Adipose tissue α-linolenic acid is inversely associated with insulin resistance in adults[1]

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ABSTRACT

Background: There is emerging evidence of the beneficial effects of n–3 (ω-3) fatty acids (FAs) on cardiometabolic risk factors. Nevertheless, not much is known about the association between adipose tissue α-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) and insulin resistance.

Objective: We determined the association between adipose tissue n–3 FAs (total n–3 FAs, ALA, and EPA plus DHA) and insulin resistance in healthy adults.

Design: In this cross-sectional study, multivariable analyses were used to assess the association between adipose tissue FAs (ALA, EPA plus DHA, and total n–3 FAs) and the homeostasis model assessment of insulin resistance (HOMA-IR) in a subset of adult participants ($n = 716$; mean age: 58 y) from the Adventist Health Study-2 (AHS-2) cohort.

Results: Compared with the lowest tertile, the third tertile ($\beta = -0.13$; 95% CI: −0.24, −0.01) of adipose tissue ALA was inversely associated with the HOMA-IR. When stratified by waist circumference, ALA continued to be inversely associated [third tertile: $\beta = -0.17$ (95% CI: −0.31, −0.02)] with the HOMA-IR in subjects with a waist circumference ≤88 cm in women or ≤102 cm in men but not in those with a larger waist circumference. No significant association was noted between adipose tissue EPA plus DHA and HOMA-IR.

Conclusions: Higher adipose tissue ALA was inversely associated with insulin resistance in this cohort of healthy adult men and women. This finding appears to be more pronounced in individuals with a normal waist circumference. *Am J Clin Nutr* 2016;103:1105–10.

Keywords: adiposity, biomarker, insulin resistance, n–3 fatty acids, waist circumference

INTRODUCTION

Insulin resistance is an important component and independent predictor of cardiometabolic risk, and it is associated with increased risk of developing cardiovascular disease and type 2 diabetes (T2D)[2] (1–3). Abdominal obesity is a substantial risk factor for cardiometabolic disease including insulin resistance (2, 4–6). Increased n–3 fatty acid (FA) intake can lower insulin resistance and cardiometabolic risk, thereby reducing the progression to cardiovascular disease or T2D (7, 8). However, the role of FAs in developing insulin resistance may be influenced by adiposity or BMI (in kg/m^2) (9, 10). There has also been some indication that an individual's metabolic response to FAs may depend on the person's adiposity state (11, 12).

The mechanisms on the role of n–3 FAs on insulin resistance have been speculative (4, 5, 8, 13–15), and evidence from human studies has remained unclear and weak. Most randomized clinical trials (16–20) have reported no effect of EPA and DHA on insulin resistance, and the findings of observational studies have been mixed (9, 21–23). In addition, EPA and DHA are not associated with reduced T2D risk (24).

With respect to α-linolenic acid (ALA), there has been limited evidence from cohort studies to suggest that ALA is associated with a lower risk of T2D (24). In terms of insulin resistance and ALA, the evidence has also been sparse. Two cross-sectional studies that showed an inverse association between ALA intake and insulin resistance either did not adjust for potential confounders such as energy intake and physical activity (21) or used a diet-history questionnaire (10), which is a tool that is imprecise and is known for underreporting intake (10, 25, 26).

Biomarkers of ALA may be more useful, but to our knowledge, there has only been one previous study, in elderly male subjects, that looked at adipose tissue ALA and insulin resistance (9). Adipose n–3 FAs are known to reflect intake for 0.5–3 y and can help overcome the bias that is inherent with self-reported intake (9, 27–32). There is a need for more studies to examine the association between adipose tissue n–3 FAs and insulin resistance that include both men and women of a wider age range. Thus, the purpose of this study was to examine the association between adipose tissue n–3 FAs (total n–3 FAs, ALA, and EPA plus DHA) and insulin resistance estimated with the use of the HOMA-IR in healthy adult men and women in the AHS-2 (Adventist Health Study-2) cohort.

METHODS

This study was a cross-sectional analysis of subjects enrolled in the calibration substudy, which is nested within the AHS-2 cohort of 96,000 church members, who were residing in Canada

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[2] Abbreviations used: AHS-2, Adventist Health Study-2; ALA, α-linolenic acid; CRP, C-reactive protein; FA, fatty acid; T2D, type 2 diabetes.

