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Original Research

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Association of dietary intake of total fat and fatty acids with the Omega-3 Index: a cross-sectional analysis of NHANES 2011–2012

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ABSTRACT

BACKGROUND/OBJECTIVES: The Omega-3 Index (O3I), which is the total eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in erythrocytes as a percentage of total fatty acids (FAs), is associated with fish intake. O3I also varies with body mass index, age, sex, and dietary factors other than the intake of n-3 polyunsaturated fatty acids (PUFAs). This study examined the relationship between the dietary intake of total fat and FA classes, and O3I, specifically regarding EPA+DHA intake.
SUBJECTS/METHODS: Data on dietary intake and serum FAs from 2,370 participants (1,192 males and 1,178 females) aged 18–79 yrs, collected during the 2011–2012 National Health and Nutrition Examination Survey, were used in this study. The O3I was estimated from the serum EPA+DHA content.
RESULTS: In the total population, O3I showed an inverse correlation with the intake of total fat (r = -0.417), saturated FAs (SFAs; r = -0.423), and monounsaturated fatty acids (MUFAs; r = -0.412) ($P < 0.01$). Similar relationships were observed among males. However, in females, only SFA intake was correlated with O3I (r = -0.386, $P < 0.05$). In contrast, no correlation was observed between n-6 PUFA intake and O3I. Multivariable regression analysis also showed that a 1% increment in energy provided by total fat, SFA, and MUFA corresponded to reductions of 0.019, 0.055, and 0.035 units in O3I, respectively ($P < 0.01$). Both SFA and MUFA intakes mediated the negative relationship between total fat intake and O3I in the total population and males. However, MUFA were not significant mediators in women.
CONCLUSION: The intakes of total fat, SFA, and MUFA negatively influenced O3I, independent of n-3 PUFA intake.

Keywords: Dietary fats; fatty acids; fatty acids, monounsaturated; fatty acids, omega-3

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Conflict of Interest
WSH is the co-developer of the Omega-3 Index test and the President of OmegaQuant, LLC, a laboratory that offers the test commercially.

Author Contributions
Conceptualization: Harris WS, Park Y; Formal analysis: Tintle NL, Hong H; Investigation: Tintle NL, Hong H; Methodology: Hong H; Supervision: Park Y, Harris WS; Validation: Jin Y, Hong H; Writing - original draft: Jin Y, Hong H; Writing - review & editing: Jin Y, Harris WS, Park Y.

INTRODUCTION

The Omega-3 Index (O3I) refers to the combined amount of eicosapentaenoic acid (EPA; 20:5n-3) and docosahexaenoic acid (DHA; 22:6n-3) in red blood cells (RBCs), represented as a percentage of the total red blood cell (RBC) fatty acids (FAs) [1]. Optimal levels of O3I (≥ 8%) exert protective effects against cardiovascular conditions [1]. The O3I is a convenient and suitable biomarker of n-3 polyunsaturated fatty acid (PUFA) status since RBC has low intra-individual variability over time and reflects long-term intake of n-3 PUFA, α-linolenic acid (ALA), EPA, and DHA [2].

Fish, as the main dietary source of n-3 PUFAs, is a key factor influencing O3I [3]. O3I is also inversely related to body mass index (BMI) [4] and age [5], and is higher in females than males [6], possibly because of estrogen [7]. However, n-3 PUFA status can be influenced by various dietary factors in addition to direct n-3 PUFA consumption [8]. Raatz *et al.* [9,10] reported that participants consuming high-fat diets had reduced levels of EPA and DHA in plasma phospholipids compared with those in participants consuming low-fat diets, despite the higher intake of n-3 PUFA in the form of ALA in the high-fat diet group.

