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Dietary fatty acids and peripheral artery disease in adults

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Abstract

BACKGROUND—Peripheral artery disease (PAD) is a debilitating condition involving atherosclerosis. Although saturated, monounsaturated and polyunsaturated fatty acids have strong associations with atherosclerosis, it is unclear if diets high in these fatty acids affect PAD.

METHODS—We studied 6,352 adults aged 40 years and older who participated in the U.S. National Health and Nutrition Examination Survey between 1999 and 2004. Ankle-brachial index (ABI) was assessed by standardized blood pressure measurements, and we defined PAD as an ABI <0.9. Fatty acid intake was assessed by validated 24-hour dietary recall. We used multivariable linear and logistic regression to estimate associations between intakes of dietary saturated fatty acids (SFAs), monounsaturated fatty acids (MFAs), marine omega-3 fatty acids (N-3), linolenic acid (LNA), and omega-6 fatty acids (N-6) and ABI/PAD.

RESULTS—The prevalence and 95% confidence interval (CI) of PAD was 5.2% (95% CI 4.6–5.8). There were no associations between ABI and intakes of marine N-3 ($p=0.83$) or N-6 ($p=0.19$) in adjusted models. In contrast, LNA was associated with higher ABI ($p=0.04$) and SFA tended to be associated with lower ABI ($p=0.06$) in adjusted models. In addition, higher SFA was associated with a higher prevalence of PAD: adjusted odds ratio 1.30 (95% CI 1.01–1.67; $p=0.04$) and a trend toward slower gait speed ($p=0.08$).

CONCLUSION—In this nationally representative sample, higher dietary intakes of LNA and SFAs were associated with higher and lower ABI, respectively. Prospective studies are needed to confirm the potential protective effects of dietary LNA and detrimental effects of dietary SFAs on PAD.

Keywords

Fatty acids; peripheral arterial disease; linolenic acid; saturated fat

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Conflict of Interest Statement:

Dr. Mukamal is the principal investigator on an ongoing study funded by Harvard Medical School for which BIDMC received a donation of docosahexaenoic acid (DHA) and placebo capsules from Martek Corporation. Drs. Davis and Naqvi are co-investigators on that trial. Martek provided no other resources or funds and has no role in the conduct or analysis of that study. Martek had no role whatsoever in the current manuscript. There are no other financial or personal interests to disclose.

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Introduction

Peripheral artery disease (PAD) is a debilitating, chronic disease caused by the accumulation of atherosclerotic plaque in the arteries of the legs. Inflammation is thought to play an important role in the pathogenesis of PAD.¹ Traditional therapies for PAD focus on targeting known risk factors, including smoking cessation, exercise, glycemic control, statins, control of hypertension, antiplatelet therapy and vascular surgery.² Dietary recommendations are primarily based upon studies on coronary heart disease, which have shown differential effects of particular fatty acids on cardiovascular disease (CVD) outcomes, but atherosclerosis in the coronary and other vascular beds is only modestly correlated.³ Moreover, there are limited studies of dietary factors and PAD.

There are multiple classes of fatty acids with various effects on CVD risk factors and outcomes. The major classes of dietary fatty acids include saturated (SFA), monounsaturated (MFA), polyunsaturated (PFA) and trans-unsaturated (TFA) fatty acids. PFAs include omega 3 (N-3s), omega 6 (N-6s) and some omega 9 (N-9s) fatty acids. PFAs have been found to have protective effects on CVD events, including myocardial infarction, coronary heart disease death, and/or sudden death in randomized controlled trials⁴ and prospective cohort studies⁵. TFA intake has consistently been associated with higher risk of clinical coronary heart disease.⁶ Intake of monounsaturated fatty acids (MFAs) has not consistently been found to be associated with incident coronary heart disease or stroke.⁵ Saturated fatty acid (SFA) intake clearly raises LDL-cholesterol,⁷ although prospective studies and trials of outcomes are still less clear.⁸

In humans, studies of PAD have been limited by size or have not provided extensive assessment of multiple classes of fatty acids.^{9–14} To our knowledge, there have been no comprehensive, large-scale studies on classes of fatty acid intake and PAD despite their strong associations with CVD risk factors and outcomes. This study aims to examine the association between these fatty acids and prevalence of PAD in a nationally representative sample of adults.

