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Plasma omega-3 and saturated fatty acids are differentially related to pericardial adipose tissue volume across race/ethnicity: The Multi-Ethnic Study of Atherosclerosis

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Abstract

BACKGROUND: Pericardial adipose tissue (PAT) is a cardiometabolic risk factor influenced by race/ethnicity, inflammation, and metabolic dysfunction. Omega-3 fatty acids (FAs) and saturated FAs (SFAs) are known to affect these latter phenomena and may influence PAT accumulation. We aimed to determine whether plasma levels of these FAs are related to PAT volume and its rate of change over a median 3-year follow-up.

METHODS: Cardiac computed tomography assessed PAT in 6,785 Multi-Ethnic Study of Atherosclerosis participants. Gas chromatography flame-ionization estimated plasma phospholipid fatty acids. Regression analyses estimated associations of FAs with PAT volume and its rate of change with adjustments for other risk factors. Race-interactions were tested.

RESULTS: In cross-section, top tertiles of omega-3 FAs and odd-chained SFAs were associated with 2.8 and 4.93 cm³ lower PAT volumes, respectively; race/ethnicity was a significant modifying variable ($p < 0.002$). Even-chained SFAs were associated with 3.5 cm³ greater PAT volume. With stratification by race/ethnicity, Chinese Americans in the top tertile of omega-3 FAs showed 10.5 cm³ greater PAT volume than those in the referent tertile. Black individuals in the top tertile of odd-chained SFAs showed 5.0 cm³ lower PAT compared to referents. Black and Chinese Americans in top tertiles of even-chained SFAs showed respective 3.7 and 5.9 cm³ greater PAT volumes compared to referents. Two associations were observed in prospective analyses among Caucasians; race interactions were non-significant.

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COMPETING INTERESTS

The authors have no competing interests to disclose.

CONCLUSIONS: Cross-sectional and prospective findings provide inconclusive evidence as to whether plasma FAs are related to PAT in healthy individuals. Cohort studies with longer follow-up periods are warranted.

Keywords

plasma fatty acids; omega-3; saturated; ectopic fat; pericardial; risk factors

Introduction

Pericardial adipose tissue (PAT) is a pathogenic ectopic fat compartment and independent cardiometabolic risk factor. Located between the visceral and parietal pericardium and distinct from the epicardial fat depot (1), PAT has been found to be independently associated with obesity (2), subclinical atherosclerosis (2), atrial fibrillation (3,4), incident coronary heart disease (5), as well as type II diabetes and pre-diabetes (6). Critically, PAT has consistently been associated with inflammation and metabolic dysfunction in intervention and cohort studies (6-9), and bioactive compounds that affect these phenomena may correspondingly influence PAT deposition. Among these, circulating levels of omega-3 fatty acids (FAs) and saturated fatty acids (SFAs) may contribute to inflammatory and metabolic environments that promote or suppress accumulation of this ectopic fat compartment.

Omega-3 FAs have been well-characterized for certain health benefits that may suppress ectopic fat deposition. Among these, omega-3's have been shown to lower circulating triglycerides (10), metabolize in to anti-inflammatory and pro-resolving mediators (11, 12), and promote insulin sensitivity (12-14). Moreover, supplementation with either omega-3 eicosapentaenoic acid (EPA) (15) or docosahexaenoic acid (DHA) (16) has been shown to modestly reduce visceral and epicardial ectopic fat volumes in cardiovascular and non-alcoholic fatty liver disease patients, respectively. Based on this evidence, it is possible that elevated plasma omega-3 FAs support an environment that suppresses PAT volume or rate of PAT accumulation—yet no studies have tested cross sectional and prospective relationships.

In contrast to omega-3 FAs, less is known about plasma levels of SFAs, though they have been shown to promote inflammation and risks of adverse metabolic outcomes. And yet, recent studies have found that, upon stratifying SFAs in to even- and odd-chained FA species, they were differentially related to disease (17, 18). While the even-chained SFAs palmitic acid and stearic acid have been shown to be directly related to markers of inflammation and metabolic dysfunction (17-19), the odd-chained SFAs pentadecylic acid and margaric acid have been found to be inversely related to inflammation, triglyceride levels, and diabetes (18-21). Whether even- or odd-chained plasma SFAs may be similarly related to PAT volume or rate of PAT accumulation is currently unknown.

