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Dietary Intake of Polyunsaturated Fatty Acids Lowers the Risk of Osteoporosis in Older Korean Females

Kyujo Lee[1], Kyeong-Rae Kim[2], Hyunjin Lee[1],Syungkyun Choi[3], Il-Tae Jang[4], Hyunwoo Kim[1]

[1]Nanoori 2bko R&D Institute, Nanoori Hospital Suwon, Gyeonggi-Do, Republic of Korea; [2]Nanoori Medical Research Institute, Nanoori Hospital Gangnam, Seoul, Republic of Korea; [3]Department of Orthopedics, Nanoori Hospital Gangnam, Seoul, Republic of Korea; [4]Department of Neurosurgery, Nanoori Hospital Gangnam, Seoul, Republic of Korea

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Corresponding Author
Hyunwoo Kim, MD
#16503 295,
Jungbu-daero, Yeongtong-gu,
Suwon-si, Gyeonggi-do,
Republic of Korea

Tel: +82-31-1688-9797
Fax: +82-31-8065-9701
E-mail: khwcool@gmail.com

Objectives: Osteoporosis is an important issue because it is associated with the risk of fractures. However, there is no study in the Republic of Korea on the relationship between PUFAs and the osteoporosis prevalence in middle-aged Korean women using public data. **Methods:** We intend to prepare basic data for osteoporosis by analyzing the prevalence of osteoarthritis in 3,294 women aged over 50 based on demographic and nutritional characteristics using the 7th KNHANES data using multiple logistic regression. **Results:** In unadjusted logistic regression analysis, the group with higher than average daily intake of PUFA had a lower prevalence of osteoporosis than the group with lower PUFA intake. In the final model, after adjustment for demographic variables such as sex and age, the group with high PUFA intake had up to 20% lower prevalence of osteoporosis than the other group. However, the effect size in the adjusted and unadjusted models was increased. **Conclusions:** A higher consumption of omega-3 and omega-6 fatty acids than the average daily intake in Korean women ages 50 years and older was negatively correlated with osteoporosis prevalence. We infer that adequate intake of PUFAs such as omega-3 and omega-6 fatty acids may help prevent osteoporosis.

Keywords: Osteoporosis, Etiology, Prevention, Polyunsaturated Fatty Acid, Bone Marrow Density.

Introduction

Osteoporosis is a very common systemic skeletal disease in middle-aged and older women, characterized by bone mass reduction and destruction of bone microstructures leading to fragile and brittle bones. Osteoporosis is defined as Bone marrow density (BMD) ≤ -2.5 [1]. In general, as people age, especially in menopausal women, bone loss occurs rapidly. Loss of bone mass deteriorates the bones' strength, increasing vulnerability to fractures from even minor trauma.

Clinically, osteoporosis is an important issue because it is associated with the risk of fractures. In the United States, 1.5 million osteoporosis-related fractures are reported annually, of which 300,000 are femoral fractures. Ninety percent of fractures in older people are attributable to osteoporosis [2]. The lifetime risk of fractures is 40% in Caucasian women [3-4], and once a fracture occurs, the risk of fractures in other sites is 50 - 100% [5]. And it has been predicted that by 2050 more than million hip fractures may occur annually worldwide due to prolonged life expectancy and increasing elderly population [6]. In particular, they predicted that 51.1% of hip fractures globally might occur in Asians.

Therefore, with increasing interest, studies on factors associated with osteoporosis have been actively conducted over the past few years. Recent large-scale studies involving female populations in Japan and Spain have claimed that increased intake of omega-3 fatty acids, the major class of polyunsaturated fatty acids (PUFAs), effectively improved BMD [7-8]. A Finnish study also reported that the intake of omega-6 fatty acids, and omega-3 fatty acids, were beneficial for improved BMD in middle-aged women [9]. Regular intake of PUFAs is known to have beneficial effects on women's health [10].

There is no study on the relationship between PUFAs and the prevalence of osteoporosis in a large population of middle-aged Korean women. Although the relationship between osteoporosis and PUFA observed in smaller studies may represent true differences, the results may be imprecise or incorrect because of the limited number of patients. Therefore, this study aimed to identify factors related to the osteoporosis prevalence, including intake of the PUFAs, omega-3 fatty acids and omega-6 fatty acids, in a nationally representative sample of Korean women aged 50 years or older.