Methods

Study Sample

This cross-sectional study used data from 6,352 adults aged 40 years and older who participated in the National Health and Nutrition Examination Survey (NHANES) between 1999 and 2004. The survey provides information on the health and nutritional status of the United States' civilian, non-institutionalized population by using a complex, stratified, multistage, probability-sampling design.^{15–17} The NHANES includes both an initial in-home interview followed by an examination and personal interview at a mobile examination center. A total of 31,126 individuals participated in the in-home interview. For this study, we excluded subjects less than 40 years of age (n=21,156; ABI was not measured in that age group), lacking or indeterminate ABI measurement (n=1,622), having missing data from covariates of interest (n=993), lacking physical exams (n=825), not meeting minimal criteria for reliability of the dietary recall (n=178), leaving 6,352 for analysis.

Peripheral Artery Disease

PAD was assessed during the physical exam by health technicians trained in the survey examination protocol.^{15–17} Briefly, after selecting the appropriate blood pressure cuff size and allowing a brief resting period, systolic blood pressure was measured on the right arm (brachial artery) and both ankles (posterior tibial arteries). If the participant had any condition that would interfere with accurate measurement or would cause discomfort, the left arm was used for the brachial pressure measurement. Systolic blood pressure was

measured two times at each site if possible for participants aged 40–59 years and once at each site for participants aged 60 years and older. The ankle brachial blood pressure index (ABI) was calculated by dividing the mean systolic blood pressure in the right or left ankle by the mean blood pressure in the arm. Since only one reading at each site for all persons 60 years and older was measured, the mean values are represented by the first recorded blood pressure reading at a site. We excluded values for ABI that were missing and those that were >1.4 ($n=34$). We defined PAD as having an ABI <0.9 .

A number of measures were taken to systematically optimize quality, including regular monitoring, periodic retraining and careful equipment maintenance. Detailed information on the NHANES lower extremity examinations for the survey periods is available elsewhere.^{15–17}

Dietary Fatty acids

Fatty acid intake in grams per day was assessed by a 24-hour dietary recall. From 1999 to 2001, dietary intake data were collected using the NHANES computer-assisted dietary interview system (CADI). The CADI is a multiple pass recall method which provides instructions to interviewers for recording information about foods. Additional information about the CADI system is provided in the NHANES 1999–2000 Dietary Interviewers Procedures manual.¹⁵ From 2002–2004, data were collected using the USDA's dietary data collection instrument, the automated multiple pass method,^{16, 17} which was found to provide valid measures of group total energy and PFA intake in twenty highly motivated premenopausal women using doubly labeled water total energy expenditure, the Block food-frequency questionnaire, the National Cancer Institute's Diet History Questionnaire and 14-day dietary record.¹⁸

We examined the following specific fatty acids (supplemental Table 5), including SFAs: dodecanoic acid ("lauric acid", SFA12), tetradecanoic acid ("myristic acid", SFA14), hexadecanoic acid ("palmitic acid", SFA16), octadecanoic acid ("stearic acid", SFA18). We did not subdivide MFAs. We assessed the following N-6s: octadecadienoic acid ("linoleic acid", LA, 18:2) and eicosatetraenoic acid ("arachidonic acid", AA, 20:4). We examined the following "marine N-3s": eicosapentaenoic acid (EPA, 20:5), docosapentaenoic acid (DPA, 22:5) and docosahexaenoic acid (DHA, 22:6). We also examined octadecatrienoic acid ("linolenic acid", LNA 18:3), which includes primarily "alpha-linolenic acid" (ALA, an N-3) and lesser amounts of "gamma-linolenic acid" (GLA, an N-6).