Overall, this study aimed to determine whether plasma omega-3 FAs, even-chained SFAs, and odd-chained SFAs are related to PAT and its rate of change over a median 3-year follow-up period in the community-based Multi-Ethnic Study of Atherosclerosis cohort. Given previous findings, it was hypothesized that plasma levels of both omega-3 FAs and odd-chained SFAs would be inversely related to PAT volume and accumulation, while even-chained SFAs were hypothesized be directly associated with PAT outcomes. Race/ethnicity

differences in PAT volumes and plasma FAs have been reported in MESA and in other cohorts (2, 22, 23), and race interactions were tested in cross-sectional and prospective analyses.

Materials and Methods

Study population

MESA design and objectives have been described previously (24), and study protocol information is available online (www.mesa-nhlbi.org). In brief, between July 2000 and August 2002 men and women aged 45 to 84 years of age without clinical cardiovascular disease were recruited across the United States from six communities (Los Angeles County, CA; New York, NY; Baltimore, MD; Chicago, IL; Forsyth County, NC; and St. Paul, MN) (N= 6,785). Study participants gave informed consent, and Institutional Review Board approval was given at all MESA sites. For prospective analyses, data collected at follow-up Exam 2 (September 2002-February 2004), Exam 3 (March 2004-September 2005) and Exam 4 (September 2005-May 2007) were utilized. Five hundred and seventy-eight individuals had missing data for omega-3 FA and even-chained SFA exposure variables, the baseline PAT outcome, or covariates (N=578), and these participants were excluded from analyses (analytic N for fully adjusted models=6,236 for plasma omega-3 FAs and even-chained SFAs); an additional 2,726 participants were missing odd-chained SFA baseline data (N=3,510 for plasma odd-chained SFAs). For prospective analyses, a number of individuals were missing baseline PAT measures, but had follow-up PAT data for analyses, resulting in nominally higher sample sizes (analytic N for fully adjusted models=6,262 for plasma omega-3 FAs and even-chained SFAs; N=3,527 for plasma odd-chained SFAs).

Laboratory measurements

Fasting blood was drawn, and serum and EDTA-anticoagulant tubes were collected and processed using a standardized protocol (25) and samples were aliquoted and stored at -70°C until time of use. Lipids were measured using standard protocols as described previously (26). Plasma phospholipid fatty acids were measured in EDTA plasma as done previously (27). Briefly, all fatty acid subfractions were initially extracted from the plasma using a chloroform/methanol method, and cholesterol esters, triglycerides, phospholipids, and free fatty acid subfractions were separated by thin layer chromatography. Phospholipid fatty acids were then harvested for analysis; they were derivatized to methyl esters and separated through gas chromatography with flame ionization detection. Generated values are expressed as percent of the total phospholipid fraction and total omega-3 FAs [alpha-linolenic acid (ALA), EPA, DHA], even-chained SFAs (myristic acid, palmitic acid, stearic acid) and odd-chained SFAs (pentadecanoic acid, heptadecanoic acid) were estimated by summing individual FAs. Coefficients of variation for FAs comprising the: 1) total omega-3 FAs: ALA (18:3): 17.9%; EPA (20:5): 3.3%; DHA (24:6): 2.7%; 2) total even-chained SFAs: myristic acid (14:0): 8.2%; palmitic acid (16:0): 2.1%; and stearic acid (18:0): 2.4%; 3) total odd-chained SFAs: pentadecanoic acid (15:0): 6.6%; heptadecanoic acid (17:0): 2.6%.

