Published in final edited form as:

Eur J Clin Nutr. 2012 May ; 66(5): 600–605. doi:10.1038/ejcn.2011.215.

Ethnicity, plasma phospholipid fatty acid composition and inflammatory/endothelial activation biomarkers in the Multi-Ethnic Study of Atherosclerosis (MESA)

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Abstract

BACKGROUND/OBJECTIVES—It has been recognized that certain long-chain polyunsaturated fatty acids (LC-PUFAs) are involved in inflammation and its resolution. It has also been shown that ethnicity may be a factor in affecting systemic inflammation, and limited evidence suggests it may influence plasma LC-PUFA composition. Given the links among these three factors, we aim to determine ethnicity-based differences in plasma LC-PUFA composition among White, Black, Hispanic and Chinese participants, and whether such differences contribute to variations in markers of inflammation and endothelial activation in a sub-cohort of the Multi-Ethnic Study of Atherosclerosis (MESA).

SUBJECTS/METHODS—Plasma phospholipid LC-PUFAs levels (%) were determined in 2848 MESA participants using gas chromatography-flame ionization detection. Enzyme immunoassays

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

determined inflammatory markers levels for high-sensitivity C-reactive protein (*n* =2848), interleukin-6 (*n* =2796), soluble tumor necrosis factor-α receptor type 1 (*n* =998), and endothelial activation markers soluble intercellular adhesion molecule-1 (*n* =1192) and soluble E-selectin (*n* =998).

The modifying influence of ethnicity was tested by linear regression analysis.

RESULTS—Chinese adults were found to have the highest mean levels of plasma eicosapentaenoic acid (EPA, 1.24%) and docosahexaenoic acid (DHA, 4.95%), and the lowest mean levels of γ-linolenic (0.10%), dihomo-γ-linolenic (DGLA, 2.96%) and arachidonic (10.72%) acids compared with the other ethnicities (all $P \leq 0.01$). In contrast, Hispanics had the lowest mean levels of plasma EPA (0.70%) and DHA (3.49%), and the highest levels of DGLA (3.59%; all $P \leq 0.01$). Significant differences in EPA and DHA among ethnicities were attenuated following adjustment for dietary non-fried fish and fish oil supplementation. Ethnicity did not modify the associations of LC-PUFAs with markers of inflammation or endothelial activation (all $P_{\text{interaction}} > 0.05$).

CONCLUSIONS—The absence of a modifying effect of ethnicity indicates that the putative benefits of LC-PUFAs with respect to inflammation are pan-ethnic. Future longitudinal studies may elucidate the origin(s) of ethnicity-based differences in LC-PUFA composition and whether certain patterns, that is, high plasma levels of DGLA and low levels of EPA/DHA, contribute to inflammation-associated health outcomes.

Keywords

race; endothelial activation; inflammation; fatty acid; omega-3; omega-6

INTRODUCTION

Dietary intake of long-chain polyunsaturated fatty acids (LC-PUFAs) has gained recent media attention, yet their benefits were recognized decades ago in studies of Greenland Inuit. High intakes of the ‘fish oil’ omega-3 (n-3) LC-PUFAs eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) were found to correspond with low incidences of cardiovascular disease (CVD) and thrombosis.[1] More recent studies have extended these findings to the omega-6 (n-6) LC-PUFAs–revealing that arachidonic acid (AA) and linoleic acid (LA) are associated with lower incidence of CVD,[2 – 5] although results are inconsistent.[6 – 8] The mechanisms by which they may affect CVD are not entirely known, but LC-PUFAs have been shown to associate with lower levels of inflammatory markers,[9] suppress pro-inflammatory cytokine production[10] and reduce hallmarks of an atherogenic lipid phenotype–high levels of triglycerides and small dense low-density lipoprotein particles.[11,12] Even more recently, LC-PUFAs have been shown to metabolize into compounds that actively resolve the inflammatory response,[13 – 15] that is, have ‘pro-resolving’ properties. Given that CVD has a strong inflammatory component, the health benefits of LC-PUFA intake may partially be a function of such anti-inflammatory, pro-resolving properties.