Covariates

We analyzed covariates that have been found to be related to PAD or CVD in previous studies.² Age was modeled as a continuous variable. We assigned self-reported race-ethnicity as white, black, Mexican-American, and other. We categorized income as $< \$20,000$, $\$20,000 - \$44,999$, $\$45,000 - \$74,999$, $\$75,000$, and unreported and education as $<$ high school, high school, and some college education. Country of birth was self-reported and grouped as within the U.S., Mexico, or other locations.

Physical activity was assessed by questions regarding any vigorous activity (i.e. jogging, sports, etc. causing a substantial increase in heart rate and heavy perspiration) and any moderate activity (i.e. brisk walking, dancing, etc. causing moderate increase in heart rate and perspiration) lasting for at least 10 minutes over the past 30 days. As in prior work,¹⁹ we divided physical activity into 3 categories: sedentary (no moderate or vigorous activity), modest activity (at least one episode of moderate activity, but no vigorous activity), and some vigorous activity (at least one vigorous episode). As a secondary measure, we included muscle strengthening activities assessed by questions on the number of episodes (at least 10

minute duration) of lifting weights, push-ups or sit-ups over the past 30 days. We categorized muscle strengthening activities based upon the median number of episodes (13) per 30 days as none, 1 to 13 times per month or >13 times per month. We categorized smoking as never, former, and current. Participants reported their general health, which we collapsed into excellent/very good, good/fair and poor. We defined hypertension as an average blood pressure reading >140/90 or if the subject had been told by a doctor that they have high blood pressure on two or more separate occasions and were taking medication for hypertension. We defined hyperlipidemia if subjects reported being told by a doctor they have a high cholesterol level and were taking a prescription medication for it or had a serum total cholesterol of >200 mg/dL. We defined diabetes if fasting glucose ≥ 126 mg/dl or if taking hypoglycemic agents or insulin to lower glucose. Cardiovascular disease included self-reported diagnoses of coronary heart disease, stroke or congestive heart failure. We categorized alcohol intake into three groups: <2 drinks/day, 2–5 drinks/day and >5 drinks/day. We used the 20-foot walk time to obtain gait speed in feet/second (ft/sec).

Statistical Analyses

We calculated descriptive statistics on the dietary intake of fatty acids and other characteristics. To facilitate comparison, we assessed each dietary fatty acid in units of its standard deviation. We tested for normality using joint tests for skewness, kurtosis and examined histograms on the outcome variables.

We first assessed the relation between dietary fatty acids and ABI in partial and fully adjusted multiple linear regression models. We also calculated odds ratios (ORs) for the relation between each dietary fatty acid intake and prevalence of PAD using two sequential multivariable logistic regression models. The first model adjusted for total energy intake (kcal/24 hr), age (yr) and sex. The second model additionally adjusted for general health status, race, smoking, origin of birth, income, education, physical activity, alcohol intake, and other fatty acids: SFA, MFA, LA, AA, DHA, DPA, EPA and LNA. Sampling weights were used to generate population-weighted effect estimates. We used SAS (v9.1, 2002, Cary, NC) SUDAAN (v10.0, 2007, Research Triangle Park, NC) to analyze dietary recall data with appropriate 6-year weight assignment from years 1999 to 2004.^{15–17}

Because CVD and its risk factors may be intermediates between diet and PAD, we adjusted all of the primary analyses additionally for cardiovascular risk factors in a “CVD model”, including a history of CVD, hypertension, diabetes and hyperlipidemia. We then examined individual SFAs for their association with PAD in partial, multivariable and CVD models. In addition, we tested for potential non-linear relationships with quadratic terms of fatty acids and found none. We also tested for interaction between fatty acids of interest and sex and N-6 fatty acids. We lastly tested the associations of fatty acid intake with gait speed after confirming its association with PAD. To ensure that our results were robust to measure of activity, we further adjusted all primary analyses for muscle strengthening activity with no material change in our results.

Results

Of the 6,352 adults studied, a total of 489 had PAD. The weighted prevalence was 5.2% (95% CI 4.6–5.8). As Table 1 shows, the study population is composed of generally healthy middle-aged adults. See Table 2 for weighted partial Pearson correlations of dietary fatty acids examined.

