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Association between Omega Fatty Acid Intake and Suicidality : Sex Differences in the General Korean Population

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ABSTRACT

Objectives : Epidemiological studies in other countries show that a low intake of omega-3 fatty acids (FAs) increases the risk of depression or suicidality. However, no studies have investigated the associations of suicidality with omega-3 FAs in Korea. Hence, this cross-sectional study aimed to investigate the effects of omega FAs on suicidality in the general South Korean population.

Methods : The data in this study were sourced from adults (n=215,860) who completed the Sixth Korea National Health and Nutrition Examination Survey (KNHANES VI), and the associations between omega FAs and suicidality were analyzed using multivariate logistic regressions.

Results : Our results demonstrated that high omega-3 FA intake was associated with a decreased risk of suicide (OR=0.83, 95% CI : 0.71−0.98) and the high omega-6 to omega-3 FA ratio was associated with an increased risk of suicide (OR=1.25, 95% CI : 1.02−1.54). Additionally, a high intake of omega-3 FAs was associated with a decreased risk of suicide in men, but not in women (OR=0.72, 95% CI : 0.59−0.88).

Conclusions : Overall, our findings suggest that a lower intake of omega-3 FA is associated with the increased risk of suicidality in the general Korean population, especially in men.

KEY WORDS : Suicide · Depression · Polyunsaturated fatty acids · Omega-3-fatty acid · Omega-6-fatty acid.

INTRODUCTION

Suicide is one of the major causes of mortality and morbidity worldwide.[1)] The annual global age-standardized suicide rate is 11.4 per 100,000 population (15.0 males and 8.0 females).[1)] In South Korea, an increased suicide rate was observed between 1990 (8.8 per 100,000 population) and 2011 (33.3 per 100,000), which is the highest recorded rate in the Organisation for Economic Co-operation and Development (OECD) database.[2)] The variability of suicidal rates across countries may be attributed to population-specific factors, such as race, environmental influences, or cultural characteristics. Dietary patterns, which are crucial determinants of the public health status, also vary across countries.[3)] Recently, nutrition-related risk factors that are associated with poor mental health, including suicidality, are attracting more attention.[4-6)] However, as compared to other risk factors, the association between nutrients and suicidality is not well understood.

18-carbon omega-3 (n-3) and omega-6 (n-6) fatty acids (FAs), which are long-chain polyunsaturated FAs, cannot be synthesized, especially in adult humans ; therefore, these FAs must be obtained from dietary sources.[7)] The three types of n-3 fatty acids involved in human physiology are alpha-linolenic acid, found in plant oils (e.g., flaxseed, linseed, canola, soy, and perilla), and eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), both commonly found in marine oils (e.g., fish, squid, and krill),[8)] n-6 fatty acids, including linoleic acid (LA) and gamma linolenic acid, are obtained from plant and vegetable seeds and oils.[9)] It is generally accepted that n-3 and n-6 FAs are converted to various forms of eicosanoids, depend-

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ing on the needs of the human body, and they function as immune and other types of chemical messengers.[10,11] As both n-3 and n-6 FAs are converted by the same enzymes, they competitively inhibit each other's metabolism. Therefore, the concentrations of both FAs should be balanced.[12,13] Each FA plays different roles in the human body. While n-3 is associated with anti-inflammatory and anti-thrombogenic interactions, n-6 act is associated with pro-inflammatory and thrombogenic interactions.[12] N-3 is also involved in the maintenance of cell membrane fluidity, suppression of cytokine production, and regulation of neurotransmitters.[10,11]

Recent epidemiological studies have demonstrated that an association between n-3 FAs deficiency and low n-3/6 ratio with depression or suicidality exists.[14,15] Lower intake of fish, which is a rich source of both n-3 and n-6 FAs, has been associated with an increased risk for depressives symptoms and suicidal thinking in cross-national and cohort-based studies.[9] While the majority of blood-based studies indicate that n-3 FAs are protective, n-6 FAs have been associated with an increased risk of suicide.[16] N-3 FAs intake may lead to decreased serotonergic neurotransmission and/or increased inflammation and subsequently influence the risk of suicide.[9]