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and the United States (33). Between 2001 and 2007, individuals were enrolled in the AHS-2 if they were English proficient, ≥30 y of age, and completed a comprehensive lifestyle questionnaire. Substudy subjects (n = 1011) were randomly selected from the parent cohort (33). Black subjects were intentionally oversampled for the substudy with the intent of increasing their proportion to one-half of the group (26). There was no significant difference between cohort and substudy subjects in terms of demographic variables, BMI, and dietary patterns (26, 34).

Between 2003 and 2007, substudy subjects participated in clinics during which anthropometric data, adipose tissue biopsies, fasting blood, and finger-prick samples were collected (35, 36). In addition, over a period of 10 mo, subjects provided six 24-h dietary recalls, which were obtained by trained dietitians with the use of Nutrition Data System for Research software 5.03 (The Nutrition Coordinating Center, University of Minnesota) (26). Nutrient compositions were based on the Nutrition Data System for Research 2008 database (http://www.ncc.umn.edu/products/database.html, The Nutrition Coordinating Center, University of Minnesota). Energy intake was estimated from 24-h dietary recalls.

Anthropometric measurements, including height, weight, and waist circumference, were collected during the clinic visit (36). Three measurements were made of height to ≤0.6 cm with the use of a Seca 214 Portable Height Rod (Seca) and of weight to ≤0.1 kg with the use of a Tanita BF-350 scale (Tanita). Waist circumference was measured 3 times at 2.5 cm above the navel with the use of an anthropometric tape from which the mean waist circumference was calculated. For the analysis, categories of waist circumference were defined on the basis of the diagnostic criteria for abdominal obesity with a normal waist circumference being equivalent to ≤88 cm in women or ≤102 cm in men and abdominal obesity being equivalent to >88 cm in women or >102 cm in men (6). Demographic data (e.g., age, race, and sex) and physical activity data were obtained from the baseline lifestyle questionnaire. For the analysis, categories of physical activity were defined as 0, >0 to <0.45, and ≥0.45 h/wk of vigorous activity. The Institutional Review Board of Loma Linda University approved the AHS-2 cohort and calibration studies, respectively.

Biochemical assessment

Adipose tissue biopsies were extracted from the upper buttocks with the use of the squeeze technique (35). An Agilent Technologies 5890A series II gas chromatograph (Agilent Technologies) was used to separate and quantify methyl esters. Gas chromatography was also used to estimate adipose tissue FA percentages from the biopsies. FA percentages that were measured in the adipose tissue included ALA (18:3), EPA (20:5), DHA (22:6), lauric acid (12:0), myristic acid (14:0), pentadecanoic acid (15:0), palmitic acid (16:0), and stearic acid (18:0). A pooled serum sample was analyzed with each batch of samples. CVs from this pooled sample were as follows: 12:0, 13%; 14:0, 10.5%; 15:0, 12%; 16:0, 1.6%; 18:0, 2.6%; 18:3, 0.7%; 20:5, 3.2%; and 22:6, 2.2%.

Deattenuated correlations between dietary ALA (24-h dietary recalls) and adipose tissue ALA were 0.66 and 0.67 in nonblack and black subjects, respectively (unpublished data). Deattenuated correlations were 0.20 and 0.28 for EPA and 0.38 and 0.54 for DHA in nonblack and black subjects, respectively (unpublished data).

High sensitivity C-reactive protein (CRP) and insulin were measured from the fasting blood samples collected at the field clinics. Serum was separated from the cells within 30 min of collection, placed on wet ice, and shipped to the central study laboratory in Loma Linda, CA, for additional processing. On arrival, aliquot of 0.5 mL were immediately stored in liquid nitrogen at −190°C until analysis. Adipose tissue aspirates were also stored on liquid nitrogen. Determinations of CRP concentrations were made in duplicate samples with the use of latex particle enhanced immunoturbidimetric assay kits (Pointe Scientific Inc.). The minimum detectable concentration was 0.1 mg/L, and the intra-assay CV and interassay CV for CRP were 8.5%, and 10.5%, respectively. Fasting insulin was assessed with the use of an Elecsys Insulin assay (Roche Diagnostics), which used 2 monoclonal insulin-specific antibodies. Fasting glucose was measured with the use of the Cholestech LDX System (Cholestech Corporation) (36).