We found that higher dietary intake of LNA was associated with higher ABI and higher dietary SFA tended to be associated with lower ABI (Table 3). Associations were strengthened with further adjustment for cardiac risk factors. Higher SFA was associated

with a higher odds of PAD in the CVD model. For MFA, a significant association in the partially adjusted model was chiefly attributable to confounding by SFA.

We did not observe an association between intakes of individual fatty acids and ABI in fully adjusted models (Table 4), except for individual SFAs. For AA, a significant association in the partially adjusted models was primarily attributable to confounding by race-ethnicity and physical activity. We found no evidence of non-linear relationships of fatty acid intake and PAD ($p>0.27$).

Given the associations of SFA and LNA with ABI, we next examined these in more detail. We found associations between two individual SFAs and prevalence of PAD in fully adjusted models (Table 4) - hexadecanoic acid (SFA16) and octadecanoic acid (SFA18). We found no evidence of interaction between sex and SFA ($p=0.63$) or LNA ($p=0.29$) in fully adjusted multivariable linear regression models. Similarly, there was no evidence of interaction between N-6 and N-3 intake on ABI ($p>0.50$).

We lastly evaluated fatty acid classes and gait speed as a consequence of PAD. We found the expected inverse association between presence of PAD and gait speed (adjusted difference -0.14 ± 0.04 ft/sec, $p<0.001$). There was no association between gait speed and LNA ($p=0.17$), marine N-3s ($p=0.39$) or N-6s ($p=0.21$). Higher SFA intake tended to be associated with slower gait speed (adjusted difference -0.07 ± 0.04 ft/sec, $p=0.08$), particularly SFA16 (adjusted difference -0.013 ± 0.004 ft/sec, $p=0.007$).

Discussion

In this nationally representative cross-sectional study of adults, dietary LNA was associated with a better ABI and SFA with a lower ABI. MFA, N-6 fatty acids and marine N-3 fatty acids were not associated with ABI. SFA was also associated with higher prevalence of PAD and with a trend toward slower gait speed, an important functional consequence of PAD.

ALA, the major constituent of LNA and the only non-marine source of omega-3 fatty acids, has been shown to have protective effects on CVD related outcomes. In animals, dietary ALA delays arterial thrombus formation by decreasing platelet aggregation to collagen and thrombin and by decreasing platelet activation.²⁰ In humans, higher dietary ALA was found to decrease risk of fatal and non-fatal ischemic heart disease in several prospective cohort studies^{21–23}, but not in others.^{24, 25} In one randomized trial, ALA as a key component of a Mediterranean diet, was found to decrease risk of cardiovascular events,²⁶ while in another trial, where margarine was supplemented with ALA, there was a trend toward decreased major cardiovascular events only amongst a pre-specified subgroup.²⁷ The only completed study of N-3 fatty acids and PAD to our knowledge was a cross-sectional study that found LNA to be associated with a lower prevalence of PAD.⁹ Our study corroborated the association of LNA with improved ABI, but we found no association with PAD. The more modest magnitude of effect that we found is due primarily to including various confounders in our multivariable models, particularly total energy, which is especially important for dietary studies of PAD.

Higher dietary SFA substituted for other macronutrients has been shown to induce early atherosclerosis in animals.²⁸ Prospective cohort studies of the association between SFA intake and CVD have yielded mixed results.⁸ We found SFA intake to be associated with a higher prevalence of PAD in a multivariable model additionally adjusted for cardiovascular-related diseases. The stronger association we observed following adjustment for CVD may have occurred because individuals diagnosed with cardiovascular diseases, who are more likely to have PAD, may have altered their diets to reduce intake of SFA after their

diagnosis. The specific saturated fatty acids responsible for the positive association with PAD were the longest carbon chain SFAs, palmitic (16-carbon) and stearic acids (18-carbon). In addition, increased saturated fatty acid intake, particularly palmitic acid, was associated with a slower gait speed.