Similar to human studies, male and ovariectomized female rats fed high-fat diets showed decreased levels of EPA and DHA in hepatic phospholipids and RBCs compared with those fed low-fat diets, despite a consistent intake of n-3 PUFA. A high-fat diet impaired the conversion of ALA to EPA and DHA by suppressing the expression of delta-6 desaturase (D6D), elongase of very-long-chain fatty acids 2 (ELOVL2), and ELOVL5 [11,12]. Furthermore, the levels of EPA and DHA in the milk of female rats fed saturated fatty acid (SFA)-rich diets were reduced compared with those fed diets with a lower SFA content, while maintaining a constant intake of ALA [13]. Male rats fed a high SFA diet also had lower levels of EPA and DHA in hepatic triacylglycerols and phospholipids than those fed a low SFA diet; however, adding more ALA to the latter diet reversed this effect [14]. Again, a higher intake of SFA reduced the conversion of ALA to EPA and DHA by downregulating the expression of D6D, D5D, ELOVL2, and ELOVL5 [13,15]. However, to the best of our knowledge, the extent to which differences in the intake of other (non-EPA/DHA) fats can affect the O3I in humans is unknown. Thus, the aim of this study was to determine the association between the consumption of total fat and each FA class (SFAs, monounsaturated fatty acids [MUFAs], and n-6 PUFAs), and O3I, in a nationally representative, cross-sectional survey from the United States (US).

SUBJECTS AND METHODS

Study population

This study utilized publicly available data from the 2011–2012 National Health and Nutrition Examination Survey (NHANES), which represents the US national population. The NHANES is structured to evaluate the nutritional status and health of Americans using a complex multistep probability sampling design [16]. The NHANES adhered to the ethical guidelines established by the Declaration of Helsinki, and all human subject procedures were approved by the National Center for Health Statistics Research Ethics Review Board (protocol #2011-17) and the Institutional Review Board of Hanyang University (HYUIRB-2021108-006). Among the 9,338 participants aged 18–79 yrs who completed the dietary survey, 2,573 had their serum FA level measured. As 203 participants had incomplete dietary data, 2,370 participants were included in the final analysis.

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Dietary assessment

The dietary recall interviews were conducted in person in a private room at the NHANES Mobile Examination Center. Using one-day dietary recall data, dietary intakes of energy, total fat, SFA, MUFA, n-6 PUFA, EPA+DHA, and ALA were obtained, and the daily intake was calculated based on the US Department of Agriculture Dietary Research Food and Nutrition Database for Dietary Studies [17]. We further calculated the percentage of energy from the total fat and each FA using the following formula:

$$\frac{\text{Fat or FA (g)} \times 9\ (\text{kcal/g})}{\text{Total Energy (Kcal)}} \times 100$$

The estimated O3I

Fasting serum samples were obtained and stored at –70°C. Serum FA content was analyzed using gas chromatography-mass spectrometry according to the Centers for Disease Control and Prevention (CDC) in the Laboratory Procedure Manual. Detailed procedures are documented in the CDC's Manual of Laboratory Procedures. Serum levels of EPA+DHA were converted from molar (mmol/L) to mass units (mg/dL), FAs were calculated, and then converted into a weight percentage of total FAs. Finally, the serum EPA+DHA weight % (x) was converted to RBC EPA+DHA content (y, i.e., estimated O3I) using the following equation [18]:

$$y = 0.0384 \times ln(x) + 0.1957\ (r^2 = 0.80)$$

Statistical analysis

Statistical analyses, including complex sample survey data analysis following NHANES guidelines, were performed using both R version 4.1.2 and SPSS version 26.0 (IBM Corp., Armonk, NY, USA). The sample weights obtained from NHANES were used to calculate an unbiased estimate of the mean and frequency representatives of the population [19]. Continuous variables were shown as mean ± SE of the mean and compared using Student's t-test. Frequencies and weighted percentages were used to represent categorical variables, and comparisons were conducted using the χ^2 test. Pearson's correlation coefficient was used to confirm the association between dietary fat intake and O3I. Multiple linear regression analysis was used to estimate the adjusted relationship between O3I and dietary fat intake, considering dietary fat intake as a continuous exposure variable [20]. We also classified dietary fat intake into quartiles, using the lowest intake quartile as the reference group, and adjusted for covariates during the assessment of the relationship between dietary fat intake and O3I. The covariates were sex, age, BMI, and dietary EPA and DHA (for sex-stratified analysis, sex was not included as a covariate). In multivariable models, covariates with $P < 0.20$ were selected as potentially confounding factors and included in the adjusted model [21].
To test whether the relationship between total fat intake and O3I was mediated by a specific class of FAs, excluding EPA+DHA, the Sobel test was conducted after adjusting for sex, age, and BMI (excluding sex in the sex-stratified analyses) [22]. The Sobel test was conducted to assess the significance of the mediator, and test how the relationship between total fat intake (independent variable) and O3I (dependent variable) was altered by introducing a potential mediator (SFA, MUFA, and n-6 PUFA) into the model.