Pericardial adipose tissue

PAT was evaluated using cardiac computed tomography in accordance with a protocol described by McClain et al. (2). In summary, the left main coronary artery superior extent was distinguished in a cross-sectional scan; slices within 15 mm above and 30 mm below this slice were included. The anterior border was identified by the chest wall and the posterior border by the aorta and the bronchus. Volume Analysis software (GE Healthcare, Waukesha, WI) was used to discern fat from the remaining portions of the heart with a threshold of -190 to -30 Hounsfield units. The volume was the sum of all voxels containing pericardial adipose tissue. Baseline PAT was used in the cross-sectional analysis and measurements from follow-up exams 2, 3 and 4 were used to tabulate rate of change from baseline (cm^3/year) with a median follow-up time of 3-years.

Covariate data collection

Demographic and lifestyle information were obtained through questionnaires, and trained staff evaluated height and weight according to standard procedures. Resting seated blood pressure was measured three times using an automated oscillometric method (Dinamap, Critikon, Milwaukee WI); the average of the second and third readings was used in analyses.

Statistical analysis

Statistical analysis was conducted using Stata (version 15.0, Stata Corp, College Station, TX). Baseline characteristics are presented as means (SD) for continuous variables and frequencies (%) for categorical variables. FA levels were categorized by tertiles, and regression analysis determined associations of plasma levels of even-chained SFAs, odd-chained SFAs, as well as omega-3 FAs with PAT volume at baseline. Tertiles of plasma phospholipid levels of FAs were evaluated with adjustments for age, sex, race/ethnicity, education, smoking status, SBP, hypertension medication use, lipid lowering medication use, exercise, and alcohol use (grams per day) as well as metabolic-related covariates including BMI, baseline fasting insulin, presence of diabetes, total cholesterol, and HDL-C. Race-stratified analyses were conducted using the same approach as above; race/ethnicity was included as an interaction term to determine any significant differences in associations among the four races/ethnicities. Interaction p-values were considered significant at $p < 0.05$.

Results

Demographic, lifestyle, and clinical characteristics of 6,785 MESA participants are stratified by quartiles of baseline PAT volume and presented in Table 1. Across successive PAT quartiles, individuals were more likely to be older, Caucasian, have type II diabetes, taking hypertension medication, consume a greater amount of alcohol, have higher blood pressure and fasting insulin levels, have a higher BMI, and have lower levels of HDL-C and intentional physical activity. Greater PAT volume was associated with greater levels of plasma even-chained SFAs and lower levels of plasma odd chained SFAs and omega-3 FAs.

Demographic, lifestyle, and clinical characteristics of 6,785 MESA participants are stratified by race/ethnicity and presented in Table 2, and numerous differences were observed across race. Relative to other races/ethnicities, Black participants were found to have the lowest

volume of baseline PAT volume, but the highest mean BMI, systolic blood pressure, prevalence of diabetes, rate of current smoking, and number of individuals on hypertension medication. Caucasians were found to have the highest amount of alcohol intake per week as well as the highest mean plasma levels of even-chained SFAs. Chinese Americans were found to have the highest mean levels of plasma omega-3 FAs, but the lowest levels of odd-chained SFAs, intentional exercise, alcohol intake, BMI, and rate of former or current smoking. Hispanics showed the lowest mean levels of pericardial fat volume, but the highest mean levels of fasting insulin and total cholesterol.

Baseline PAT volumes for all participants and races/ethnicities are shown across tertiles of plasma phospholipid FAs in Table 3. For all participants, individuals in top tertiles of plasma omega-3 FAs and odd-chained SFAs were associated with respective 2.8 and 4.93 cm³ lower PAT volumes compared to those in the referent tertiles after multivariate adjustments. By contrast, participants in the top tertile of even-chained SFAs were found to have an estimated 3.5 cm³ greater PAT volume compared to those in the bottom tertile. Upon stratifying by race/ethnicity, Chinese Americans with omega-3 FAs in the top tertile were found to have a significant 10.5 cm³ greater PAT volume than those in the bottom tertile. For odd-chained SFAs, Black individuals in the top tertile were found to have 5.0 cm³ lower PAT than Black individuals in the bottom tertile. Finally, Black and Chinese Americans in top tertiles of even-chained SFAs were found to have 3.7 and 5.9 cm³ greater PAT volumes than those in respective bottom tertiles. Race/ethnicity was found to modify associations between PAT volume and plasma omega-3 FAs (p for race interaction=0.002). No race/ethnicity interactions were observed for odd- or even-chained SFAs in cross-sectional analyses.