Insulin resistance

Insulin resistance was calculated with the use of the homeostasis model assessment calculator 2.2.2 (The Oxford Center for Diabetes Endocrinology and Metabolism, Oxford, United Kingdom) (37). Fasting glucose and insulin values were inputted into the Excel version of the homeostasis model assessment calculator 2 (37). The HOMA method has previously been used to measure insulin resistance in >150 epidemiologic studies (38). Furthermore, the correlation between the more-sensitive euglycemic clamp and the HOMA method ranges from 0.73 to 0.88 (38).

Statistics

As per the AHS-2 research protocol, we excluded subjects from the analysis if they consumed <500 kcal/d (2093 kJ/d) or >4500 kcal/d (188,833 kJ/d) (n = 9) because these extremes are implausible, and the data may have been unreliable. Subjects were excluded from the analysis if they indicated that they were currently smoking at the time of recruitment (n = 8). Subjects were also excluded for improbable or extreme variable values (n = 13). Furthermore, the exclusion of subjects with missing HOMA-IR values (n = 121) or adipose tissue n–3 FA values (n = 44) reduced the sample size to 823 subjects. This sample was used for the crude analyses. Spearman correlations were ascertained between the HOMA-IR and adipose tissue ALA, EPA plus DHA, and total n–3 FAs. After the exclusion of subjects with missing covariates (total: n = 107 total; race: n = 37; sex: n = 37; age: n = 4; adipose tissue SFA: n = 42; physical activity: n = 99; waist circumference: n = 41; and CRP: n = 67), a final analytic sample of 716 subjects (mean: 34%; black: 41%) was available for the multivariable analyses. Descriptive data were represented as either means ± SDs, geometric means with 95% CIs for log-transformed variables, or medians with IQRs (representing the range of data between first and third quartiles) for skewed variables. A difference in characteristics between men and women was assessed with the use of Wilcoxon 2-sample tests comparing means and median 2-sample tests for comparing medians.

The dependent variable HOMA-IR was log transformed to achieve an approximate normality. The independent variables

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included adipose tissue ALA, adipose tissue EPA plus DHA, and total adipose tissue n–3 FAs. The independent variables were analyzed as continuous variables, and categorical variables (tertiles in the cases of ALA and total n–3 FAs and dichotomous with the median as the cutoff for EPA plus DHA). The first, second, and third tertiles of adipose tissue ALA were ≤1.15%, >1.15 to 1.45%, and >1.45%, respectively. The first, second, and third tertiles of adipose tissue total n–3 FAs were ≤1.37%, >1.37 to 1.72%, and >1.72%, respectively. The median cutoff of adipose tissue EPA plus DHA was 0.20%.

Multivariable analyses were done to assess the association between dependent and independent variables. Explanatory variables that were considered for adjustment in the multivariable regression analyses included age, sex, race, energy intake, adipose tissue SFA [which was a combination of lauric acid (12:0), myristic acid (14:0), pentadecanoic acid (15:0), palmitic acid (16:0), and stearic acid (18:0)], physical activity, waist circumference, and mean CRP. Mean CRP was log transformed to improve the distribution of the variable. Variables were considered for adjustment on the basis of known biological associations with either independent or dependent variables or statistical associations with independent and dependent variables.

Model 1 was used for the regression analysis and included age, sex, race, and energy intake as covariates. Model 2 included model 1 covariates and physical activity, adipose tissue SFA, and CRP. Model 3 included model 2 covariates and waist circumference. Visceral adiposity, which can be estimated by measuring waist circumference, is a more-sensitive indicator of insulin resistance than BMI is (6). Education level and current alcohol use were considered as possible covariates; however, they did not contribute to confounding in this sample and were not included in the final model.

A stratified analysis was done by waist circumference with a cutoff for abdominal obesity that was equivalent to >88 cm in women or >102 cm in men (6). In addition, because a previous analysis of the association between adipose tissue FA and insulin resistance was not done in female subjects, sensitivity analyses were done to assess the measure of the association in men and women. Assumptions were not violated after regression diagnostics. The statistical analysis was done with the use of SAS 9.4 software (SAS Institute Inc.).