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RESULTS

Characteristics of participants

Males were younger, consumed more energy, had a lower percentage of total energy from ALA, and a lower O3I compared with those of females (**Table 1**). The difference in BMI between males and females was not statistically significant; however, obesity was higher in females than that in males. The intake of total fat, SFA, MUFA, n-6 PUFA, and EPA+DHA as a percentage of total energy was not significantly different between males and females.

Associations between dietary fat and FA intake, and the O3I

O3I was inversely correlated with the intake of total fat, SFA, and MUFA, but positively correlated with ALA and EPA+DHA intake, following adjustment for potential confounders (**Table 2**). When comparing the results by sex, findings from males mirrored those of the

Table 1. Characteristics of participants

Characteristics	Total (n = 2,370)	Male (n = 1,192)	Female (n = 1,178)	*P*-value[1]
Age (yrs)	47 ± 0.38	46 ± 0.38	47 ± 0.54	0.030
BMI (kg/m^2)	28.65 ± 0.14	28.19 ± 0.17	29.11 ± 0.22	0.444
< 18.5	3.38 (0.14)	2.43 (0.16)	4.33 (0.21)	0.004
18.5–24.9	30.04 (0.06)	29.87 (0.09)	30.22 (0.09)	
25–29.9	31.18 (0.05)	35.82 (0.07)	26.49 (0.08)	
≥ 30	31.40 (0.19)	31.88 (0.15)	38.96 (0.28)	
Energy (kcal/day)	2,136.19 ± 20.19	2,430.13 ± 30.03	1,838.74 ± 24.03	< 0.001
Total fat (% of energy)[2]	32.69 ± 0.18	32.42 ± 0.24	32.96 ± 0.27	0.329
SFA (% of energy)[3]	10.43 ± 0.08	10.30 ± 0.11	10.57 ± 0.12	0.282
MUFA (% of energy)[3]	11.66 ± 0.07	11.71 ± 0.11	11.61 ± 0.11	0.365
n-6 PUFA (% of energy)[3]	6.97 ± 0.06	6.81 ± 0.08	7.14 ± 0.09	0.108
EPA+DHA (% of energy)[3]	0.050 ± 0.003	0.048 ± 0.004	0.051 ± 0.004	0.800
ALA (% of energy)[3]	0.74 ± 0.01	0.71 ± 0.01	0.76 ± 0.01	0.001
Omega-3 Index (%)[4]	4.63 ± 0.03	4.40 ± 0.05	4.86 ± 0.05	< 0.001

Data are presented as % (SE) or mean ± SE, with unweighted sample sizes provided for the total and subgroup analyses. A complex sample design was employed and a weighted analysis was performed.
BMI, body mass index; SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid; ALA, α-linolenic acid.
[1]*P*-value was determined through an independent *t*-test for continuous variables and a χ^2 test for categorical variables.
[2](Total Fat × 9 kcal)/Energy × 100.
[3](Fatty Acid × 9 kcal)/Energy × 100.
[4]Omega-3 Index, a sum of EPA and DHA in red blood cells.