Rates of pericardial adipose tissue accumulation (cm³/year) across tertiles of plasma FAs over a median 3-year follow-up period are shown in Table 4. No significant associations were observed for the entire cohort. After stratifying by race/ethnicity, two associations were found in Caucasian participants. Those in the top tertiles of plasma omega-3 FAs and even-chained SFAs showed 0.61 and 0.74 cm³/year lower accumulations of PAT than those in bottom tertiles. Null findings were observed for odd-chained SFAs across all groups. No significant race/ethnicity interactions were observed.

Discussion

In this large multi-ethnic cohort, elevated levels of plasma omega-3 FAs and odd-chained SFAs were associated with significantly, albeit incrementally, lower PAT volumes. By contrast, plasma even-chained SFAs were related to significantly greater PAT volume. Upon stratifying by race/ethnicity, differential cross-sectional associations were observed, and race/ethnicity was found to be a significant modifying variable for plasma omega-3 FAs. In prospective analyses, significant associations were only found in Caucasians; however, no race interactions were evident. When considered together, these results provide an unclear picture as to whether these FAs are independently related to PAT; however, the cross-sectional results for omega-3 FAs and even-chained SFAs are corroborated by previous findings.

Omega-3 FAs and ectopic fat

Previous intervention studies have demonstrated that fish oil omega-3 FAs affect ectopic fat stores—albeit in specific patient populations. A six-month non-blinded intervention study in individuals with cardiovascular disease showed that 1.8 grams of EPA per day resulted in 11.6 cm³ and 7.3 cm³ reductions in respective visceral and epicardial fat compartments compared to controls (15). Similarly, a six-month double-blind placebo-controlled randomized trial in children with non-alcoholic fatty liver disease showed that a modest dose of 250 mg of DHA per day resulted in significant 5.6% and 12.5% reductions in respective visceral and epicardial fat volumes compared to those given a placebo (16). While these studies were conducted in distinct patient populations and ectopic fat compartments, they support a beneficial effect of EPA and DHA in reducing ectopic fat stores.

Our cross-sectional findings in this community-based cohort of relatively healthy, free-living individuals largely agree with results from the above intervention studies insofar as study participants with greater plasma omega-3 FA levels showed significantly less PAT volume at baseline independent of demographic, lifestyle, and metabolic risk factors. Numerous mechanisms may explain the current cross sectional and intervention study findings including omega-FA effects on suppressing adipose cell proliferation and differentiation (26, 28) as well as countering inflammatory pathways (10, 11, 29) and insulin resistance (12-14; 30, 31) related to ectopic fat accumulation. It must be acknowledged that the direct relationship between omega-3 FAs and PAT observed in Chinese American participants was unexpected; however, given the wide confidence intervals in the 2nd and 3rd tertiles—a reflection of the small sample size of this group—replication in Chinese individuals and those with Chinese ancestry is critical before making firm conclusions.

For prospective associations, the null findings in all groups except a borderline association in Caucasians ($p=0.04$) are inconsistent with any influence of plasma omega-3 FAs on PAT in healthy individuals. Several factors may account for the null results. First, over the 3-year follow-up period, change in PAT volume averaged 1.03 cm³/year with a plausible value range for the slopes between -4.94 and 7.00 cm³/year. This nominal change in PAT, coupled with the wide plausible value range and the abbreviated follow-up period, may have constrained our ability to discern associations with plasma FAs independent of metabolic risk factors—BMI in particular. In addition, the omega-3 FA exposure variable may have been a limiting factor since individuals in the US show a modest level of plasma EPA and DHA. A comparative study in the ERA JUMP cohort showed that plasma EPA and DHA levels in US individuals were approximately half of those found in native Japanese individuals (32). Relatedly, it is possible that elevated EPA and DHA levels through supplementation or consistent seafood consumption are required to achieve an identifiable PAT-related benefit over time. Taken together, these factors may have limited our ability to observe relationships in prospective analyses, and confirmation in other cohorts is warranted.