RESULTS

The mean age of the study subjects was 58 y (**Table 1**). Caloric intake, waist circumference, glucose, insulin, and HOMA-IR were significantly higher in men than in women. The medians (IQRs) of adipose tissue ALA and EPA plus DHA in the sample were 1.28% (0.49) and 0.20% (0.17), respectively, and did not differ between men and women. CRP was significantly lower in men. Additional descriptive data on the subjects are presented in Table 1. Crude correlations (n = 823) between the HOMA-IR and adipose tissue ALA, EPA plus DHA, and total n–3 FAs were −0.31 ($P < 0.0001$), 0.07 ($P = 0.0392$), and −0.26 ($P < 0.0001$), respectively.

We showed an inverse linear association between adipose tissue ALA and the HOMA-IR after adjustment for age, sex, race, and energy intake (model 1) (**Table 2**). After additional adjustment for physical activity, adipose tissue SFA, CRP, and waist circumference (model 3), the magnitude of the association was reduced, but it remained significant (Table 2).

When adipose tissue ALA was split into tertiles, a dose-dependent inverse relation appeared between ALA and the HOMA-IR (**Table 3**). We showed a significant inverse association with the HOMA-IR for the third tertile of adipose tissue ALA compared with the first (reference) and second tertiles after adjustment for the full model (model 3).

We showed no significant association between adipose tissue EPA plus DHA and the HOMA-IR (Tables 2 and 3). The association between adipose tissue total n–3 and the HOMA-IR was inverse and of a lesser magnitude than our findings of the association between adipose tissue ALA and the HOMA-IR.

The stratified analysis by waist circumference revealed an inverse association between adipose tissue ALA and the HOMA-IR although this association was significant only for subjects with both a normal waist circumference (≤88 cm in women or ≤102 cm in

TABLE 1
Characteristics of participants in the AHS-2 calibration study[1]

Characteristics	All (n = 716)	Men (n = 242)	Women (n = 474)
Age, y	58 ± 13[2]	60 ± 13***	57 ± 13
Caloric intake/d, kJ/d	6690 ± 2159	7640 ± 2301***	6192 ± 1908
Waist circumference, cm	93.07 ± 15.95	98.40 ± 13.84***	90.35 ± 16.31
Glucose, mg/dL	94.68 ± 26.64	96.86 ± 20.32***	93.57 ± 29.30
Insulin, μU/mL	9.76 ± 7.67	10.99 ± 9.00***	9.13 ± 6.83
HOMA-IR	1.01 (0.96, 1.06)[3]	1.12 (1.02, 1.22)***	0.96 (0.90, 1.02)
Adipose tissue ALA, %	1.28 (0.49)[4]	1.32 (0.50)	1.26 (0.47)
Adipose tissue EPA plus DHA, %	0.20 (0.17)	0.20 (0.16)	0.20 (0.17)
Adipose tissue total n–3 FAs, %	1.52 (0.59)	1.53 (0.59)	1.52 (0.59)
Adipose tissue SFA, %	26.28 (4.14)[5]	26.81 (3.84)***	26.01 (4.26)
CRP, mg/dL	1.85 (1.65, 2.08)	1.63 (1.34, 1.97)***	1.98 (1.72, 2.29)

[1]Differences between men and women were assessed with the use of the Wilcoxon 2-sample test to compare means and with the use of median 2-sample tests for comparing medians. ***Significantly different from women, $P < 0.05$. AHS-2, Adventist Health Study-2; ALA, α-linolenic acid; CRP, high-sensitivity C-reactive protein; FA, fatty acid.
[2]Mean ± SD (all such values).
[3]Geometric mean; 95% CI in parentheses (all such values)
[4]Median; IQR in parentheses (all such values for skewed distributions of adipose tissue n−3 FAs).
[5]Mean ± SD; IQR in parentheses (all such values).

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TABLE 2
Association between adipose tissue n–3 FAs and insulin resistance in the AHS-2 calibration study (n = 716)[1]

FA	Model 1	Model 2	Model 3
ALA	−0.40 (−0.50, −0.29)*	−0.28 (−0.40, −0.17)*	−0.13 (−0.23, −0.02)***
EPA plus DHA	−0.12 (−0.44, 0.20)	−0.17 (−0.48, 0.14)	0.01 (−0.28, 0.25)
Total n–3 FAs	−0.34 (−0.44, −0.25)*	−0.24 (−0.34, −0.14)*	−0.10 (−0.19, −0.01)***

[1]All values are β coefficients; 95% CIs in parentheses. Associations were determined with the use of a multivariable regression analysis. Model 1 was adjusted for age, sex, race, and energy intake. Model 2 was adjusted as for model 1 and for physical activity, adipose tissue SFA, and high-sensitivity C-reactive protein. Model 3 was adjusted as for model 2 and for waist circumference. *,***Significant association between insulin resistance and adipose tissue FAs: *$P < 0.0001$, ***$P < 0.05$. AHS-2, Adventist Health Study-2; ALA, α-linolenic acid; FA, fatty acid.

men) and within the highest tertile of adipose tissue ALA after adjustment for model 2 covariates (β = −0.17; 95% CI: −0.31, −0.02).