Table 2. Correlation between dietary intake of total fat and fatty acids with the Omega-3 Index[1]

Dietary intakes	Total (n = 2,370)		Male (n = 1,192)		Female (n = 1,178)	
	r[2]	*r*[3]	*r*[2]	*r*[3]	*r*[2]	*r*[3]
Total fat (% of energy)[4]	−0.105***	−0.417***	−0.161**	−0.430**	−0.063	−0.381
SFA (% of energy)[5]	−0.145***	−0.423***	−0.195***	−0.436***	−0.118**	−0.386*
MUFA (% of energy)[5]	−0.095**	−0.412**	−0.130*	−0.422**	−0.055	−0.379
n-6 PUFA (% of energy)[5]	−0.001	−0.405	−0.045	−0.404	−0.032	−0.378
ALA (% of energy)[5]	0.089**	0.408*	0.095*	0.406	0.055	0.378
EPA+DHA (% of energy)[5]	0.253***	0.400***	0.255***	0.399***	0.259***	0.367***

SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; ALA, α-linolenic acid; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.
[1]A complex sample design was employed, and a weighted analysis was conducted.
[2]Unadjusted Pearson's correlation coefficient (*r*).
[3]Pearson's correlation coefficient (*r*) was adjusted for age, sex, BMI, dietary EPA, and DHA in the total population; adjusted for age, BMI, dietary EPA, and DHA in males and females; and excluded for dietary EPA and DHA in EPA+DHA.
[4](Total Fat × 9 kcal)/Energy × 100.
[5](Fatty Acid × 9 kcal)/Energy × 100.
$^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$.

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Table 3. Multiple linear regression analysis of dietary intake of total fat and fatty acids on the Omega-3 Index according to continuous and quartile intake

Variables	Total fat (% of energy)[1]		SFA (% of energy)[2]		MUFA (% of energy)[2]		n-6 PUFA (% of energy)[2]		ALA (% of energy)[2]		EPA+DHA (% of energy)[2]	
	Cutoff	β	Cutoff	β	Cutoff	β	Cutoff	β	Cutoff	β	Cutoff	β
Total												
Q1[3]	≤ 27.11	1.00 (ref.)	≤ 7.69	1.00 (ref.)	≤ 9.13	1.00 (ref.)	≤ 4.77	1.00 (ref.)	≤ 0.47	1.00 (ref.)	≤ 0.004	1.00 (ref.)
Q2	27.11 < to ≤ 32.87	−0.002	7.69 < to ≤ 10.24	−0.159	9.13 < to ≤ 11.48	−0.260	4.77 < to ≤ 6.55	−0.037	0.47 < to ≤ 0.65	−0.074	0.004 < to ≤ 0.010	−0.177
Q3	32.87 < to ≤ 38.47	**−0.152***	10.24 < to ≤ 12.96	**−0.393****	11.48 < to ≤ 14.03	**−0.483*****	6.55 < to ≤ 8.70	−0.023	0.65 < to ≤ 0.90	−0.251	0.010 < to ≤ 0.031	0.055
Q4	> 38.47	**−0.496*****	> 12.96	**−0.568*****	> 14.03	**−0.436*****	> 8.70	−0.045	> 0.90	−0.194	> 0.031	**0.729*****
Continuous (β)[4]	**−0.019*****		**−0.055*****		**−0.035****		−0.006		0.076		**3.383*****	
Male												
Q1[3]	≤ 27.06	1.00 (ref.)	≤ 7.73	1.00 (ref.)	≤ 9.27	1.00 (ref.)	≤ 4.72	1.00 (ref.)	≤ 0.45	1.00 (ref.)	≤ 0.004	1.00 (ref.)
Q2	27.06 < to ≤ 32.91	−0.389	7.73 < to ≤ 10.21	**−0.439***	9.27 < to ≤ 11.51	**−0.601***	4.72 < to ≤ 6.46	0.052	0.45 < to ≤ 0.63	−0.036	0.004 < to ≤ 0.010	−0.127
Q3	32.91 < to ≤ 37.90	**−0.419***	10.21 < to ≤ 12.72	**−0.647****	11.51 < to ≤ 14.04	**−0.683****	6.46 < to ≤ 8.54	−0.056	0.63 < to ≤ 0.87	−0.328	0.010 < to ≤ 0.031	0.043
Q4	> 37.90	**−0.681****	> 12.72	**−0.784*****	> 14.04	**−0.611****	> 8.54	−0.101	> 0.87	−0.232	> 0.031	**0.633****
Continuous (β)[4]	**−0.032****		**−0.081*****		**−0.059****		−0.028		0.099		**3.123****	
Female												
Q1[3]	≤ 27.16	1.00 (ref.)	≤ 7.66	1.00 (ref.)	≤ 9.04	1.00(ref.)	≤ 4.78	1.00 (ref.)	≤ 0.49	1.00 (ref.)	≤ 0.004	1.00 (ref.)
Q2	27.16 < to ≤ 32.85	0.393	7.66 < to ≤ 10.27	0.105	9.04 < to ≤ 11.42	0.108	4.78 < to ≤ 6.66	−0.136	0.49 < to ≤ 0.66	−0.027	0.004 < to ≤ 0.010	−0.098
Q3	32.85 < to ≤ 37.29	0.084	10.27 < to ≤ 13.15	−0.142	11.42 < to ≤ 14.02	−0.272	6.66 < to ≤ 8.80	−0.094	0.66 < to ≤ 0.93	−0.173	0.010 < to ≤ 0.031	−0.003
Q4	> 37.29	−0.272	> 13.15	**−0.368***	> 14.02	−0.276	> 8.80	0.053	> 0.93	−0.085	> 0.031	**0.837*****
Continuous (β)[4]	−0.009		**−0.035***		−0.015		0.010		0.040		**3.700****	