Odd- and even-chained SFAs and ectopic fat

In contrast to the omega-3 FAs, no previous studies have examined ectopic fat and plasma SFAs; yet, even- and odd-chained SFAs have been associated with metabolic endpoints that would putatively influence ectopic fat deposition including β -cell function, insulin sensitivity, and type II diabetes development (17-21). Critically, direct effects of SFAs on inflammatory cascades (33) and insulin resistance have also been reported (34-37). Indeed, the observed cross-sectional associations of even- and odd-chained SFAs in the entire cohort corresponds with these phenomena. While the null findings in prospective analyses challenge the hypothesis that SFAs have a substantial influence on PAT accumulation, the limited rate of change in PAT over the 3-year period likely constrained our ability to observe associations and increased the likelihood of type II errors. Given the few studies conducted to date, confirmation of these findings in other cohorts is warranted; however, it is possible that even-chained SFA plasma FA profiles reflect adiposity and metabolic status—the primary contributors to PAT accumulation.

Implications of study findings

Differential results between cross-sectional and prospective analyses provide inconclusive evidence as to whether plasma omega-3 or SFA levels are important variables in PAT deposition in an outwardly healthy cohort of individuals. Yet the significant interactions for omega-3 FAs in cross-section were remarkable and raise the possibility that these may have benefits depending upon race/ethnicity. Given their novelty, the race interactions require confirmation in other cohort studies as well as other ectopic adipose tissue compartments. Prospective studies over longer follow-up periods are also needed to determine whether these may be mediating exposure variables or whether they have limited associations compared to other risk factors.

In terms of additional studies, plasma omega-3 FAs and odd-chained SFAs are partially determined by their dietary consumption, e.g. non-fried fish or fish oil supplements and dairy fats, respectively. Observational or interventional dietary studies with longer follow-ups would also be well-suited to determine whether these fatty acids are related to ectopic fat accumulation. By contrast, plasma even-chained SFA levels have been shown to be unrelated to their dietary consumptions (38, 39) and are largely synthesized *de novo* from other macronutrient sources. Of these, carbohydrates have been found to be related to plasma phospholipid and cholesterol ester SFA levels (40, 41). If further research over longer study periods shows evidence of prospective associations between these FA exposures and pericardial PAT outcomes, it is possible that dietary consumptions of omega-3 FAs, dairy fats, and carbohydrates may differentially influence ectopic fat deposition.

Strengths and limitations

The present study provides the largest cross-sectional and prospective analyses of plasma FAs and PAT outcomes in a large multi-ethnic cohort. Pericardial fat measures were carried out with a high degree of reproducibility and observed intra-class correlation coefficients for intra-reader and inter-reader reliability were 0.999 and 0.997, respectively. In terms of limitations, only baseline plasma FA levels were assessed, and potential changes in plasma FA profile over the study period cannot be evaluated. As discussed above, the lower

mean levels of plasma omega-3 FAs in MESA participants compared to other cohorts, the abbreviated follow-up period, and nominal changes in PAT accumulation over this time may have constrained our ability to observe prospective associations. Covariate adjustments were included for demographic, lifestyle, and clinical factors in statistical models, but the potential for residual confounding remains. Finally, the present findings may not be generalizable to other global populations since MESA is a U.S.-based cohort.

Conclusion

The disparate findings between cross-sectional and prospective findings provide equivocal evidence as to whether plasma FAs may influence PAT in healthy individuals. The significant interaction observed in cross-sectional analyses suggest that race/ethnicity may be an important modifying variable for future multi-ethnic studies involving FAs or ectopic adipose tissue depots. There remains limited research in this area, and both cohort and intervention studies of FAs and ectopic adipose tissue are warranted.

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Table 1.

Demographic, lifestyle, and clinical characteristics of 6,785 MESA participants* stratified by quartiles of baseline pericardial fat volume.