Clearly, LC-PUFA composition is not the only factor that affects an inflammatory phenotype or disease risk. A host of additional lifestyle factors such as physical activity

levels and obesity, as well as non-lifestyle factors such as ethnicity, have been shown to influence inflammation. Indeed, certain ethnicities appear to be more predisposed toward chronic inflammation than others–for example, Black adults have been shown to have higher levels of inflammatory markers compared with Hispanics, Whites or Asians in a number of studies,[16 – 19] including the Multi-Ethnic Study of Atherosclerosis (MESA).[20,21] Further, some ethnic groups have been shown to have a higher prevalence of diseases that have been associated with inflammation–for example, higher prevalences of diabetes, hypertension and increased left ventricular mass have been noted in Blacks compared with Hispanics and Whites, with the lowest prevalence among Asians.[22 – 24] LC-PUFAs are known to affect the inflammatory response and are associated with inflammation in relatively homogenous study populations;[25,26] thus, a greater understanding of LC-PUFA variation among a heterogeneous study population may provide insight into the development of inflammatory conditions such as CVD.

Using a large multi-ethnic cohort of MESA participants, the present study aims to determine differences in plasma LC-PUFA compositions, as well as inflammatory and endothelial activation markers among Black, White, Hispanic and Chinese–American participants. Further, the study aims to determine whether ethnicity modifies the relations of plasma LC-PUFAs with inflammatory and endothelial activation markers.

MATERIALS AND METHODS

Population

The primary aim of MESA is to investigate the development and progression of subclinical CVD. The study design and methods have been described,[27] and information about the MESA protocol is available online (www.mesa-nhlbi.org). Briefly, 6814 men and women between the ages of 45 and 84 years without clinical evidence of CVD were recruited from six communities in the United States (Baltimore, MD; Chicago, IL; Forsyth County, NC; Los Angeles County, CA; New York, NY; and St Paul, MN). During recruitment, questions on ethnicity were asked based on the United States 2000 census questionnaire. Subjects who self-reported their ethnic group as White or White, Black or African American, Chinese, or Spanish/Hispanic/Latino were potentially eligible. Institutional Review Board approval was obtained at all MESA sites, and all participants gave informed consent. Recruitment and baseline examinations began in July 2000 and were conducted over a 24-month period. The present cohort was composed of 2848 MESA participants who gave informed consent (MESA Genetics Candidate Gene Evaluation Cohort); each race was represented relatively equally, African American (n =703), Asian (of Chinese descent n =712), Hispanic (n =709) and White (n =722) participants.

Measurements

Questionnaire information was obtained regarding age, sex, ethnicity, education and lifestyle factors including smoking status, physical activity and dietary intake. Physical activity is represented by the sum of intentional exercise in metabolic equivalent-min/week, including walking for exercise, sports, dancing and conditioning activities. Usual dietary intake over the previous year was assessed through a self-administered, 120-item food frequency

questionnaire in which responses were given as never/rare to frequently (≥2 times per day), and serving sizes were listed as small, medium or large. Height and weight were measured according to standard procedures.[27] Fasting blood was drawn and serum and EDTA-anticoagulant tubes were collected and processed using a standardized protocol.[27] The serum and plasma samples were aliquoted and stored at −70 °C until time of use.

Plasma fatty acid profile—Phospholipid fatty acids were extracted from EDTA plasma (*n* =2848) using the method previously described by Cao *et al*.[28] In brief, lipids were extracted from the plasma using a chloroform/methanol extraction method, and the cholesterol esters, triglyceride, phospholipids and free fatty acids were separated by thin layer chromatography. Fatty acids from the phospholipids were derivatized to methyl esters and detected by gas chromatography flame ionization. The fatty acids detected were expressed as a percent of total fatty acids. The following representative correlation values were obtained from intra-laboratory quality control (*n* =20): LA 2.6%; α-LA, 2.4%; AA, 2.4%; EPA, 3.3%; DPA, 2.9% and DHA, 2.7%.