Materials and Methods

Subjects

TThe Korea National Health and Nutrition Examination Survey (KNHANES) consists of 4 parts: the 'health interview' focusing on disease prevalence, activity limitations, injuries caused by accidents, and healthcare utilization; the 'health behavior survey' concerning drinking and smoking habits; the 'health examination'; and the 'dietary survey'.

The target subjects of this study were stratified according to the administrative districts (dong/eup or myeon) of the regional strata (seven metropolitan cities and the six regional provinces of Gyeonggi, Gangwon, Chungcheong, Jeolla, Gyeongsang, and Jeju) and housing type (apartment or general housing) based on data from the Population and Housing Census. Household samples were extracted in proportion to the population in each stratum using systematic sampling. Subsequently, all female members aged 50 and above of the selected households were enrolled as subjects of this study.

Among 16,120 individuals enrolled in 2016 and 2017, individuals below 50 years of age, those not surveyed for PUFA intake, those not surveyed for the other analyzed parameters, outliers, those with singular values, and those with chronic diseases were excluded, leaving a total of 3,294 participants for this study.

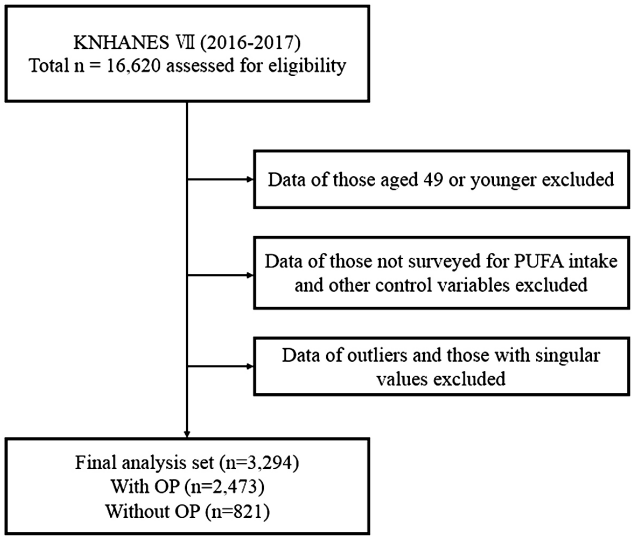

Figure 1. Flow diagram of the selection process from the 7th KNHANES (2016 - 2017) KNHANES = Korea National Health and Nutrition Examination Survey, PUFA = polyunsaturated fatty acids, OP = osteoporosis

Empirical analysis variables

TThe dependent variable in this study was the presence or absence of osteoporosis confirmed by a physician. This outcome variable was defined as those who responded with "Yes" or with "No" to the question, "Did you get an accurate diagnosis of osteoporosis from your doctor?" Subjects who responded with "I don't know" were excluded from the analysis. Control variables included basic demographic and socioeconomic variables of sex, income, residential area, age, level of education, nature of work, marital status, private health insurance status, income-generating activity, drinking status, smoking status, and body mass index.

PUFA intake was used as the independent variable in the logistic regression model. Based on PUFA intake, subjects were classified into three groups: those with PUFA intake ≤ 8.99 g (1), those with PUFA intake of 9 g to 17.99 g (2), and those with PUFA intake ≥ 18 g (3). A study by Song (2019) reported that the average PUFA intake in women between 50 and 64 years and women age 65 years or older was 9.0 g and 9.1 g, respectively. Based on this, a reference value was set, and the subjects were divided into three groups: those with lower than average intake, those with higher than average intake, and those with higher than twice the average intake. All the variables used in this study were verified as appropriate variables by the Mantel-Haenszel chi-square test for categorical data.