Characteristic	Quartiles of pericardial adipose tissue				p-value
	1	2	3	4	
Volume (cm ³), mean (SD)	37.4 (8.2)	60.1 (6.1)	83.7 (8.2)	137 (100)	
Age (years), mean (SD)	58.7 (10.0)	61.6 (10.2)	63.6 (9.9)	64.7 (9.8)	<0.001
Sex, female n (%)	1153 (68.0)	1012 (59.7)	868 (51.2)	557 (32.9)	<0.001
Race, n (%)					<0.001
Black	647 (38.1)	526 (31.0)	433 (25.5)	278 (16.4)	
Caucasian	622 (36.7)	561 (33.1)	632 (37.3)	797 (47.1)	
Chinese American	169 (10.0)	264 (15.6)	221 (13.0)	142 (8.4)	
Hispanic	258 (15.2)	345 (20.3)	409 (24.1)	476 (28.1)	
Education, n(%)					<0.001
<High school	206 (12.2)	287 (17.0)	352 (20.8)	372 (22.0)	
Completed high school/GED	268 (15.9)	294 (17.4)	312 (18.5)	354 (21.0)	
Some college	384 (22.7)	416 (34.8)	412 (24.4)	378 (22.4)	
Associate degree	107 (6.3)	89 (5.3)	73 (4.3)	70 (4.1)	
Bachelor's degree	360 (21.3)	282 (16.7)	264 (15.6)	258 (15.3)	
Graduate or professional school	364 (21.6)	322 (19.1)	276 (16.3)	257 (15.2)	
Smoking status, n (%)					<0.001
Never	943 (55.8)	894 (52.9)	842 (49.9)	720 (42.6)	
Former	516 (30.5)	563 (33.3)	625 (37.0)	769 (45.5)	
Current	231 (13.7)	233 (13.8)	222 (13.1)	200 (11.8)	
Exercise (Met-min/wk), mean (SD)	1806 (2470)	1614 (2556)	1493 (2183)	1299 (2109)	<0.001
Alcohol intake (g/d), mean (SD)	3.9 (8.2)	4.2 (9.1)	4.7 (12.0)	7.1 (17.1)	<0.001
SBP (mm Hg), mean (SD)	102.3 (58.9)	123.9 (80.5)	140.4 (99.0)	159.4 (100)	<0.001
On hypertension medicine, n (%)	444 (26.2)	567 (33.4)	710 (41.9)	797 (47.1)	<0.001
BMI (kg/m ²), mean (SD)	25.3 (27.2)	27.2 (4.8)	29.3 (5.2)	31.6 (5.2)	<0.001
Fasting insulin (mU/L), mean (SD)	7.8 (15.8)	9.6 (23.9)	11.1 (11.4)	13.2 (9.7)	<0.001
Diabetes, n (%)	175 (10.3)	175 (10.3)	250 (14.8)	322 (19.0)	<0.001
Total cholesterol (mmol/L), mean (SD)	5.0 (0.88)	5.08 (0.93)	5.02(0.94)	4.99 (0.94)	0.01
HDL-C (mmol/L), mean (SD)	1.51 (0.43)	1.35 (0.38)	1.25 (0.33)	1.16 (0.29)	<0.001
Plasma FAs (% total), mean (SD)					
Even-chained SFAs	39.2 (2.7)	39.5 (2.7)	39.8 (2.5)	40.1 (2.6)	<0.001
Odd-chained SFAs	0.67 (0.8)	0.61 (0.1)	0.60 (0.1)	0.60 (0.2)	0.001
Omega-3 FAs	5.1 (2.2)	5.1 (2.2)	4.8 (2.0)	4.5 (1.8)	<0.001

* Individuals with missing covariate data were excluded from the analysis

Table 2.

Demographic, lifestyle, and clinical characteristics of 6,785 MESA participants* stratified by race/ethnicity.