Several studies have shown that n-3 and n-6 FAs play important roles in multiple neural pathways.[17] Omega FAs can be metabolized into various signaling molecules that influence neural pathways in the brain.[17] For instance, EPA and DHA have been reported to be associated with the membrane composition of the brain[18] and play a crucial role in brain development.[17] Additionally, n-3 FAs is involved in the regulation of neurotransmitters.[5] The consumption of n-3 FAs has been associated with chronic psychiatric disorders, including depression,[4] bipolar disorder,[19] and anxiety disorders.[20] Several studies showed the lower level of n-3 FAs in depression compared to healthy controls.[20,21] In clinical study, consumption of n-3 FA dietary supplements significantly decreased depressive symptoms in major depressive patients.[22]

However, as most current researches are derived from other countries, there is little evidence that supports the association between nutritional factors and suicidality in Korea. As stated above, dietary patterns are crucial determinants of the public health status[23] ; therefore, the association between FA intake and suicidality may provide insight into the nutritional and mental health status in South Korea. Hence, the current study examined the associations between omega FA intake and the risk of suicide in a nationally representative sample of the Korean population. We hypothesized that the consumption of omega-3 FAs would be associated with a decreased risk of suicidality. Additionally, we evaluated the effect of omega FA intake on suicidality between sexes.

MATERIALS AND METHODS

1. Participants and procedures

Data from the sixth Korea National Health and Nutrition Examination Survey (KNHANES VI), 2013 and 2015, and Korea Centers for Disease Control and Prevention were used. The KNHANES is a nationwide cross-sectional statistical survey that is performed annually to assess the nutritional and health status of Koreans.[24] Using stratified multistage clustered probability sampling, nutritional status and health-related information was obtained from clinical examination, face-to-face interviews, and self-report questionnaires. Estimated nutrient intake data, which were calculated using the Korean National Rural Living Science Institute and Korea Health Industry Development Institute databases[25,26] was obtained by trained dietitians in homes of the participants from surveys on one-day (24 hours) dietary recalls. The food intake questionnaire has been designed as an open-ended survey for reporting various dishes and foods using the 24-h recall method with various measuring aids. A detailed description of this survey is available elsewhere.[26]

A total of 22,948 individuals (10,411 men and 12,537 women) participated in the survey, and there was a 78.8% response rate. We excluded 12,359 participants who were under 19 years of age and participants who did not provide both one-day dietary recall and suicide-related data. As a result, the total number of eligible participants was 10,589 (4,529 men and 6,060 women).

The KNHANES was reviewed and approved by the Institutional Review Board of Korea Centers for Disease Control and Prevention (2013-07CON-03-4C ; 2013-12EXP-03-5C ; 2015-01-02-6C), and the data that was used in this study is openly available. The statistical design and process were also approved by the Institutional Review Board of the National Center for Mental Health (Seoul, Republic of Korea) (Institutional Review Board no. 116271-2018-07).

2. Measurements

1) Predictor variables

Amounts (g) of n-3 FA and n-6 FA intakes were obtained from one-day dietary recall data. n-6 to n-3 FAs ratios were also calculated.

2) Covariates

Sociodemographic variables included age (continuous), sex,

marital status [married, separated (i.e., living apart from their spouse), bereaved, divorced], education (elementary, middle, high school, university), and house income (lowest, low-middle, high-middle, highest quartile groups).

Lifestyle and nutrition related variables included severity of alcohol use, which was determined using the Alcohol Use Disorder Identification Test[27] ; smoking status (smoker who had smoked more than 100 cigarettes during their lifetime and currently smoke or non-smoker), total daily calorie intake (kcal/day), amount (g) of monosaturated and saturated FA intake, and body mass index (BMI, kg/m^2). Information on comorbid medical illness were obtained from self-reported health questionnaires. Patients were coded as "yes" if they had any of the following diseases : hypertension, types 1 or 2 diabetes, myocardial infarction, angina, arthritis, pulmonary tuberculosis, asthma, thyroid disease, renal failure, liver cirrhosis, or cancer. Otherwise, patients were coded as "no."