Analysis of inflammatory markers/cytokines adhesion/endothelial activation markers

High-sensitivity C-reactive protein (hsCRP) was measured (*n* =2848) on a BNII nephelometer (N High-Sensitivity CRP; Dade Behring Inc., Deerfield, IL, USA) using a particle-enhanced immuno-nephelometric assay. Interleukin-6 (IL-6; *n* =2796), tumor necrosis factor-α soluble receptor 1 (sTNF-R1; *n* =998), soluble intercellular adhesion molecule-1 (sICAM-1; *n* =1192) and soluble E-selectin (sE-selectin; *n* =998) were measured using the quantitative sandwich enzyme immunoassay technique of enzyme-linked immunosorbent assay assays (Quantikine HS Human IL-6 Immunoassay, Quantikine Human sTNF-RI Immunoassay, Parameter Human sICAM-1 Immunoassay, Parameter Human sE-Selectin Immunoassay, respectively; R&D Systems, Minneapolis, MN, USA). Importantly, significant differences in sICAM-1 were not evaluated in all ethnic groups, as a previous report[29] indicates that a common single-nucleotide polymorphism of sICAM-1 in Black individuals results in an underestimation of sICAM-1.

Statistical analysis

All analyses were conducted using SAS (version 9.2, SAS Institute, Inc., Cary, NC, USA). Body mass index was calculated as weight in kg divided by height in (m) squared. Baseline characteristics are presented as means (s.d.) for continuous variables and frequencies (%) for categorical variables and stratified by ethnic group. Levels of biomarkers with skewed distributions were log-transformed before analysis, and results were back-transformed and presented as geometric means. Generalized linear regression analysis further evaluated levels of biomarkers and plasma phospholipid fatty acids according to the ethnic group, adjusting for potential confounding factors known to affect these measures, including age, gender, field center, socioeconomic status with highest education level attained, smoking, physical activity, energy intake, non-fried fish intake, body mass index, high-density lipoprotein –cholesterol, low-density lipoprotein– cholesterol, triglycerides and diagnosed diabetes. MESA dietary data for fish intake are more fully detailed by Chung *et al*.[30] Interaction terms were included in the models to determine whether ethnic group modified

the association between plasma phospholipid fatty acids and biomarkers adjusting for potential confounding factors. Statistical tests were considered significant at $P \leq 0.01$.

RESULTS

Baseline characteristics are shown in Table 1. Overall, the cohort was made up of 25.4% White, 24.7% Black, 24.9% Hispanic and 25.0% Chinese participants. Average age was 62.1±10.2 years, over 50% was female, and the majority of adults had greater than a high school education.

Markers of inflammation and endothelial activation were significantly different among ethnicities after adjusting for confounding factors including body mass index (Table 2). Generally, Chinese adults had the lowest mean levels of these markers compared with those of other ethnicities, except for sE-selectin. No other differences were observed among other ethnic groups for inflammatory markers hsCRP or IL-6. sE-selectin levels did not differ significantly among study participants. Differences in sICAM-1 in Black individuals could not be evaluated and is discussed in the limitations section.

Significant differences in plasma phospholipid LC-PUFA composition were found across ethnicities after adjusting for potential confounding factors (Table 3). Chinese adults had the highest relative levels of plasma n-3 fatty acids EPA and DHA, as well as n-6 LA levels, but the lowest levels of GLA (18:3, n-6), dihomo-γ-linolenic (DGLA; 20:3, n-6) and AA (20:4, n-6) compared with other ethnicities. To evaluate whether differences in EPA and DHA levels were primarily a function of non-fried fish intake and fish oil supplementation, these covariates were included in an additional statistical model. Differences in plasma EPA levels were found to be dependent on non-fried fish intake and fish oil supplementation, as no significant race differences were observed following adjustment. Likewise, differences in DHA levels were attenuated, and only found to be higher in Chinese compared with Hispanics ($P = 0.02$) after adjustment for non-fried fish intake and fish oil supplementation. Hispanics initially showed the lowest levels of plasma EPA and DHA, but again no statistical significance was shown following further adjustment for confounding factors. Notably, the highest levels of DGLA were found in Hispanic participants, whereas the highest levels of plasma GLA (18:3, n-6) were observed among White participants. Finally, Black participants had the highest levels of plasma AA, but, along with Chinese adults, the lowest levels of GLA (18:3, n-6) and DGLA (20:3, n-6). No significant differences were observed in plasma α-LA (18:3, n-3).