Empirical analysis model

A theoretical review of binary logistic analysis was conducted to investigate the effects of nutrient intake on osteoporosis in relation to risk factors. The most distinguishing feature of logistic regression from general regression is that the outcome variable's value is 0 or 1. Therefore, a logit transformation was performed on the linear regression equation whose value range was [-∞, + ∞], so that the result value range can be [0,1]. The procedure to find a logistic function is as follows:

$$\text{logit}(\mathbb{E}|[\text{Y}_i|x_{1,i}, \dots, x_{m,i}]) = logit(p_i) = ln\frac{p_i}{1-p_i}$$

As a result, the logit transform in logistic regression is the same as the linear function for x

logit(pi), the functional formula is as follows:

$$\text{logit}(p_i) = \beta_0 + \beta_1 x_{1,i} + \cdots + \beta_m x_{m,i} = \beta \cdot X_i$$

If a linear combination is made, the formula is as follows:

$$ln\frac{p_i}{1-p_i} = \beta \cdot X_i$$

Therefore, when a specific explanatory variable, x, is given, the probability that the outcome variable is in the category of 1 is as follows:

$$\text{p}_i = logit^{-1}(\beta \cdot X_i) = \frac{1}{1+e^{-\beta \cdot x_i}}$$

Our study analyzed the effects of PUFA intake on osteoporosis using the above formula [11].

Statistical analysis

In this study, statistical analysis was performed using data from the 7th KNHANES (2016 - 2017 Korea National Health and Nutrition Examination Survey). The proportion of osteoporosis cases and non-osteoporosis cases in relation to demographic variables was calculated. Significance tests for the groups and the categorical variables were performed using the Mantel-Haenszel chi-square test. Moreover, the presence or absence of osteoporosis, which was adjusted for all covariates, was divided into 'yes' (no problem) and 'no' (there is a problem) for each parameter, and logistic regression analysis was performed.

Specifically, the odds ratio of the prevalence of osteoporosis for each model with each control variable and its 95% confidence interval (CI) were determined using multivariable logistic regression analysis after adjusting for confounding variables. All statistical analyses were performed using STATA/SE 13.0 version (Stata Statistical Software: Release 13; StataCorp LLC, College Station, TX, USA).

Ethical statement

This study was conducted in compliance with the Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects. The use of the 7th KNHANES was approved by the Institutional Review Board of the Korea Centers for Disease Control and Prevention, and all the participants provided written informed consent.

Results

The differences in sociodemographic characteristics between the osteoporosis group and the non-osteoporosis group are shown in Table 1.

Analyzing each group's age, those with osteoporosis tended to be older and those without tended to younger (= 282.682, $p < 0.001$).

Table 1. Sociodemographic characteristics of the study subjects stratified by osteoporosis status

		Non-Osteoporosis cases (%)	Osteoporosis cases (%)		p-value
Total		2473	821		
Place of residence					
Rural	0	531 (21.4)	229 (27.8)	14.317	0.000
Urban	1	1942 (78.5)	592 (72.1)		
Age					
50-59	0	1036 (41.8)	120 (14.6)	282.682	0.000
60-69	1	804 (32.5)	258 (31.4)		
Over 70	2	633 (25.5)	443 (53.9)		
Income					
Low	0	573 (23.1)	217 (26.4)	5.863	0.118
Low-moderate	1	624 (25.2)	213 (25.9)		
Moderate-high	2	620 (25.0)	202 (24.6)		
High	3	656 (26.5)	189 (23)		
Education level					
≤6 years	0	965 (38.6)	539 (65.5)	196.772	0.000
7-9 years	1	399 (16.1)	119 (14.4)		
10-12 years	2	717 (28.9)	110 (13.3)		
≥ 13 years	3	392 (15.8)	53 (6.4)		
Marital status					
Married	0	30 (1.2)	12 (1.4)	0.302	0.591
Single	1	2443 (98.7)	809 (98.5)		
Private health insurance status					
No	0	706 (28.5)	395 (48.1)	106.015	0.000
Yes	1	1767 (71.4)	426 (51.8)		
Income-generating activity					
No	0	1275 (51.5)	553 (67.3)	62.302	0.000
Yes	1	1198 (48.4)	268 (32.6)		
Drinking status					
2 drinks/month to 3 drinks/week	0	578 (23.3)	274 (33.3)	32.154	0.000
4 drinks/week	1	1895 (76.6)	547 (66.6)		
Smoking status					
Non-smoker or ex-smoker	0	2402 (97.1)	801 (97.5)	0.434	0.301
Current smoker	1	71 (2.8)	20 (2.4)		
BMI					
≥ 23		813 (32.8)	280 (34.1)	0.420	0.272
23 <		1660 (67.1)	541 (65.8)		

Concerning the location of residence, a higher proportion of patients with osteoporosis lived in rural areas (= 14.317, p < 0.001). Regarding income, there was no difference between the two groups (= 5.863, p = 0.118).