To assess the history of depression, participants were asked the following question: "In the past year, has there been a period of time when you were feeling depressed or down for as long as 2 week?" Participants were instructed to answer "yes" or "no." Perceived stress was assessed using a 4-point Likert scale (very much, much, not really, not at all) regarding the response to the following question : "How often do you feel stress in your daily life?" Participants were categorized into two groups based on stress level : "high level" (very much or much) and "low level" (not really or not at all).

3) Outcome variables

Suicidal ideation and attempt were assessed using the three following questions : 1) "Have you ever seriously thought about suicide in the last year?" (suicidal ideation), 2) Have you ever made a plan to commit suicide in the last year?" (suicidal plan), and 3) "Have you ever actually attempted to commit suicide in the last year?" (suicidal attempts). Participants who answered "yes" to any one of the three questions were assigned to the suicidality group, and patients who answered "no" to all questions were assigned to the control group.

3. Statistical analyses

All statistical analyses were performed using STATA/IC version 15.0 (Stata Corporation, TX, USA). Given the complex and multistage sampling design, all analyses were weighted to adjust for the non-response rate using post-stratification. The estimated prevalence and associations with robust standard errors were calculated with survey command (svy) in STATA. We considered variables with $p<0.05$ to be statistically significant. Energy-adjusted nutrient values were calculated in accordance with the residual approaches of Willett.[28] Additionally, the following variables were log-transformed to normalize their skewed distributions : n-3 and n-6 FA intake, monosaturated and saturated FA intake, BMI, and total daily calorie intake.

Univariate logistic regressions were performed to compare sociodemographic and clinical characteristics between the control and suicidality groups. To analyze the association between omega FA intake and suicidal risk, odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using univariate and multivariate logistic regression tests. We used two multivariate models that are described below. The first model was constructed using covariates that included age, sex, marital status, education, and household income. The second model included all covariates within the first model, along with additional covariates: severity of alcohol use, smoking status, total calorie intake, monosaturated and saturated FA intake, BMI, history of depression, and perceived stress. In addition, separated logistic regressions were performed to assess the interaction between sex and omega FA intake on suicidality.

RESULTS

1. Association of suicidality with demographic and clinical characteristics

A total of 595 (5.6%) participants were assigned to the suicidality group. Table 1 depicts the participants' sociodemographic characteristics and the associations between these characteristics and suicidality. Participants who were assigned to the suicidality group were more likely to be female (OR=1.64, 95% CI : 1.32−2.05). Widowed (OR=2.54, 95% CI : 1.94−3.32) and divorced (OR=4.33, 95% CI : 2.96−6.34) marital statuses significantly increased suicidal risk, compared to married subjects. Regarding education level, risks were reduced in high school (OR=0.22, 95% CI : 0.16−0.31) and middle school graduates (OR=0.41, 95% CI : 0.32−0.52), compared to university graduates. The lowest quartile group in household income showed an increased risk, compared to other quartile groups, such as the low-middle (OR=0.53, 95% CI : 0.40−0.71), high-middle (OR=0.32, 95% CI : 0.24−0.42), and highest quartiles (OR=0.25, 95% CI : 0.19−0.36), respectively. Lifestyle factors, including current smoking (OR=1.32, 95% CI : 1.01−1.72), were significantly associated with an increased risk of suicide. As expected, the risk of suicide was 16-fold greater for participants who had a history of depressive symptoms (OR=16.81, 95% CI : 13.41−21.07) and 5-fold greater for those with perceived stress (OR=5.58, 95% CI : 4.52−6.88).