DISCUSSION

In this large cross-sectional study of adult men and women, an inverse association was observed between adipose tissue ALA and insulin resistance assessed by homeostasis model assessment. This association remained even after adjustment for various factors including inflammation and adiposity. Our findings corroborate the results of one other study that showed an inverse association between dietary ALA and insulin resistance (10). Previous observations related to adipose tissue ALA in elderly men (9) were also apparent in our study, which was inclusive of both adult men and women with a wider age range. Although sex differences were not considered, there was a nonsignificant inverse association, with similar point estimates, between adipose tissue ALA and insulin resistance for both men and women. We did not observe any association between EPA plus DHA and insulin resistance. The mean adipose tissue ALA (1.34%) of our study subjects was ∼20% higher than that reported by others (9, 28, 39, 40) and may have partly explained the significant protective effect of adipose ALA on insulin resistance. However, intake of EPA and DHA in our cohort was lower, which resulted in lower amounts of these FAs in adipose tissue (0.25%) than in other cohorts (0.3–0.45%) that typically consume more fatty fish (9, 31, 40).

These differences in the proportion of adipose tissue ALA, EPA, and DHA compared with those reported by other researchers may have been related to dietary intake differences. Mean intakes of ALA were 1.7 and 1.5 g/d (reported in white and black subjects, respectively) on the basis of 24-h dietary recalls collected from a sample of the AHS-2 cohort (26). Comparatively, Muramatsu et al. (10), whose findings were similar to ours, reported mean intake of 1.9 g ALA/d. In a study that reported lower intakes (0.73% of energy) of ALA than in our study (0.94% of energy), there was no association between ALA and insulin resistance (15). There may be a certain threshold in ALA intake or deposition in adipose tissue before it influences insulin resistance.

Intake from the diet plus supplements was 29 and 70 mg EPA/d and 46 and 130 mg DHA/d in AHS-2 white and black subjects, respectively (26), which were lower than US mean intake (72 mg/d) of EPA but as high or higher than US mean intake (41 mg/d) for DHA (41). With regard to EPA plus DHA, the amount of intake may not influence insulin resistance. Even in studies that reported a substantially higher intake of EPA plus DHA than in our study,

TABLE 3
Association between categories of adipose tissue n–3 FAs and insulin resistance in the AHS-2 calibration study (n = 716)[1]

Category of FA	FA category,[2] %	Model 1	Model 2	Model 3
ALA				
First tertile	0.97	Reference	Reference	Reference
Second tertile	1.28	−0.20 (−0.32, −0.08)[3],***	−0.12 (−0.24, −0.008)***	−0.05 (−0.15, 0.05)
Third tertile	1.73	−0.44 (−0.56, −0.32)*	−0.30 (−0.43, −0.18)*	−0.13 (−0.24, −0.01)***
EPA plus DHA				
Below median	0.14	Reference	Reference	Reference
Above median	0.31	−0.03 (−0.13, 0.07)	−0.04 (−0.14, 0.05)	−0.01 (−0.10, 0.07)
Total n–3 FAs				
First tertile	1.18	Reference	Reference	Reference
Second tertile	1.54	−0.17 (−0.29, −0.05)***	−0.08 (−0.19, 0.04)	−0.03 (−0.14, 0.07)
Third tertile	2.04	−0.38 (−0.50, −0.26)*	−0.25 (−0.38, −0.12)*	−0.08 (−0.20, 0.03)

[1]Associations were determined with the use of a multivariable regression analysis. Model 1 was adjusted for age, sex, race, and energy intake. Model 2 was adjusted as for model 1 and for physical activity, adipose tissue SFA, and high-sensitivity C-reactive protein. Model 3 was adjusted as for model 2 and for waist circumference. *,***Significant association between insulin resistance and adipose tissue FAs: *$P < 0.0001$, ***$P < 0.05$. AHS-2, Adventist Health Study-2; ALA, α-linolenic acid; FA, fatty acid.