Analysis of educational levels also revealed that osteoporosis was proportionally more common in the less educated (= 196.772, p < 0.001). In contrast, a higher proportion of those without osteoporosis had private health insurance (= 106.015, p < 0.001. There was no difference in the marital status of the groups (= 0.302, p = 0.591). There was a similar statistical difference in economic activity between the two groups (= 62.302, p < 0.001).

There was a difference between the two groups in drinking status, indicating health risk behavior, with higher consumption in proportionally more women with osteoporosis (= 32.154, p < 0.001). In contrast, there was no difference in the frequency of smoking between the two groups (= 0.434, p = 0.301). Finally, there was no statistically significant difference in BMI between the two groups (= 0.420, p = 0.272).

Next, we analyzed the differences between the two groups based on PUFA intake, which was the explanatory variable of interest used in the model. This explanatory variable was also treated as a categorical variable and was analyzed using the Mantel-Haenszel chi-square test. The results of the analysis are depicted in Table 2.

Table 2. The effect of polyunsaturated fatty acid consumption on osteoporosis

		Non-Osteoporosis cases (%)	Osteoporosis cases (%)		p-value
Total		2473	821		
PUFA intake					
≤ 8.99g	0	1418 (57.3)	591 (71.9)		
9g to 17.99g	1	779 (31.5)	182 (22.2)	57.774	0.000
≤ 18g	2	276 (11.2)	48 (5.9)		

PUFA = polyunsaturated fatty acids

We noted a difference in PUFA intake between the two groups (= 57.774, p < 0.001). As the PUFA intake increased, the number of the subjects in each group decreased, but proportionately more so in the osteoporosis group.

Logistic regression analyses were performed using the set of explanatory variables described above, and the results are shown in Table 3.

Table 3. The multiple logistic regression results of potential factors affecting osteoporosis.

	Unadjusted			Adjusted					
	Model 1			Model 2†			Model 3‡		
	Odds ratio	CI		Odds ratio	CI		Odds ratio	CI	
		Min	Max		Min	Max		Min	Max
Place of residence									
Rural§									
Urban				0.798*	0.651	0.892	0.884	0.737	1.059
Age									
50 - 59§									
60 - 69				1.897**	1.586	2.019	1.460*	1.169	1.823
Over 70				2.159**	2.058	2.301	1.886*	1.453	2.447
Income									
Low§									
Low - moderate				1.024	0.899	1.157	1.075	0.868	1.332
Moderate - high				1.055*	1.011	1.072	1.089	0.874	1.357
High				0.991	0.698	1.231	1.008	0.799	1.272
Education level									

	Unadjusted			Adjusted					
	Model 1			Model 2†			Model 3‡		
	Odds ratio	CI Min	CI Max	Odds ratio	CI Min	CI Max	Odds ratio	CI Min	CI Max
≤ 6 years§									
7 - 9 years							0.530**	0.417	0.672
10 - 12 years							0.322**	0.251	0.413
≥ 13 years							0.262**	0.186	0.370
Marital status									
Married§									
Single							0.636	0.300	1.348
Private health insurance status									
No§									
Yes							0.743	0.850	1.257
Income-generating activity									
No§									
Yes							0.574**	0.482	0.682
Drinking status									
2 drinks/month to 3 drinks/week§									
4 drinks/week							0.920	0.772	1.096
Smoking status									
Non-smoker or ex-smoker§									
Current smoker							0.907	0.557	1.478
BMI									
≥ 23§									
23 <							0.833*	0.710	0.977
PUFA intake									
≤ 8g§									
≥ 9g to ≤ 17.99g	0.561**	0.465	0.676	0.747**	0.612	0.911	0.800*	0.653	0.980
≥ 18g	0.417**	0.303	0.575	0.605**	0.433	0.846	0.666*	0.474	0.936
Constant	0.417			0.152			0.303		
Cox-Snell R^2	0.168			0.359			0.583		