Though significant associations were observed between phospholipid LC-PUFAs and biomarkers (Table 4), ethnicity did not modify these associations (all $P_{interaction} > 0.05$). The highest levels of GLA and DGLA corresponded with the highest levels of IL-6, and either sTNFR-1 or hsCRP. Levels of GLA and DGLA were also positively associated with higher concentrations of sE-selectin and sICAM-1, respectively. In contrast, significant inverse associations were found between IL-6 and EPA, as well as DHA. In addition, EPA was inversely associated with sTNF-R1, and plasma levels of the n-6 fatty acid LA were inversely associated with hsCRP and sE-selectin.

DISCUSSION

In this cross-sectional analysis, significant differences among ethnicities were observed in plasma phospholipid LC-PUFA composition, as well as markers of inflammation and endothelial activation. Contrary to our hypothesis, the associations between LC-PUFAs and markers of inflammation and endothelial activation were not modified by ethnicity.

Plasma phospholipid LC-PUFA composition differs among ethnicities

The current study is the largest to examine plasma LC-PUFA composition of White, Black, Hispanic and Chinese adults, though previous investigators have reported differences in plasma LC-PUFAs in other ethnically diverse populations.[31 – 33] Nogi *et al*.[32] observed that Japanese individuals had three-fold higher plasma EPA levels as well as two-fold higher plasma DHA levels compared with Mongolian individuals, with levels for Korean individuals falling between them. Van Eijsden *et al*.[33] found significant differences in n-3 and n-6 LC-PUFAs among Dutch, Turkish, Moroccan, Surinamese, Ghanaian and Antilean participants. Finally, Young *et al*.[31] found that Canadian Inuit had significantly increased levels of plasma phospholipid EPA and remarkably lower levels of DGLA, AA and total n-6 fatty acids compared with non-Inuit in the same region. Notably, the variations in fatty acid composition were found to be independent of diet, despite the large inter-group variation in fish and marine fatty acid dietary intakes. In contrast, no differences in LC-PUFA levels were observed between Whites and Hispanics in a study by Haffner *et al*.,[34] though limited sample size may have contributed to the null findings. The origin(s) for variations in LC-PUFA composition among ethnicities is not entirely clear, but a number of genetic and environmental factors have been found.

It is currently known that plasma phospholipid and membrane fatty acids partially reflect dietary intake, particularly the fatty acids associated with fish (EPA and DHA).[30,35] Differences in fish consumption have been noted among ethnicities in the MESA population,[36,37] and EPA + DHA levels were found to correlate with non-fried fish consumption in a sub-cohort of MESA participants.[30] Adjustments were therefore made in our statistical models for non-fried fish intake and fish oil supplementation. Following this adjustment, plasma EPA and DHA levels were not significantly different among ethnicities, with one notable exception: plasma DHA levels were higher in Chinese compared with Hispanic participants. Though fish/fish oil intake largely accounted for the differences in plasma EPA and DHA among ethnicities, it is likely that other factors such as fatty acid bioavailability and/or metabolism contribute to variations in plasma n-6 fatty acid and DHA levels among ethnic groups, in agreement with Chung *et al*.[30]