2. Association between suicidality and omega-3 and omega-6 FA intakes

Table 2 contains the results from the logistic regressions that analyzed the association between omega FA intake and the risk of suicide. In the univariate analysis, n-3 (OR=0.75, 95% CI : 0.65−0.88) and n-6 FA intake (OR=0.65, 95% CI :

Table 1. Odds ratios for suicidality depending on demographic and clinical characteristics in all study population (n=10,589)

	Control (n=9,994, 94.4%)	Suicidality (n=595, 5.6%)	Odds ratio (95% CI)
Age	46.24 (SE 0.28)	51.28 (SE 0.90)	1.02 (1.01−1.02)*
Sex (%)			
Men	96.8	3.9	
Women	93.7	6.3	1.64 (1.32−2.05)*
Marriage (%)			
Married	95.8	4.3	
Separated	91.4	5.6	2.12 (0.81−5.54)
Widowed	89.9	10.3	2.54 (1.94−3.32)*
Divorced	83.9	16.1	4.33 (2.96−6.34)*
Education (%)			
Elementary school	89.4	10.6	0.72 (0.50−1.03)
Middle school	92.1	7.9	0.41 (0.32−0.52)*
High School	95.3	4.7	0.22 (0.16−0.31)*
University	97.4	2.6	
Household income (%)			
Lowest quartile	89.3	10.7	
Low-middle quartile	94.0	6.0	0.53 (0.40−0.71)*
High-middle quartile	96.3	36.8	0.32 (0.24−0.42)*
Highest quartile	97.0	3.0	0.25 (0.19−0.36)*
Smoking (%)			
Non-smoker	95.2	4.8	
Current smoker	93.8	6.3	1.32 (1.01−1.72)*
Alcohol use (AUDIT score)	6.26 (SE 0.92)	7.02 (SE 0.50)	1.02 (0.99−1.04)
Depressive symptoms in the past year (%)			
No	97.8	2.2	
Yes	72.8	27.2	16.81 (13.41−21.07)*
Perceived stress in daily life (%)			
Low level	97.5	2.5	
High level	87.5	12.5	5.58 (4.52−6.88)*
Existence of comorbid medical illness	26.6	44.1	2.03 (1.67−2.47)*
Total energy intake (calories)	2135.46 (14.68)	1811.51 (53.50)	1.00 (0.98−0.99)*
Monounsaturated fatty acid (g/day)	15.10 (0.22)	11.18 (0.67)	0.98 (0.96−0.98)*
Saturated fatty acid (g/day)	13.75 (0.19)	10.42 (6.78)	0.98 (0.96−1.00)*

* : $p<0.05$. AUDIT : Alcohol Use Disorder Identification Test

Table 2. Unadjusted and adjusted odds ratio for suicidality by n-3 and n-6 fatty acid intakes

Dependent variable	Control (n=9,994)	Suicidality (n=595)	Univariate model		Multivariate model 1		Multivariate model 2	
			OR (95% CI)	p	Adjusted OR (95% CI)	p	Adjusted OR (95% CI)	p
n-3 FA intake (g/day, median)	1.09	0.84	0.75 (0.65−0.88)	<0.001	0.82 (0.71−0.95)	0.007	0.82 (0.70−0.97)	0.020
n-6 FA intake (g/day, median)	7.22	5.47	0.65 (0.56−0.76)	<0.001	0.79 (0.67−0.94)	0.007	0.92 (0.68−1.24)	0.566
n-6 to n-3 FA ratio (median)	7.30	7.38	0.97 (0.82−1.15)	0.749	1.08 (0.92−1.029)	0.317	1.26 (1.03−1.55)	0.029

All dietary values were adjusted for total energy intake using residual methods. Dependent variables were log transformed due to the skewness of the distribution. Model 1 : Odds ratios adjusted for age, sex, marital status, education, household income. Model 2 : Odds ratios adjusted for age, sex, marital status, education, household income, alcohol consumption, current smoking, history of depressive symptoms, perceived stress, existence of comorbid medical illness, log-transformed monounsaturated fatty acid (g/day), log-transformed saturated fatty acid (g/day), and log-transformed body mass index (kg/m^2). FA : fatty acid, SE : standard error, OR : odds ratios, CI : confidence interval