Marine N-3 fatty acids have been found to have protective effects on cardiovascular risk factors in animal studies,²⁸ and with cardiovascular disease outcomes in prospective cohort studies and randomized controlled trials.²⁵ In a small, case-control study in an Edinburgh population, DPA (the least common marine N-3) was found to be protective for PAD.¹⁴ We found no association between DPA or other marine N-3 fatty acids and ABI or prevalence of PAD. The previously positive findings may reflect chance, given the very low levels of usual DPA intake. Alternatively, the null associations between marine N-3 intake and PAD in this study may be due to relatively low marine N-3 intake and/or misclassified marine N-3 intake due to lack of information regarding farm versus wild sources of fatty fish.

Limitations of our study include the cross-sectional design, which permits the detection of associations but not a temporal relationship nor causation. Individuals' dietary intakes vary from day to day, so a 24-hour dietary recall does not necessarily provide an ideal estimate of an individual's long-term average or "usual" daily intake. However, dietary recalls tend to provide highly reliable estimates of recent intake, and the mean of a group's recent intake yields a reasonable estimate of the mean of the group's usual nutrient intake if the dietary recalls are collected on all days of the week and seasons of the year, as is the case with NHANES. As with most other methods of dietary ascertainment, dietary recall relies on memory and subjects may under-report portion sizes. However, the 24-hour dietary recall used in this study was found to provide valid measures of group total energy and PFA intake in twenty highly motivated premenopausal women using other methods, including doubly labeled water total energy expenditure, which does not share these limitations.

Lastly, ALA and GLA are combined into one variable, linolenic acid, which could represent opposing effects on chronic inflammation since ALA is an n-3, whereas GLA is an n-6 fatty acid.²⁹ However, the great majority of dietary LNA intake is from ALA.³⁰ In addition, GLA was found in one small randomized controlled trial to reduce gingival inflammation.³¹

Strengths of our study include the large and representative sample of civilian, US adults. Also, detailed ABI assessments were conducted with a number of quality control procedures, including calibration of technicians prior to and tri-annually throughout the survey. Finally, detailed information on potentially confounding covariates was available in a systematic manner.

In summary, we found that higher dietary intakes of LNA was associated with higher ABI and higher dietary intake of SFA, particularly the 16 and 18 carbon length subtypes, are positively associated with PAD in the US population. Prospective cohort studies are needed to confirm the potential protective effects of dietary LNA and detrimental effects of SFA on PAD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- In a nationally representative sample of Americans, higher dietary intake of linolenic acid was associated with higher ABI.
- Higher dietary intake of saturated fatty acids was positively associated with prevalence of PAD in models further adjusted for CVD risk factors.
- Other fatty acids were not substantially associated with ABI or prevalence of PAD.

Table 1

Sample characteristics among U.S. adults 40 years and older; NHANES 1999–2004; n=6,352

Characteristic	n (%)	Mean (SD)
SFA, gm/d		25.5 (15.7)
MFA, gm/d		28.2 (17.4)
mN-3, gm/d		0.1 (0.3)
LNA, gm/d		1.3 (1.0)
N-6, gm/d		13.4 (9.5)
Age group, years		
40–59	3030 (63)	
60–79	2710 (32)	
80	612 (5)	
Sex		
Male	3134 (51)	
Female	3218 (49)	
Race/ethnicity		
Non-Hispanic white	3430 (78)	
Non-Hispanic black	1119 (9)	
Mexican American	1381 (5)	
Other	422 (8)	
Education		
<High school	2144 (20)	
High school	1504 (26)	
Some college	2704 (54)	
Smoking status		
Never	2951 (46)	
Former	2185 (34)	
Current	1216 (20)	
Activity level		
Sedentary	2988 (38)	
Modest	1959 (34)	
Some vigorous	1405 (27)	
Health status		
Excellent/very good	2572 (49)	
Good	2056 (31)	
Fair/poor	1724 (21)	
Cardiovascular disease		
No	5360 (87)	
Yes	992 (13)	
Hypertension		
No	2963 (53)	
Yes	3389 (47)	