The metabolism of DHA and n-6 LC-PUFAs involves a multitude of pathways and enzymes, the Δ5 and Δ6 desaturases and elongases among them.[38] In addition, LC-PUFAs are substrates for eicosanoid generation, including the prostaglandins, prostacyclins, leukotrienes and lipoxins, as well as the newly discovered ‘non-classic’ eicosanoids including the resolvins, protectins and maresins. Evidence has suggested that gene polymorphisms of these metabolic enzymes may contribute to differences in LC-PUFA composition.[39 – 41] Observed in the InCHIANTI study, cluster polymorphisms encoding Δ6 desaturase (*FADS* gene) partially accounted for the variance in plasma AA levels,[39] and the

ELOVL2 gene was found to be involved in the homeostasis of longer chain n-3 fatty acids. The Genetics of Coronary Artery Disease in Alaska Natives study revealed that genetic variations in *APOJ*, *LPL* and *TNFRSF10B* genes significantly influenced plasma fatty acid distribution.[40] Ultimately, future MESA studies may provide evidence as to whether such distinct gene polymorphisms contribute to the differences in LC-PUFA composition observed here.

Inflammatory and endothelial activation markers differ across ethnicities

In agreement with Stowe *et al*.,[16] but in contrast to other studies,[18,21] we did not observe higher levels of hsCRP in Blacks compared with Whites or Hispanics after adjusting for confounders. However, we did find that hsCRP was lower in Chinese compared with Whites, Blacks and Hispanics, as found by a number of previous studies.[18,19,21] In general, Chinese participants showed the lowest levels of endothelial activation and inflammatory markers among the ethnic groups studied here. As high levels of these biomarkers are widely considered risk factors for CVD, previous findings and ours may partially explain the lower incidence of CVD in individuals of Chinese or Asian descent.[42]

Strengths and limitations

The present study avoided the inherent problems of relying on dietary questionnaires by directly measuring plasma phospholipid levels of fatty acids. Further, plasma phospholipid fatty acids are considered a reflection of membrane fatty acids–thus, observed differences are inclusive of the multitude of metabolic processes associated with fatty acids, which is not the case with dietary fatty acid intake data.

The cross-sectional study design limits our ability to determine the temporal relation between levels of LC-PUFAs and selected biomarkers. Additionally, plasma fatty acids, sTNF-R1, IL-6, sICAM-1 and sE-selectin were only measured in a subset of individuals enrolled in the MESA study; consequently, the study may have been underpowered to find true associations in some instances. Finally, we adjusted for several confounding factors in our statistical model; however, it is possible that residual confounders remain.

CONCLUSIONS

It was found that the inverse associations of certain n-3 and n-6 LC-PUFAs with inflammatory/endothelial markers are not based on ethnicity, and benefits of these LC-PUFAs would therefore be expected to be pan-ethnic. Dietary fish and fish oil supplementation largely accounted for differences in phospholipid EPA +DHA levels among ethnicities. Future studies examining gene variants in fatty acid metabolism may provide the basis for the observed race/ethnicity based differences in plasma DHA and n-6 LC-PUFA composition. Future longitudinal studies will better define the consequences of LC-PUFA composition variation and whether certain patterns, that is, high levels of DGLA and low levels of EPA/DHA found here, contribute to long-term chronic inflammation and associated health outcomes in MESA participants.

Acknowledgments

We thank the other investigators, staff and participants of the MESA study for their valuable contributions. A full list of participating MESA investigators and institutions can be found at http://www.mesa-nhlbi.org. This research was supported by the following contracts, N01-HC-95159 through N01-HC-95169 from the National Heart, Lung and Blood Institute.