Bold values indicate a statistically significant difference with $P < 0.05$.

SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; ALA, α-linolenic acid; EPA, eicosapentaenoic acid; DHA, docosahexaenoic acid.

[1](Total fat×9 kcal)/Energy×100.

[2](Fatty acid×9 kcal)/Energy×100.

[3]Multiple linear regression analysis was adjusted for age, BMI, sex, dietary EPA, and DHA in the total population; adjusted for age, BMI, and dietary EPA and DHA in males and females; and excluded dietary EPA and DHA in EPA+DHA. A complex sample design was employed and a weighted analysis was performed.

[4]Each point corresponds to a 1% increase in energy from dietary intake of total fat or each fatty acid.

$^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$.

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total population, whereas among females, only the intake of SFA and EPA+DHA exhibited a statistically significant relationship with O3I (inverse and direct, respectively). The intake of n-6 PUFA showed no significant correlation with O3I.

In a multiple linear regression analysis with quartiles of dietary total fat and FAs as independent variables, adjusted for covariates, the O3I differences between participants in the highest and lowest quartiles were −0.50% for total fat, −0.57% for SFA, −0.44% for MUFA, and 0.73% for EPA+DHA. In an adjusted multiple linear regression analysis of dietary fat and FA intake as continuous variables on O3I, a 1% increment in energy provided by total fat, SFA, and MUFA predicted decreases of 0.02%, 0.06%, and 0.04% in O3I, respectively (**Table 3**). Conversely, a 1% increase in the percentage of energy from EPA+DHA predicted an increase of 3.4 units in the O3I. In females, O3I was inversely associated with SFA intake and positively associated with EPA+DHA, but not with the intake of total fat and MUFA. The association between n-6 PUFA intake and O3I was weak and nonsignificant.

Mediating effect of FAs

We further conducted a mediation analysis to determine whether FAs (other than EPA+DHA) mediated the association between total fat intake and O3I. Mediation analysis indicated that the association between total fat and O3I was significantly and negatively mediated by both SFA and MUFA, with a smaller effect observed for n-6 PUFA (**Fig. 1**). The mediating effects of SFA and MUFA differed by sex, with a significant negative indirect effect of SFA observed in both males and females, whereas MUFA showed a significant negative indirect effect only in males.

DISCUSSION

The present study demonstrated that the intake of total fat, SFA, and MUFA was inversely associated with O3I (when EPA+DHA intake was constant). Unsurprisingly, EPA and DHA intake were directly related to O3I. Based on the mediation analysis from the Sobel test, the negative effect of total fat intake on O3I can be attributed primarily to the intake of SFA and MUFA, with n-6 PUFAs having only a minor effect. When comparing the results by sex, only SFA mediated the effect of total fat on O3I in females.