0.56−0.76) were associated with a significantly decreased risk of suicide. However, the ratio of n-6 to n-3 FAs was not significantly associated with suicidality (OR=0.97, 95% CI : 0.82−1.15). After adjusting for sociodemographic variables (age, sex, marital status, education, and house income), n-3 and n-6 FA intake continued to be associated with a significant decreased risk of suicide (n-3 FAs, OR=0.82, 95% CI : 0.71−0.95 ; n-6 FAs, OR=0.79, 95% CI : 0.67−0.94). In the final analysis with all covariates, n-3 FA intake (OR=0.82, 95% CI : 0.70−0.96) demonstrated a significant association with a reduced risk of suicide. The ratio of n-6/n-3 was also significantly associated with an increased risk of suicide (OR=1.26, 95% CI : 1.03−1.55)

3. The effects of sex on suicidality and omega FA intake

A significant interaction was observed between sex and n-3 intake (p=0.027), but not between sex and n-6 intake (p=0.555) or between sex and the n-6/3 ratio (p=0.210) (Table 3). The adjusted odds ratios for suicidality in n-3 intake were 0.74 (95% CI : 0.60−0.96) in men and 0.91 (95% CI : 0.74−1.12) in women (Table 3, Fig. 1).

DISCUSSION

The purpose of this study was to evaluate the association

Table 3. Associations of omega-3 and omega-6 fatty acid intakes with suicidality by gender

Dependent variable	Men				Women				Gender interaction	
	Control (n=4,322)	Suicidality (n=207)	Adjusted OR (95% CI)	p	Control (n=5,672)	Suicidality (n=388)	Adjusted OR (95% CI)	p	F (df)	p
n-3 FA Intake (g/day, median)	1.31	1.00	0.74 (0.60−0.96)	0.008	0.94	0.75	0.91 (0.74−1.12)	0.839	F (2, 358)=3.64	0.027
n-6 FA Intake (g/day, median)	8.76	6.54	0.84 (0.60−1.17)	0.304	6.18	4.85	0.96 (0.68−1.36)	0.835	F (2,358)=0.59	0.555
n-6 to n-3 FA Ratio (median)	7.44	7.34	1.19 (0.95−1.48)	0.130	7.20	7.41	1.20 (0.98−1.48)	0.083	F (2,358)=1.57	0.210

All dietary values were adjusted for total energy intake using residual methods. Dependent variables were log transformed due to the skewness of the distribution. Odds ratios adjusted for age, sex, marital status, education, household income, alcohol consumption, current smoking, history of depressive symptoms, perceived stress, existence of comorbid medical illness, log-transformed monounsaturated fatty acid (g/day), log-transformed saturated fatty acid (g/day), log-transformed body mass index (kg/m^2). FA : fatty acid, SE : standard error, OR : odds ratios, CI : confidence interval