Characteristic	n (%)	Mean (SD)
Diabetes		
No	5395 (89)	
Yes	957 (11)	
Hyperlipidemia		
No	2271 (35)	
Yes	4081 (65)	

Abbreviations: NHANES: National Health and Nutrition Examination Survey, SD: Standard deviation, SFA: Saturated fatty acid intake, MFA: Monounsaturated fatty acid intake, N-6: Omega-6 fatty acid intake: linoleic acid and arachidonic acid; mN3: Marine Omega-3 fatty acid intake: Docosahexaenoic acid, Docosapentaenoic acid and Eicosapentaenoic acid; LNA: Linolenic acid

Table 2

Weighted partial Pearson correlations of dietary exposures; n=6,352

Variable	SFA	MFA	mN3	LNA	N6
SFA	1.00				
MFA	0.60	1.00			
mN3	-0.10	0.00	1.00		
LNA	0.14	0.28	0.13	1.00	
N6	0.05	0.45	0.09	0.73	1.00

Abbreviations: SFA: Saturated fatty acid intake, MFA: Monounsaturated fatty acid intake, mN3: Marine omega-3 fatty acid intake, LNA: Linolenic acid intake, N6: Omega-6 fatty acid intake

Table 3

Fatty Acid Intake and Prevalence of PAD/ABI (linear) per SD increment; n=6,352

	Odds Ratios of PAD (95% CI)		Change in ABI	
		p-value	Beta (+/-SE)	p-linear
SFA				
Partial adjustment ^a	1.47 (1.13, 1.92)	0.006	-0.008 (0.003)	0.007
Multivariable ^b	1.27 (0.98, 1.65)	0.07	-0.007 (0.004)	0.06
Cardiovascular ^c	1.30 (1.01, 1.67)	0.04	-0.007 (0.004)	0.05
MFA				
Partial adjustment ^a	1.49 (1.17, 1.90)	0.01	-0.008 (0.004)	0.04
Multivariable ^b	1.24 (0.91, 1.71)	0.17	-0.002 (0.004)	0.55
Cardiovascular ^c	1.21 (0.89, 1.65)	0.22	-0.002 (0.004)	0.54
N-6				
Partial adjustment ^a	1.02 (0.87, 1.21)	0.78	-0.001 (0.003)	0.81
Multivariable ^b	1.03 (0.69, 1.53)	0.90	-0.005 (0.004)	0.19
Cardiovascular ^c	1.03 (0.68, 1.55)	0.89	-0.005 (0.004)	0.18
Marine N-3				
Partial adjustment ^a	1.00 (0.91, 1.10)	0.99	0.001 (0.001)	0.65
Multivariable ^b	1.04 (0.92, 1.17)	0.55	-0.000 (0.001)	0.83
Cardiovascular ^c	1.04 (0.92, 1.17)	0.50	-0.000 (0.001)	0.90
LNA				
Partial adjustment ^a	0.99 (0.87, 1.12)	0.41	0.003 (0.002)	0.24
Multivariable ^b	0.90 (0.67, 1.23)	0.51	0.006 (0.003)	0.04
Cardiovascular ^c	0.90 (0.66, 1.24)	0.51	0.006 (0.002)	0.02

Abbreviations: PAD: Peripheral Artery Disease; ABI: Ankle Brachial Index; CI: Confidence Interval; SD: Standard Deviation; SE: Standard Error; SFA: Saturated fatty acid intake; MFA: Monounsaturated fatty acid intake; N-6: Omega-6 fatty acid intake: linoleic acid (LA) and arachidonic acid (AA); Marine N-3: Omega-3 fatty acid intake from marine sources: Docosahexaenoic acid (DHA), Docosapentaenoic acid (DPA) and Eicosapentaenoic acid (EPA); LNA: Linolenic acid

^aPartial model: Adjusted for age, sex and total energy intake (kcal/day)

^bMultivariable model: Adjusted for age, sex, total energy intake (kcal/day), race/ethnicity, smoking, education, income, physical activity, self-reported health status, origin of birth, alcohol intake and other fatty acids: SFA, MFA, LA, AA, DHA, DPA, EPA, LNA

