |
| Other foods (5%)[f] | Other foods (1%) | Chicken (3%) | Chicken (3%) | Chicken (3%) |
| Margarine | Margarine | Other foods (8%) | Other foods (14%) | Other foods (7%) |
| Chocolate | | Margarine | Cookies | Margarine |
| | | Olive oil | Sweet bread | Sweet bread |
| | | Avocado | Margarine | Olive oil |
| | | Cookies | Chocolate | Cookies |
| | | Sweet bread | Tamales | |

[a]Numbers in parentheses indicate percentage of a given fat contributed by each food/food group.
[b]Mostly 1 and 2% fat milk.
[c]Includes ice cream, sour cream, custard and butter; butter includes *lactocrema*, a mixture of butter and margarine.
[d]Red meat refers to beef and pork.
[e]Palm oil and soybean oil are the major oils used for cooking and frying in Costa Rica.
[f]Includes only foods that contributed at least 1% of fat.

**Table 6** Risk of nonfatal acute MI across quintiles of top five food sources of saturated fat in 485 cases and 508 controls, Costa Rica, 1995–1998

| | *OR and 95% CI by quintiles of dietary intake* | | | | | |
|---|---|---|---|---|---|---|
| *Major food source of saturated fat*[a] | *1 (lowest)* | *2* | *3* | *4* | *5 (highest)* | P *for trend* |
| Cheese | | | | | | |
| Median (servings/day)[b] | 0 | 0.14 | 0.43 | 0.80 | 1.43 | |
| Basic model[c] | 1.0 | 1.01 (0.61–1.69) | 1.08 (0.72–1.62) | 1.23 (0.78–1.96) | 2.13 (1.37–3.32) | 0.0002 |
| Multivariate[d] | 1.0 | 0.92 (0.50–1.69) | 1.38 (0.84–2.28) | 1.57 (0.90–2.73) | 3.07 (1.74–5.39) | <0.0001 |
| Milk[e] | | | | | | |
| Median (servings/day) | 0 | 0.14 | 0.43 | 1.00 | 2.50 | |
| Basic model[c] | 1.0 | 0.97 (0.61–1.53) | 1.21 (0.82–1.79) | 0.99 (0.66–1.47) | 1.02 (0.67–1.55) | 0.65 |
| Multivariate[d] | 1.0 | 0.96 (0.55–1.70) | 0.91 (0.57–1.46) | 0.76 (0.47–1.23) | 0.81 (0.47–1.38) | 0.49 |
| Other dairy[f] | | | | | | |
| Median (servings/day) | 0 | 0.08 | 0.14 | 0.43 | 1.14 | |
| Basic model[c] | 1.0 | 1.28 (0.80–2.05) | 1.27 (0.84–1.91) | 1.45 (0.94–2.23) | 1.48 (0.96–2.29) | 0.20 |
| Multivariate[d] | 1.0 | 1.19 (0.68–2.09) | 1.55 (0.94–2.56) | 1.79 (1.04–3.06) | 1.58 (0.94–2.67) | 0.27 |
| Meat and pork | | | | | | |
| Median (servings/day) | 0.28 | 0.66 | 1.08 | 1.57 | 2.45 | |
| Basic model[c] | 1.0 | 0.84 (0.54–1.31) | 0.72 (0.46–1.13) | 1.14 (0.73–1.77) | 1.79 (1.13–2.83) | 0.0007 |
| Multivariate[d] | 1.0 | 0.79 (0.46–1.36) | 0.72 (0.41–1.24) | 1.04 (0.60–1.80) | 1.69 (0.93–3.06) | 0.02 |
| Fried foods | | | | | | |
| Median (servings/day) | 4.57 | 6.00 | 6.62 | 7.78 | 9.75 | |
| Basic model[c] | 1.0 | 0.96 (0.63–1.46) | 1.16 (0.75–1.80) | 1.24 (0.79–1.94) | 1.22 (0.77–1.94) | 0.33 |
| Multivariate[d] | 1.0 | 0.86 (0.50–1.48) | 1.01 (0.59–1.75) | 1.15 (0.66–2.03) | 1.06 (0.59–1.91) | 0.65 |

[a]All the five major food sources of saturated fat were entered into the model simultaneously.
[b]Serving size: 28 g for cheese (one slice); 72 g for ice cream (1/2 cup); 72 g for sour cream (1/2 cup); 5 g for butter (one pat); 244 ml for milk (one glass); 53 g for red meat (one small patty).
[c]OR adjusted for age, gender and county of residence through matching.
[d]Adjusted for smoking (never, past, <10 and ≥10 cigarettes/day), alcohol intake (never, past, three tertiles of current drinkers), history of diabetes, history of hypertension, history of angina, waist-to-hip ratio, physical activity, socioeconomic status (in tertiles), years living at current residence since age 18, and intake of dietary fiber, total energy, and *trans*-fat.
[e]Mostly 1 and 2% fat milk.
[f]Includes ice cream, sour cream and butter. Butter includes *lactocrema*, a mixture of butter and margarine.

saturated fat with *cis*-unsaturated fat in the diet may be more effective in reducing CVD risk than attempting to reduce total fat intake (Hu *et al*, 2001).