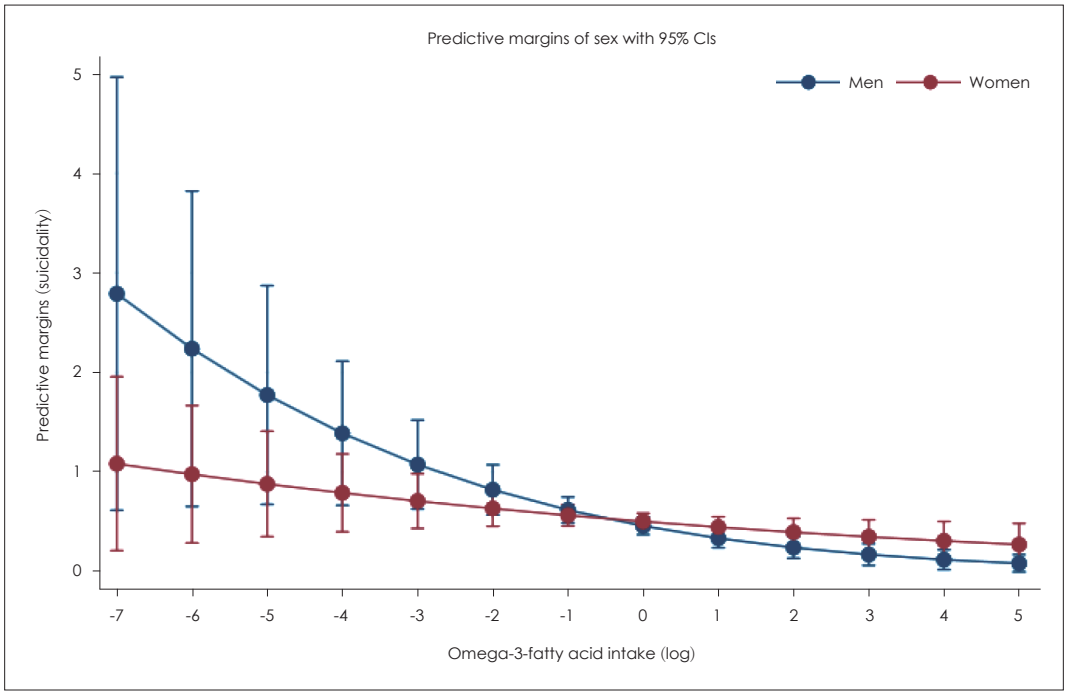

Fig. 1. Predictive margins of sex predicting suicidality by n-3 FA intake. Caption : The predictive margins were adjusted for covariates in the final model of logistic regression analysis. There was a significant interaction between sex and n-3 FA intake with respect to suicidality (p=0.043). In stratified analyses, a significant protective association was present only in men (p=0.016), but not in women.

between the consumption of omega FAs and suicidality. Using data from a nationally representative survey, we found that higher n-3 intake and n-3/n-6 ratio were associated with a lower risk of suicidality. These results remained significant after adjusting for confounders that were identified after multiple regression modeling with sociodemographic, behavioral, nutritional, and mental variables. The relationship between n-3 FA intake and suicidality was significant only in men.

According to a previous study, low intake levels of n-3 FAs have been associated with an increased prevalence of depression and worsening of depressive symptoms.[29] A recent systematic review[30] suggested that both lower n-3 FA dietary intake and a higher n-6/n-3 intake ratio could predict the risk of suicide among depressed patients without medication. We also discovered a significant association between n-3 FA intake and the n-6/n-3 ratio with suicidality, including suicidal ideation, planning, and attempts in the general population, after correcting for depressive symptoms. Additionally, our findings are compatible with several epidemiological studies for the general population in other countries.[31-33] The data from the third National Health and Nutrition Examination Survey of U.S. demonstrated that suicide attempters consumed a lower amount of omega FAs than non-attempters.[33] Suicidal attempters also had lower levels of red blood cell (RBC) EPA or serum DHA as compared to non-attempters.[31,32] Additionally, there was a dose-dependent relationship between low EPA levels in red blood cells and suicidal risk.[31] Furthermore, although there were few participants for whom FA levels were tested in serum phospholipids, a significant correlation was observed in a Belgian cohort between seasonal variations of EPA or DHA in serum phospholipids and the occurrence of suicide.[34] However, the trend between DHA or omega-FAs levels in the brains of suicide victims was not significantly different with controls in a post-mortem study.[30] The post-mortem study was limited to 20−60 subjects, and the DHA and omega FA concentrations were assessed in one brain region (the concentration may not directly reflect the n-3 FA intake when the victims were alive). The current study evaluated the relationship between current n-3 FA intake and patients' symptoms (suicidality) ; therefore our results were different than the results of the post-mortem study. The direct biochemical mechanism underlying the relationship between n-3 FAs and suicidality remains unclear. Among polyunsaturated FAs, n-3 FAs are known to be essential for neural function and affect cognitive function, emotional states, and mental health.[35] Several potential biochemical mechanisms may explain the association between n-3 FAs and depression.[21] For example, the anti-inflammatory properties of n-3 FAs may mitigate increased activity of the immune system, which is associated with depression.[36] There is a considerable amount of literature that focuses on the roles of PUFA in the nervous system.[36-38] Fatty acids are implicated as regulators of gene transcription within the central nervous system[37] and may play a role in neural membrane fluidity and receptor binding.[21,39,40] N-3 FAs, specifically EPA and DHA, are concentrated in neural tissues and play a key role in modulating neurotransmitters, neurogenesis, and myelination.[38] Subette et al.[41] demonstrated that low plasma DHA levels, which are associated with hyperfunction of the limbic forebrain and hypofunction of the parietal and temporal cortex, strongly predict future suicide risk in patients who are diagnosed with major depression. Furthermore, reduced dietary DHA has been associated with reduced cortical serotonin and dopamine.[36]