Previous studies have suggested a similar pattern in the association between total fat and SFA intake and O3I in several countries [23-25]. The intake of n-3 PUFA (> 550 mg/day) was similar in Korea, Japan [26], and Spain [27]; however, O3I was higher in Korea (11.3%) than that in Japan (8.9%) [23] and Spain (7.1%) [27]. Consistent with our hypothesis, the Japanese and Spanish cohorts consumed a greater percentage of energy as total fat and SFA than those of Koreans (i.e., 25% and 38.5% vs. 21%; and 8.4% and 12% vs. 5.9%, respectively) [24]. Another observation suggests that a general relationship exists between Belgium and South Africa. The intake of n-3 PUFA was higher in Belgium (200–249 mg/day) than that in South Africa (< 50 mg/day) [26]; however, O3I (4%) was similar [23]. This similarity may be due to the fact that the intake of total fat and SFA was higher in Belgium (37% and 15.4% of energy) than that in South Africa (27% and 8.6% of energy) [24,25]. In a previous study [28], dietary EPA+DHA, which has been considered the primary determinant of O3I [3,28-30], explained only 12% of the variability in O3I in a multivariable model including other FAs. This suggests that total fat and SFA intake may also play a role in influence O3I.

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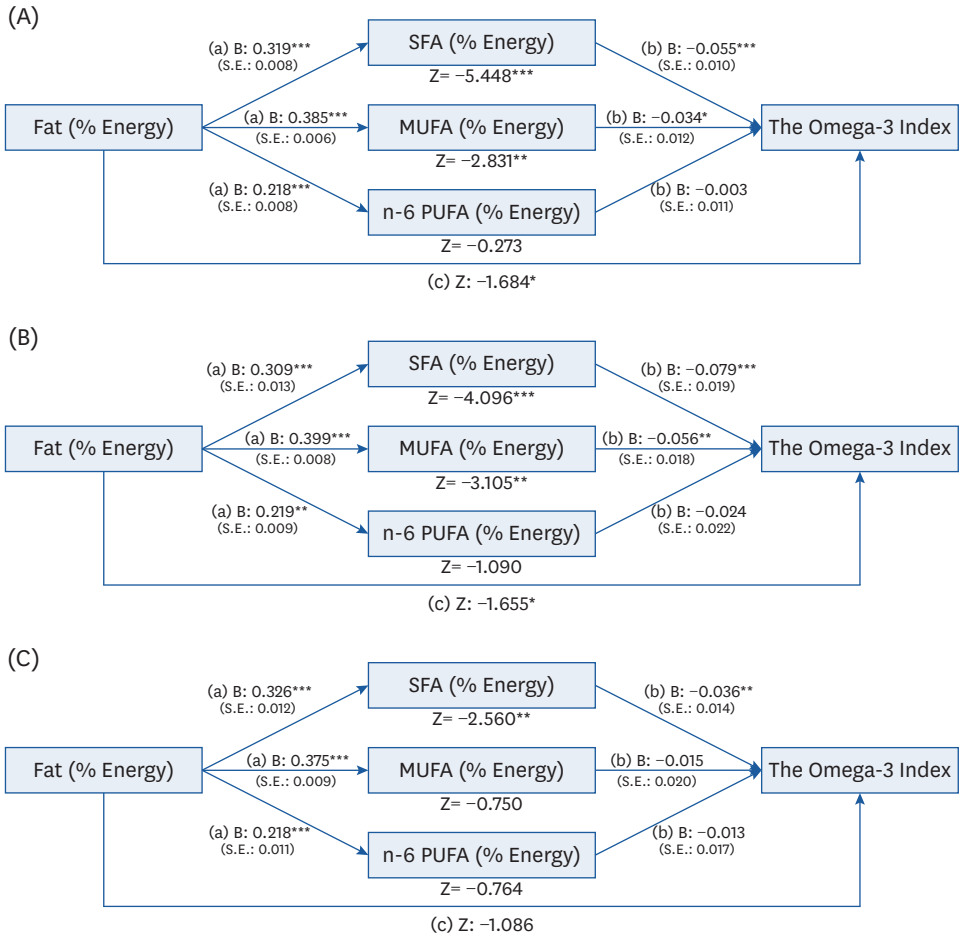

Fig. 1. Mediation effects of mediating variable (SFA, MUFA, and n-6 PUFA) intake on the association between fat intake (independent variable) and the Omega-3 Index (dependent variable) by Sobel tests adjusting factors. (A) Total population, (B) male, and (C) female; (a) path: effect of fat intake on SFA, MUFA, and n-6 PUFA intake; (b) path: effect of SFA, MUFA and n-6 PUFA intake on the Omega-3 Index; (c) path: indirect effect in total; Z: For statistically significant indirect effects in each variable.
SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid.
$^{*}P < 0.05$; $^{**}P < 0.01$; $^{***}P < 0.001$.