[2]All values are medians.

[3]β coefficient; 95% CI in parentheses (all such values).

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no significant association was shown between EPA, DHA, or EPA plus DHA intake and insulin resistance (10, 15). Thus, it is possible that, even if adipose tissue or dietary intake of EPA plus DHA was higher, the association with HOMA-IR may still not have been apparent.

AHS-2 subjects reported mean linoleic acid intake of 12.9 and 13.2 g/d (in black and white subjects, respectively) (26), which translated to n–6 to n–3 FA ratio of ∼8:1. Research has indicated that, with a ratio of n–6:n–3 of 2:1, a substantial conversion of ALA to EPA is possible (42), but conversion to DHA is still limited (42) unless a direct source of DHA is provided. Therefore, because of the relatively high n–6:n–3 in our subjects, we speculated that the conversion of ALA to EPA and DHA would have been limited, thereby indicating a direct role of ALA in modifying insulin resistance.

Consistent with previous findings of an inverse association between dietary ALA and insulin resistance only in subjects with BMI <25 (10), we also observed an inverse association between adipose tissue ALA and insulin resistance only in subjects with a normal waist circumference (lean individuals). The variation of adipose tissue ALA was smaller in the abdominally obese than in lean individuals, which could possibly have accounted for the lack of an association with insulin resistance. After stratified analyses were conducted, Iggman et al. (9) showed that adipose tissue DHA was significantly positively correlated with insulin sensitivity in men with BMI >25. Although NS, we showed similar trends in our findings (results not shown) regarding the association between adipose tissue EPA plus DHA and HOMA-IR after stratifying for abdominal obesity.

The impact of adiposity on the association of adipose tissue n–3 FAs and HOMA-IR may be related to its role in the development of insulin resistance. Free FAs are released from adipose tissue as it exceeds the storage capacity during weight gain (2, 6). Elevated free FAs lead to insulin resistance by reducing the clearance of glucose from the blood which causes hyperinsulinemia and β cell dysfunction (2, 43). Obesity may also contribute to reduced insulin sensitivity by inhibiting AMP-activated protein kinase (43). The lack of a significant association between adipose tissue ALA and the HOMA-IR in subjects with abdominal obesity or obese subjects may have been due to the strength of association between adiposity and insulin resistance overwhelming the contrary effects of individual FA. In addition, it is possible that the mechanism(s) by which n–3 FA reduce insulin resistance are diminished in overweight or obese individuals. n–3 FAs have been shown to have differential effects in mice depending on the presence or absence of genetically predetermined obesity (11). Additional studies are needed to clarify these issues.

Weaknesses of this study included the cross-sectional nature of the analysis, which precluded an evaluation of a cause-effect relation between adipose tissue n–3 FAs and the HOMA-IR. Although the HOMA method for estimating insulin resistance may not be the most robust method, it is a practical measure to use in a study of this type (38). In addition, adipose tissue n–3 FAs are a relative measure rather than an absolute measure with weight loss, fat intake, and insulin sensitivity all possibly affecting the FA composition (9, 44). The proportion and range of adipose tissue EPA and DHA were also relatively low in this sample. Finally, there may be limited generalizability of the results because the AHS-2 cohort is made of up relatively healthy individuals (33).

One of the strengths of this study was the use of waist circumference as a measure of adiposity. Adipose tissue concentrations and dietary intakes of ALA were relatively high in our subjects. Members of the AHS-2 cohort, from whom the sample was selected, have limited alcohol intake, which markedly reduced confounding by this dietary factor (33). Black subjects were oversampled (33), which increased the applicability of study findings to members of that demographic. The sample also included both men and women, which was useful for the expansion of previous findings in men on the association between adipose tissue FAs and HOMA-IR. Although limitations have been noted for adipose tissue FA measurements, the measures have the strength of reflecting intake over long periods of time (9, 27, 29–31).

In conclusion, this study confirms that there is an inverse association between adipose tissue ALA and the HOMA-IR. This association may be stronger in subjects without abdominal obesity. For individuals who are lean, increasing dietary ALA may be a simple way of preventing insulin resistance. These findings should be confirmed through randomized controlled trials in the future.

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