Taken together, these findings suggest that the proper intake of n-3 FAs might be related to suicidality. Caution should be exercised when assessing causal directionality due to the use of a cross-sectional design. The present study could not determine whether suicidality preceded or succeeded low intake of n-3 FAs. However, our results may constitute evidence to support the association of n-3 FA intake with suicidality.

Some cohort studies have reported that the dietary intake of n-3 FAs is not associated with suicidality, and the consumption of FAs did not reduce suicidal risk in the general Japanese,[16] American,[42] and Finnish populations.[43] While these studies evaluated the effects of n-3 FAs on risk of completed suicide, our study evaluated the relationship between n-3 FA intake and suicidality. The discrepancies between our results indicate that a low n-3 FA intake may be linked to suicidal ideation or planning, but this may not be sufficient to complete suicide. The risk of suicidal ideation was significantly lower among frequent fish consumers than among infrequent fish consumers in Northern Finland.[44] Furthermore, Poudel-Tandukar et al.[16] reported that a significantly increased risk of suicide was associated with very low fish or EPA+DHA intake. This suggested that extremely low intake of fish or n-3 FAs alone may increase the risk of completed suicide ; results from a randomized controlled intervention trial in suicidal patients support this reasoning. According to the results of the study by Hallahan et al.,[45] suicidal thinking was significantly decreased in the group that received n-3 FAs supplementation, compared with placebo group. Most randomized trials have employed preparations with EPA+DHA dosages exceeding 1 g/day and the n-3 FAs Subcommittee of the American Psychiatric Association recommended that people with depres-

sive disorders should consume at least 1 g of EPA+DHA per day.[46] The different amounts of n-3 FA intake between studies may have caused differences in results. In our study, the mean baseline daily intake of n-3 FAs was 1.72±0.35 g/day for participants in the control group and 1.33±0.10 g/day for participants in the suicidality group. However, in a three cohort study in the US, the median EPA+DHA consumption of participants was less than 1 g/day, which is the dosage that is used for treating depression.[47] Instead of n-3 FA intake, frequent fish consumption (at least twice per week) was used as the independent variable in a study that was conducted in Finland.[43] The subjects' age in a cross-sectional study with similar results to those of our study was 19−30 years, whereas the subjects' ages in three other cohort studies were 40−69 years (Japan),[16] above 30 years (US),[42] and 50−60 years (Finland).[43] The effects of n-3 FA intake on neuronal or psychiatry function may be more obvious in studies that include a younger sample of participants.

Interestingly, we found that a low intake of n-3 FAs was associated with a significantly increased risk of suicide in men, but not in women. However, our results are not compatible with the results of a US cross-sectional study,[48] which indicated that female suicide attempters, but not male suicide attempters, consumed a lower number of fish servings than non-attempters. Further, in a prospective Japanese study, a very low intake of fish was associated with a significant increased risk of suicidal death in women, but not in men.[16] The reasons for these sex differences are unclear. However, in Japan, n-3 FA intake was not different between men and women. In the current study, the n-3 FAs mean intake of men was higher than that of women (men ; 1.92±0.04 g / day, women; 1.44± 0.02 g/day).