In addition to total dietary fat and SFA, dietary MUFA were inversely associated with O3I in this study. Dietary MUFA can come from both plant-based and animal-based sources, with animal sources (e.g., red meats and dairy products) also contributing particularly to SFA intake [31]. According to NHANES 2005–2006 data, chicken and processed meats ranked among the top 3 food sources of oleic acid (18:1), the major MUFA in the US diet [32]. Moreover, animal-based MUFA intake was highly correlated with SFA intake in 2 large prospective studies of US males and females [33], supporting similar relationships between SFA and MUFA intake and O3I, as shown in this study. In a previous study by Sala-Vila *et al.* [28] in a Mediterranean population with a higher intake of MUFA, primarily from olive oil, no specific associations were found with individual FAs, except for EPA+DHA and O3I. The MUFA intake in Spain is approximately 20.5% [28], as opposed to approximately 11.7% in the US [28]. This suggests that the inverse relationship between MUFA intake and O3I in the US may, in part, reflect a spillover effect from meat-derived SFAs and not be due to MUFAs themselves. In addition, we observed a slightly weaker association between MUFA intake and O3I in females compared with that in males. Another study, using NHANES 2007–2008 data, reported that US females

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had a relatively higher energy intake from oil and nuts, the main contributors to plant-based MUFA, than males [34]. Consequently, the variations in dietary intake across food categories by sex could, in part, explain the small sex differences in the associations between the intake of MUFA and O3I observed in this study.

It is well known that n-3 and n-6 PUFAs are metabolized by the same enzymes, and a surplus of one may significantly impair the conversion of the other into longer-chain or oxygenated metabolites [35]. However, there has been controversy regarding the effect of consumption of n-6 PUFA, predominantly linoleic acid (80–90%) [26], on the reduction of O3I [28,36]. We found a weaker association between n-6 PUFA intake and O3I. The conversion of ALA to EPA and DHA is insufficient, therefore, consumption of EPA+DHA-rich foods and supplements is directly related to O3I [37]. Additionally, 18-carbon species (linoleic acid; 18:2n-6, ALA; 18:3n-3) have different physiological properties from those of 20- or 22-carbon species (arachidonic acid; 20:4n-6, EPA; 20:5n-3, DHA; 22:6n-3) [38]. Owing to the imprecise and nonspecific nature of the n-6/n-3 PUFA ratio [39], the use the arachidonic acid/EPA ratio has been proposed, which distinguishes one PUFA from each class [40]. Further research is warranted to explore the interactions between each member of the n-6 PUFA family with different carbon species and O3I in a population with relatively high linoleic acid consumption.

A key strength of this study was the use of data from a formal US-wide survey that has been validated and includes both dietary and blood biomarker results. However, there were some limitations. First, a 1-day diet recall may not properly capture overall dietary patterns, as it reflects intake on a single day rather than providing a comprehensive representation of habitual dietary intake. Second, O3I in this study was calculated from serum FA composition and was not directly measured. Third, although various confounding factors were adjusted, some residual confounding factors remained. Finally, a cause-and-effect relationship between total fat, SFA, and MUFA intakes and O3I could not be determined because of the cross-sectional design of the present study. In conclusion, the present study found that the intake of total fat, especially SFA and MUFA, might negatively influence the levels of O3I independent of EPA+DHA intake, and that this effect could differ by sex. These findings indicate that reducing the dietary fat or SFA content increases EPA+DHA levels in the body, potentially explaining the health benefits of a low-fat diet. Further studies and clinical trials are needed to investigate whether these observations can be confirmed in other populations with different fat intake ranges.

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