Characteristic	Race/ethnicity				p-value
	Black	Caucasian	Chinese Am	Hispanic	
Age (years), mean (SD)	62.1 (10.1)	62.6 (10.3)	62.3 (10.3)	61.3 (10.3)	<0.001
Sex (female), n (%)	1049 (55.4)	1363 (52.0)	413 (51.4)	774 (51.8)	NS
Education, n(%)					<0.001
<High school	229 (12.1)	129 (4.9)	199 (24.9)	668 (44.7)	
Completed high school/GED	359 (19.1)	442 (16.9)	130 (16.2)	305 (20.4)	
Some college	536 (28.3)	625 (23.9)	112 (13.9)	321 (21.5)	
Associate degree	118 (6.3)	119 (4.6)	49 (6.1)	53 (3.5)	
Bachelor's degree	325 (17.3)	581 (22.3)	182 (22.7)	83 (5.6)	
Graduate or professional school	311 (16.6)	715 (27.4)	130 (16.2)	65 (4.3)	
Smoking status, n (%)					<0.001
Former	691 (36.8)	1155 (44.2)	153 (19.1)	485 (32.4)	
Current	338 (18.0)	301 (11.5)	45 (5.6)	203 (13.6)	
Exercise (Met-min/wk), mean (SD)	1712 (2785)	1687 (2301)	1149 (1518)	1336 (2110)	<0.001
Alcohol intake (grams/day), mean (SD)	3.4 (8.1)	8.0 (15.1)	1.5 (6.4)	3.4 (11.9)	<0.001
SBP (mm Hg), mean (SD)	131.7 (21.6)	123.5 (20.4)	124.6 (21.6)	126.7 (21.9)	<0.001
On hypertension medicine, n (%)	950 (50.3)	866 (33.1)	231 (28.8)	486 (32.5)	<0.001
BMI (kg/m ²), mean (SD)	30.2 (5.9)	27.7 (5.1)	24.0 (3.3)	29.4 (5.1)	<0.001
Fasting insulin (mU/L), mean (SD)	11.4 (25.5)	9.2 (5.6)	9.5 (12.3)	11.8 (15.4)	<0.001
Diabetes, n (%)	343 (18.1)	165 (6.3)	107 (13.3)	265 (17.7)	<0.001
Total cholesterol (mmol/L), mean (SD)	4.89 (0.94)	5.06 (0.91)	4.98 (0.82)	5.12 (0.97)	<0.001
HDL-C (mmol/L), mean (SD)	1.36 (0.40)	1.35 (0.41)	1.28 (0.33)	1.23 (0.34)	<0.001
Plasma FAs (% total), mean (SD)					
Even-chained SFAs	39.3 (2.8)	40.0 (2.6)	39.3 (2.1)	39.8 (2.7)	<0.001
Odd-chained SFAs	0.62 (0.74)	0.62 (0.15)	0.56 (0.11)	0.62 (0.13)	NS
Omega-3 FAs	5.3 (1.9)	4.6 (1.9)	6.5 (2.5)	4.0 (1.6)	<0.001
Pericardial fat volume (cm ³)	67.5 (34.7)	85.1 (46.1)	73.7 (31.4)	88.3 (43.8)	<0.001
PAT change rate (cm ³ /year), mean (SE) [†]	0.81 (0.11)	1.07 (0.20)	0.97 (0.13)	1.63 (0.14)	<0.001

* Individuals with missing covariate data were excluded from the analysis

[†] Rates of PAT change (and SEs) were estimated using a linear mixed model. P-value was based on the interaction between follow-up time and sex.

Definitions: SBP=systolic blood pressure; BMI=body mass index; HDL-C=high density lipoprotein-cholesterol; FAs=fatty acids; SFAs=saturated fatty acids; PAT=pericardial adipose tissue

Table 3.

Baseline pericardial adipose tissue volume (cm³) across tertiles of plasma levels of omega-3 fatty acids (FAs), monounsaturated FAs, odd-chained saturated FAs (SFAs), and even-chained SFAs among 6,236 Multi-Ethnic Study of Atherosclerosis participants.