In our study, high n-6 to n-3 FAs ratio was associated with an increased risk of suicide significantly, and there was a tendency that the risk of suicidality increased based on higher intake of n-6 FAs. With respect to similar findings, elevated n-6/3 have predicted suicidal behavior in patients who were diagnosed with major depression without medication.[31,41] Another study revealed that n-6 FA intake was not significantly different between suicide attempters and participants in the control group,[31] and n-6 FA intake did not increase the risk of suicide.[42] However, in a study of 234 pregnant women, higher serum levels of n-6 FAs (LA and AA) were associated with greater likelihood of suicide.[49] This may be due to variable concentrations of other lipid species ; n-6 FAs compete with n-3 FAs in a variety of signaling and inflammatory pathways. The higher the n-6 to n-3 ratio, the more inflammation associated with suicide risk can be promoted. Therefore, focusing on n-3 FA intake alone is not sufficient. If people consume large amounts of n-6 FAs, the effects of eating n-3 FAs that promote mental health appear to be relatively low. In the modern diet, n-6 FAs are abundant in many plant-based oils and meats from animals that are fed corn-based diets, but the major source of n-3 FAs is seafood.[50,51] The mean daily intake of n-6 FAs was 10.23±0.15 g/day for participants in the control group and 7.38±0.38 g/day for participants in the suicidality group; both were higher than those of n-3 FAs in each group. Overall, n-3 FA intake is important for managing and promoting mental health.

There were several limitations of the current study that should be mentioned. The first limitations of the present study were related to its cross-sectional design. We were unable to explain the causal relationship between n-3 FA intake and suicidality, because the reference period for the questions regarding suicidal ideation and attempts was 1 year prior to the day when the 24-hour recall was performed. In addition, low intake of n-3 FAs and suicidality may be influenced by undefined factors. Second, we estimated n-3 and n-6 FA intakes from one-day (i.e., 24 hours) dietary recalls; however, a single assessment of dietary intake may not accurately reflect long-term intake.[28] This may contribute to misclassification of intake, which weakens the strength of detected associations. Third, both depression and perceived stress were assessed using a simple question in the KNHANES VI, rather than validated instruments. As in all research using self-reported measurements, under-reporting might be a concern for suicidality because the interviewee's response is influenced by the perception of societal desirability. Additionally, information regarding potential confounding factors, including medication for depression and other mental illnesses, was insufficient in our study. Further validated studies are needed to confirm our hypothesis. Finally, dietary intake of subtype n-3 FAs (DHA and EPA) and alpha-linolenic acid might be more relevant to mental status and behavior.[52] KNHANES data did not include information regarding subtypes ; thus, the conclusion of the present study is less specific. Caution is needed when interpreting our results, due to the potential effects of other dietary factors that were not considered in our analysis. A recent meta-analysis suggested that the intake of fruit and vegetables could reduce the risk of depression.[53] Sugar consumption may also be related to mood symptoms.[54] Future studies with additional dietary information related to mental health are needed to determine the relationships of n-3 and n-6 FAs with suicidality. Our study had an important strength, in

that, to the best of our knowledge, this was the first study to evaluate the relationship between n-3 and n-6 FAs and suicidality in the general Korean population. The participants in the KNHANES VI were randomly selected from among the community-dwelling population ; therefore, our results can be generalized to adults in Korea. It is important to identify a protective factor for suicide, which is a major social problem, and the worst outcome of psychiatric disease

Overall, our findings suggest that a lower intake of n-3 FAs was associated with an increased risk of suicidality in the general Korean population, especially in men. Our results also highlight the importance of n-3 FA intake for promoting and maintaining mental health. Additionally, future prospective studies should clarify whether n-3-FAs plays a causal role in suicidality and if n-3 FA intake can be manipulated to reduce the risk of suicide.

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Conflicts of Interest

The authors have no financial conflicts of interest.

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