^cCVD model: Adjusted for all multivariable model covariates and cardiovascular disease, hypertension, diabetes mellitus and hyperlipidemia

Table 4

Individual Fatty Acid Intake and Prevalence of PAD/ABI per SD increment; n=6,352

	Odds Ratios of PAD (95% CI)		Change in ABI	
	mean (SD)	p-value	Beta (+/-SE)	p-linear
<u>Omega-6:</u>				
LA	13.9 g/d (9.7)			
Partial adjustment ^a	1.04 (0.89, 1.23)	0.62	-0.001 (0.003)	0.83
Multivariable ^b	1.03 (0.69, 1.55)	0.88	-0.005 (0.004)	0.18
Cardiovascular ^c	1.04 (0.68, 1.57)	0.86	-0.005 (0.004)	0.17
AA				
Partial adjustment ^a	1.08 (0.92, 1.26)	0.34	-0.004 (0.002)	0.08
Multivariable ^b	0.94 (0.74, 1.19)	0.62	0.002 (0.003)	0.54
Cardiovascular ^c	0.94 (0.74, 1.19)	0.58	0.002 (0.003)	0.42
<u>Marine Omega-3:</u>				
DHA	0.08 g/d (0.2)			
Partial adjustment ^a	1.00 (0.90, 1.10)	0.93	0.000 (0.001)	0.78
Multivariable ^b	0.91 (0.68, 1.21)	0.50	-0.001 (0.004)	0.73
Cardiovascular ^c	0.92 (0.68, 1.24)	0.57	-0.002 (0.004)	0.62
DPA				
Partial adjustment ^a	1.03 (0.95, 1.12)	0.37	-0.001 (0.001)	0.62
Multivariable ^b	1.09 (0.96, 1.25)	0.19	-0.002 (0.002)	0.25
Cardiovascular ^c	1.09 (0.95, 1.24)	0.22	-0.002 (0.002)	0.24
EPA				
Partial adjustment ^a	0.05 g/d (0.17)			
Multivariable ^b	1.01 (0.92, 1.10)	0.47	0.001 (0.001)	0.38
Cardiovascular ^c	1.07 (0.89, 1.30)	0.45	0.002 (0.003)	0.37
Cardiovascular ^c	1.07 (0.87, 1.32)	0.53	0.003 (0.002)	0.23
<u>Saturated:</u>				
SFA12	0.7 gm/d (1.0)			
Partial adjustment ^a	0.96 (0.83, 1.11)	0.58	0.001 (0.002)	0.38

	Odds Ratios of PAD (95% CI)		Change in ABI	
	mean (SD)	p-value	Beta (+/-SE)	p-linear
Multivariable ^b	0.91 (0.78, 1.07)	0.25	0.002 (0.002)	0.42
Cardiovascular ^c	0.93 (0.79, 1.09)	0.34	0.001 (0.002)	0.55
SFA14	1.9 gm/d (1.7)			
Partial adjustment ^a	1.15 (0.96, 1.37)	0.12	-0.002 (0.002)	0.47
Multivariable ^b	1.08 (0.89, 1.31)	0.40	-0.003 (0.003)	0.32
Cardiovascular ^c	1.10 (0.92, 1.33)	0.29	-0.003 (0.003)	0.27
SFA16	13.1 gm/d (8.1)			
Partial adjustment ^a	1.58 (1.19, 2.10)	0.002	-0.011 (0.003)	<0.001
Multivariable ^b	1.38 (1.00, 1.91)	0.05	-0.011 (0.004)	0.01
Cardiovascular ^c	1.40 (1.03, 1.91)	0.03	-0.010 (0.004)	0.009
SFA18	6.1 gm/d (4.0)			
Partial adjustment ^a	1.70 (1.20, 2.42)	0.004	-0.011 (0.003)	0.003
Multivariable ^b	1.66 (1.04, 2.65)	0.03	-0.010 (0.005)	0.05
Cardiovascular ^c	1.70 (1.07, 2.68)	0.03	-0.010 (0.004)	0.04