Our results are similar to those of the Nurses Health Study (NHS) (Hu *et al*, 1999), in that palmitic acid was the major type of saturated fat in the diet but the food sources in the two study populations are different. In our study, palmitic acid as well as total saturated fat are derived mainly from fried foods, where as the major sources of saturated fat in the US are dairy and meat products (Hu *et al*, 1999). Dairy and meat products are also the major sources of saturated fat in European countries such as Spain (Aranceta, 2001). The ranges of intake and OR for 1% increase in energy from palmitic acid in our study were consistent with those reported in the NHS (Hu *et al*, 1999). In contrast, the OR for 1% increase in energy from lauric, myristic and stearic acid were higher than those in the NHS. This could be due, in part, to differences in the ranges of intake of these fatty acids. For instance, in the reference quintiles, the median intake of the sum of lauric and myristic acid in our study *vs* the NHS was 0.42 *vs* 0.98% of energy while it was 1.68 *vs* 2.14% in the top quintiles (Hu *et al*, 1999). If dietary saturated fat has a threshold effect, it may then be more likely to observe higher effects in populations with lower saturated fat intakes compared to those with high intakes.

Consumption of cheese, a major source of lauric and myristic acid, was associated with a three-fold increase in risk of MI, while a positive trend was observed for consumption of ice cream, sour cream and butter. Although there are no studies reporting the risk of MI associated with consumption of cheese by itself, high-fat dairy products collectively (whole milk, cheese, ice cream and butter) were weakly associated with coronary heart disease (Hu *et al*, 1999). Of note is the reference category in our study population, which included only subjects who were nonconsumers (0 servings/day) of high-fat dairy products. In contrast, the reference group for high-fat dairy products in the NHS (0.28 servings/day) is comparable to the second or third quintile in our study. Similar to what we observed for individual fatty acids, these data suggest a threshold effect for high-fat dairy products. Fried foods were not associated with increased risk of MI. One explanation is the narrow range of the frequency of consumption of fried foods, being 4.57 and 9.75 servings/day in the lowest and the highest quintiles of fried foods, respectively. Frying is the most common way of preparing food in Costa Rica and most foods are fried. As a result of lack of a reference group with subjects who do not consume fried foods or those who fry less frequently, it may be appropriate to investigate the relation between frequency of consumption of fried foods and risk of MI in another population.

These results are not likely to have been confounded by smoking, physical activity, socioeconomic status and dietary risk factors because we adjusted the estimates of risk for these variables. Also, the study subjects are not likely to have changed their lifestyle and dietary habits since data collection, for most cases (81%) were completed within $<14$ days from the date of discharge from the hospital. In addition, the subjects were visited in their homes and the type of oil used for cooking and frying was confirmed by visual identification.

It is noteworthy that nutrient intakes in our study were similar to those reported for the Costa Rican adolescent population in another study, where dietary information was collected by a 3-day food record (Monge-Rojas, 2001). For instance, the nutrient densities in our study *vs* those in the study by Monge-Rojas (2001) were 34 *vs* 31% for total fat, 12 *vs* 11% for total saturated fat, 6 *vs* 5% for polyunsaturated fat and 11 *vs* 12 g/1000 kcal for total fiber. Saturated fat intakes in our study were very similar to those reported in the US Third National Health and Nutrition Examination Survey (Anon, 1994), but were lower than intakes in Spain (Serra-Majem *et al*, 2001). Consistent with higher CVD mortality rates (178.8/100,000 population) in Costa Rica (Anon, 2002), saturated fat intake in Costa Rica was higher than in Guatemala (Torun *et al*, 2002), Mexico (Lopez-Carrillo *et al*, 1999) and Korea (Suh *et al*, 2001), where CVD mortality rates are lower (Anon, 2002; Suh *et al*, 2001).

In the analysis by quintiles, subjects in the second *vs* the first quintile of intake of total and all individual SFAs showed an increase in risk of nonfatal acute MI; and yet the median saturated fat intake was 10.5% of energy in the second quintile. This suggests that the current recommendation of 10% energy from saturated fat may be high for this population.

The high potency of SFAs from dairy and red meat products (mainly lauric and myristic acids) observed in this study suggests that small increases in the intake of these products could result in a significant increase in CVD risk. However, high consumption of low potency SFAs such as palmitic acid could also result in increased risk. This highlights a need for public health educators to emphasize the potential increase in risk of CVD resulting from high consumption of animal fats and vegetable oils that are high in saturated fat.

These data suggest that primary prevention of CVD should include strategies to lower the intake of saturated fat for example, through substitution of highly saturated vegetable oils with oils low in saturated fat, and a reduction of consumption of meat and dairy products.

## Conclusion

High total and individual SFAs, including stearic acid, are independently associated with increased risk of nonfatal acute MI in Costa Rica. Lauric, myristic and stearic acids were more potent than palmitic acid. Palmitic acid was the most abundant saturated fatty acid, derived mainly from fried foods, red meat, and dairy products.

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