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Table 1

Baseline characteristics of MESA participants, *n* =2846

Characteristic	All (*n* =2846)	White (*n* =722)	Black (*n* =703)	Hispanic (*n* =709)	Chinese (*n* =712)
Age, years (s.d.)	62.1 (10.2)	62.0 (10.5)	62.0 (9.8)	61.5 (10.1)	62.8 (10.4)
Gender, n *(%)*					
Female	1517 (53.3)	381 (52.8)	385 (54.8)	382 (53.9)	369 (51.8)
Education, n *(%)*					
<HS	619 (21.7)	32 (4.4)	89 (12.8)	324 (45.7)	172 (24.2)
HS	512 (18.0)	125 (17.4)	123 (17.6)	143 (20.2)	120 (16.9)
Some college	794 (27.9)	206 (28.6)	268 (38.4)	177 (25.0)	140 (19.7)
College, 4 year	473 (16.6)	170 (23.6)	107 (15.3)	35 (4.9)	160 (22.5)
College, 5+ year	450 (15.8)	187 (26.0)	111 (15.9)	30 (4.2)	119 (16.7)
Current smoker, *n* (%)	390 (13.7)	113 (15.7)	134 (19.1)	105 (14.8)	38 (5.3)
BMI, kg/m^2 (s.d.)	27.9 (5.5)	27.8 (5.3)	30.1 (5.8)	29.6 (5.0)	24.0 (3.3)
Physical activity, MET-min/week (s.d.)	1454 (2145)	1693 (2391)	1730 (2509)	1279 (1983)	1114 (1502)
Fish oil supplements, *n* (%)	119 (4.2)	21 (2.9)	17 (2.4)	19 (2.7)	59 (8.3)
Energy intake, kcal (s.d.)	1622 (814)	1693 (708)	1724 (946)	1769 (917)	1329 (582)
Non-fried fish intake, servings/day	0.13 (0.19)	0.11 (0.15)	0.13 (0.22)	0.07 (0.14)	0.20 (0.21)

Abbreviations: BMI, body mass index; HS, high school; MESA, Multi-Ethnic Study of Atherosclerosis; MET, metabolic equivalent.

Eur J Clin Nutr. Author manuscript; available in PMC 2014 July 15.

Table 2

Geometric mean levels[a] of biomarkers for inflammation and endothelial activation by ethnicity: MESA, *n* =2846

Marker	*N*	White	Black	Hispanic	Chinese
Inflammation					
HsCRP (pg/ml)	2846	1.87[c] (1.72, 2.04)	2.07[c] (1.89, 2.28)	1.89[c] (1.71, 2.09)	1.14[bhw] (1.02, 1.27)
IL-6 (pg/ml)	2796	1.15[c] (1.10, 1.21)	1.26[c] (1.19, 1.33)	1.25[c] (1.18, 1.33)	0.99[bhw] (0.93, 1.05)
sTNF-R1 (pg/ml)	998	1.34[bch] (1.31, 1.38)	1.18[cw] (1.13, 1.23)	1.19[cw] (1.14, 1.24)	1.05[bhw] (0.99, 1.12)
Endothelial activation					
sE-selectin (pg/ml)	998	46.92 (44.8, 49.2)	51.31 (47.8, 55.1)	52.66 (47.9, 55.6)	50.31 (45.2, 56.0)
sICAM-1 (pg/ml)	1192	284.25[c] (277.9, 290.7)	N/A[b]	280.87[c] (271.5, 290.5)	240.36[hw] (229.3, 250.9)

Abbreviations: b, Black; c, Chinese; h, Hispanic; hsCRP, high-sensitivity C-reactive protein; MESA, Multi-Ethnic Study of Atherosclerosis; N/A, not applicable; sE-selectin, soluble E-selectin; sTNF-R1, tumor necrosis factor-α soluble receptor 1; sICAM, soluble intercellular adhesion molecule-1; w, White. Difference among groups ($P \leq 0.01$): b, c, h, w, 95% confidence intervals ( ).

[a] Adjusted for age, sex, education, field center, smoking, energy intake, physical activity, BMI, HDL, LDL, triglycerides, and diabetes.

[b] Quantification of sICAM-1 in Black individuals cannot be evaluated (see Materials and Methods, section 2.4).