Fatty acids	All N=6236	Black N=1641	Caucasian N=2440	Chinese American N=782	Hispanic N=1373
Omega-3 FAs*					
Tertile 1	referent	referent	referent	referent	referent
Tertile 2	-1.45 (-3.41 - 0.50)	-1.31 (-5.06 - 2.44)	0.80 (-2.25 - 3.85)	10.39 (3.36 - 17.4) 0.004	-4.29 (-8.39 - -0.19) 0.04
Tertile 3	-2.80 (-4.90 - -0.71) 0.009	-2.17 (-5.99 - 1.65)	-1.03 (-4.39 - 2.33)	10.52 (3.94 - 17.1) 0.002	-4.19 (-9.44 - 1.06)
Odd-chained SFAs					
Tertile 1	referent	referent	referent	referent	referent
Tertile 2	-3.56 (-6.19 - -0.93) 0.008	-2.10 (-6.16 - 1.97)	-1.99 (-5.89 - 1.90)	-0.35 (-14.3 - 13.6)	-6.77 (-13.2 - -0.34) 0.04
Tertile 3	-4.93 (-7.62 - -2.24) <0.001	-4.99 (-9.35 - -0.62) 0.03	-2.15 (-6.05 - 1.74)	9.84 (-6.71 - 26.4)	-5.82 (-12.4 - 0.74)
Even-chained SFAs					
Tertile 1	referent	referent	referent	referent	referent
Tertile 2	1.90 (0.0 - 3.81) 0.05	3.09 (-0.09 - 6.26)	2.37 (-0.93 - 5.67)	2.19 (-1.63 - 6.00)	-1.13 (-5.61 - 3.34)
Tertile 3	3.53 (1.59 - 5.46) <0.001	3.69 (0.26 - 7.11) 0.04	1.17 (-2.05 - 4.40)	5.93 (1.71 - 10.2) 0.006	3.17 (-1.32 - 7.67)

Model adjustments for age, gender, education, smoking status, systolic blood pressure, hypertension medication use, lipid lowering medication use, exercise, alcohol use, body mass index, fasting insulin, diabetes, total cholesterol, and HDL-C. Regression model for 'All' participants additionally adjusted for race/ethnicity.

* Significant interaction across race/ethnicity (p=0.002)

Table 4.

Rates of pericardial adipose tissue accumulation (cm^3/year) across tertiles of plasma levels of omega-3 fatty acids (FAs), monounsaturated FAs, odd-chained saturated FAs (SFAs), and even-chained SFAs over a median 3-year follow-up period.

Fatty acids	All	Black	Caucasian	Chinese American	Hispanic
Omega-3 FAs					
Referent	referent	referent	referent	referent	referent
Tertile 2	0.09 (-0.21 - 0.39)	0.30 (-0.38 - 0.99)	-0.059 (-0.59 - 0.47)	-0.79 (-2.39 - 0.81)	0.18 (-0.43 - 0.79)
Tertile 3	-0.14 (-0.44 - 0.16)	0.32 (-0.37 - 1.00)	-0.61 (-1.18 - -0.039)	-1.41 (-2.87 - 0.053)	-0.30 (-1.05 - 0.46)
Odd-chained SFAs					
Referent	referent	referent	referent	referent	referent
Tertile 2	-0.13 (-0.55 - 0.29)	0.009 (-0.68 - 0.70)	-0.56 (-1.317 - 0.195)	1.09 (-1.77 - 3.95)	0.14 (-0.82 - 1.10)
Tertile 3	0.01 (-0.41 - 0.43)	-0.14 (-0.88 - 0.60)	0.07 (-0.66 - 0.80)	0.25 (-2.93 - 3.43)	0.18 (-0.80 - 1.16)
Even-chained SFAs					
Referent	referent	referent	referent	referent	referent
Tertile 2	-0.16 (-0.46 - 0.14)	-0.27 (-0.85 - 0.31)	-0.25 (-0.84 - 0.34)	-0.025 (-0.93 - 0.88)	-0.12 (-0.80 - 0.55)
Tertile 3	-0.30 (-0.60 - 0.007)	-0.016 (-0.62 - 0.59)	-0.74 (-1.31 - -0.17)	0.01 (-1.50 - 0.46)	0.043 (-0.62 - 0.71)

Model adjusted for age, gender, education, smoking status, systolic blood pressure, hypertension medication use, lipid lowering medication use, exercise, alcohol use, body mass index, fasting insulin, diabetes, total cholesterol, and HDL-C. Regression model for 'All' participants additionally adjusted for race/ethnicity.