Abbreviations: PAD: Peripheral Artery Disease; ABI: Ankle Brachial Index; CI: Confidence Interval; SE: Standard Error; SFA: Saturated fatty acid intake; LA: linoleic acid; AA: arachidonic acid; DHA: Docosahexaenoic acid; DPA: Docosapentaenoic acid; EPA: Eicosapentaenoic acid; SFA14: tetradecanoic acid, SFA16: hexadecanoic acid, SFA18: octadecanoic acid

^aPartial model: Adjusted for age, sex and total energy intake (kcal/day)

^bMultivariable model: Adjusted for age, sex, total energy intake (kcal/day), race/ethnicity, smoking, education, income, physical activity, self-reported health status, origin of birth, alcohol intake and other fatty acids: SFA, MFA, LA, AA, DHA, DPA, EPA, LNA

^cCVD model: Adjusted for all multivariable model covariates and cardiovascular disease, hypertension, diabetes mellitus and hyperlipidemia

Table 5

Fatty acids assessed in NHANES 24 hour Dietary Recall

Category (subclass)		Systematic Name # Carbons/double bonds	Trivial Name (* isomer names)	Food Sources
SFA				
	4:0	Butanoic acid	Butyric acid	butter, parmesan cheese
	6:0	Hexanoic acid	Caproic acid	animal fats & oils
	8:0	Octanoic acid	Caprylic acid	animal milk
	10:0	Decanoic acid	Capric acid	coconut & palm kernel oil
	12:0	Dodecanoic acid	Lauric acid	coconut & palm kernel oil
	14:0	Tetradecanoic acid	Myristic acid	nutmeg & palm kernel oil
	16:0	Hexadecanoic acid	Palmitic acid	palm/palm kernel/coconut oil
	18:0	Octadecanoic acid	Stearic acid	animal & veg. fats/oils
MFA				
	16:1	Hexadecenoic acid:		
(N-7)			Palmitoleic acid	animal/veg./marine oils
(N-10)			Sapienic acid	human sebum
	18:1	Octadecenoic acid:		
(N-9)			Ricinoleic acid	Castor plant/oil
(N-9)			Oleic acid	olive/pecan/peanut oil
Trans (naturally occurring)			Vaccenic acid	ruminant fats & dairy
(N-7)			Cis- vaccenic acid	Sea Buckthorn oil
Trans (industrial)			Elaidic acid	Hydrogenated veg. oils
(N-9)	20:1	Eicosenoic acid	Arachidic acid (AA)	Peanut oil
(N-9)	22:1	Docosenoic acid	Urucic acid	rape/wallflower/mustard seed
PFA				
(N-6)	18:2	Octadecadienoic acid	Linoleic acid (LA)	Common veg. oils
	18:3	Octadecatrenoic acid	Linolenic acid (LNA):	
(N-3)			α-linolenic acid (ALA)	Common veg. oils
(N-6)			γ-linolenic acid (GLA)	Rare veg. oils
	18:4	Octadecatetraenoic acid:		
(N-3)			Stearidonic acid	hemp/blackcurrant seed
(N-3)			α-parinaric acid	Makita seeds
(N-6)	20:4	Eicosatetraenoic acid	arachidonic acid (AA)	meat, eggs, dairy
(N-3)	20:5	Eicosapentaenoic acid (EPA)		Fatty fish
(N-3)	22:5	Docosapentaenoic acid (DPA); clupanodonic acid		Seal oil
(N-3)	22:6	Docosahexaenoic acid (DHA)		Fatty fish

Abbreviations: SFA: Saturated fatty acid intake, MFA: Monounsaturated fatty acid intake, DHA: Docosahexaenoic acid, DPA: Docosapentaenoic acid, EPA: Eicosapentaenoic acid, LNA: Linolenic acid, LA: Linoleic acid, AA: Arachidonic acid Subclass: Refers to the first desaturated carbon from the methyl end of the carbon chain or if the fatty acid is in the trans-unsaturated conformation

* Not assessed separately in NHANES