Table 3

Mean levels[a] of individual plasma phospholipid fatty acids (%) by ethnic groups: MESA, *n* =2846

Fatty acid[b] (%)	White (*n* =722)	Black (*n* =703)	Hispanic (*n* =709)	Chinese (*n* =712)
LA 18:2, n-6	20.93 bch	19.95 chw	21.97 bcw	22.95 bhw
ALA 18:3, n-3	0.18	0.17	0.18	0.17
GLA 18:3, n-6	0.120 bch	0.107 cw	0.107 cw	0.097 bhw
DGLA 20:3, n-6	3.39 bc	3.05 hw	3.48 bc	2.92 hw
AA 20:4, n-6	12.04 bch	13.53 chw	11.56 bcw	10.84 bhw
EPA 20:5, n-3				
Model 1[a]	0.99 ch	0.95 ch	0.75 bcw	1.20 bhw
Model 2[c]	1.68	1.06	1.12	1.81
DHA 22:6, n-3				
Model 1[a]	3.83 bch	4.51 chw	3.58 bcw	4.95 bhw
Model 2[c]	4.97	5.35	4.37 c	5.56 h

Abbreviations: AA, arachidonic acid; ALA, α-linolenic acid; b, Black; c, Chinese; DGLA, dihomo-γ-linolenic acid; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; GLA, γ-linolenic acid; h, Hispanic; HDL, high-density lipoprotein; LA, linoleic acid; LDL, low-density lipoprotein; MESA, Multi-Ethnic Study of Atherosclerosis. Difference observed between groups ($P_{diff} \leq 0.01$): b, c, h, w.

[a] Adjusted for age, sex, education, field center, smoking, energy intake, physical activity, BMI, HDL, LDL, triglycerides and diabetes.

[b] LA, ALA, GLA, DGLA, AA, EPA, DHA.

[c] EPA and DHA levels were further adjusted for non-fried fish intake and fish oil supplements.

Table 4

Mean[a] levels of biomarkers of inflammation and endothelial function across tertiles of phospholipid fatty acids, MESA, *n* =2846

Fatty acids[b] Biomarkers[c]	Biomarker levels (pg/ml) expressed by phospholipid fatty acid tertiles			P_{trend}	% difference T1:T3
	1	2	3		
LA(18:2, n-6)					
hsCRP	1.89	1.66	1.66	0.01	−12.2
Eselectin	50.9	51.8	46.9	0.02	−7.9
GLA (18:3, n-6)					
IL-6	1.10	1.22	1.20	0.001	+9.1
sTNF-R1	1.16	1.22	1.23	0.01	+6.0
Eselectin	47.6	49.6	53.3	0.01	+12.0
DGLA (20:3, n-6)					
hsCRP	1.42	1.68	2.21	<0.001	+55.6
IL-6	1.11	1.15	1.24	0.006	1.24
sICAM-1	260.4	262.1	279.4	0.001	11.7
EPA (20:5, n-3)					
IL-6	1.21	1.17	1.12	0.02	−7.4
sTNF-R1	1.25	1.18	1.16	0.002	−7.2
DHA (22:6, n-3)					
IL-6	1.24	1.20	1.06	<0.001	−14.5

Abbreviations: AA, arachidonic acid; ALA, α-linolenic acid; DHA =docosahexaenoic acid; DGLA, dihomo-γ-linolenic acid; EPA, eicosapentaenoic acid; GLA, γ-linolenic acid; hsCRP, high-sensitivity C-reactive protein; IL, interleukin; LA, linoleic acid; MESA, Multi-Ethnic Study of Atherosclerosis; sTNF-R1, tumor necrosis factor-α soluble receptor 1; sICAM, soluble intercellular adhesion molecule-1. Only significant associations are reported.

[a] Adjusted for age, sex, education, field center, smoking, energy intake, physical activity, BMI, HDL, LDL, triglycerides, and diabetes.

[b] LA, ALA, GLA, DGLA, AA, EPA, DHA.

[c] Sample size for biomarkers hsCRP, *n* =2846; IL-6, *n* =2796; sTNF-R1, *n* =998; sE-selectin, *n* =998; sICAM-1, *n* =1192.