*p < 0.05, **p < 0.001, §reference category, with a value of 1
†Only the place of residence, age and income were included in the control variables of the model
‡The final logistic analysis model that included all the control variables such as age and income
CI = 95% confidence interval, BMI = body mass index, PUFA = polyunsaturated fatty acids

In the analysis of Model 1 without any control variables, higher than the average PUFA intake was found to lower the risk of osteoporosis compared to lower levels of PUFA intake. A higher than twice than average PUFA intake was found to lower the risk of osteoporosis further. This indicates that consuming higher than average PUFA intake was associated with a lower risk of osteoporosis.

In the analysis of Models 2 and 3, in which more control variables were incrementally applied to increase the model's ability to partition the variance, higher than average PUFA intake was found to lower the risk of osteoporosis compared to lower PUFA intake. Incrementally adding these additional factors in the models increased their R2, indicating improved explanatory power compared to the odds ratios for model 1.

Discussion

PUFAs typically include omega-3 fatty acids and omega-6 fatty acids. Omega-3 fatty acids and omega-6 fatty acids are characterized by the presence of a double bond of three or six atoms away from the terminal methyl group in their chemical structure [12] Omega-3 fatty acids are important constituents required for lipid metabolism and typically include α-linolenic acid (ALA) found in vegetable oils, and eicosapentaenoic acid (EPA) as well as docosahexaenoic acid (DHA) found in marine oils [13].

Common sources of vegetable oils containing α-linolenic acid include various seeds and nuts (walnuts, chia seeds, flaxseeds) and plant-based oils (flaxseed oil, soybean oil, and canola oil). EPA and DHA sources include fatty fish (i.e., salmon, mackerel, sardine, herring, etc.) [14-17]. Omega-6 fatty acids are typically known to have anti-inflammatory effects in the body [18]. Linoleic acid, the shortest-chain omega-6 fatty acid, is one of the most common omega-6 fatty acids and is classified as an essential fatty acid because it is not synthesized in the human body. Vegetable oil is a primary linoleic acid source and is rich in soybeans and sunflower seeds [19].

Omega-3 fatty acids and omega-6 fatty acids compete as substrates for the same enzymes, and some scientists have argued in favor of the importance of the ratio of omega-6 to omega-3 fatty acids in the diet [20]. Another study reported that a higher proportion of omega-6 to omega-3 fatty acids was associated with lower BMD, and suggested that the relative intake of PUFAs may be important [21].

In our study, when the models above were set up and analyzed, the results showed that those who consumed higher than the average PUFA intake also had a reduced risk of osteoporosis compared to those who did not. This finding was consistent with a study reporting that higher PUFA intake is required to prevent osteoporosis [22]. Additionally, this finding was also consistent with Harris' results in 2015, indicating that dietary PUFA intake was negatively associated with total bone mineral density in postmenopausal women [23].

Our study has some limitations. Data used in this study were based on the 24-hour food consumption recall data. Additionally, our study's results were obtained by investigating only the variations in PUFA intake under the assumption that the intake of other nutrients was the same. Hence, it is difficult to draw definite conclusions. However, this study is significant. We identified a significant correlation between PUFA intake and the prevention of osteoporosis and secured its representativeness as a cross-sectional study using nationally representative data.

Conclusions

This study showed that adequate omega-3 and omega-6 fatty acid intake was negatively correlated with the osteoporosis prevalence. Therefore, we recommend the consumption of fish rich in omega-3 fatty acids and vegetable oils containing omega-6 fatty acids. However, some studies have reported that omega-3 and omega-6 fatty acids have opposing physiological effects and that if the intake ratio of omega-6 to omega-3 fatty acids is excessively high, it may induce osteoporosis. Therefore, it might be advisable to avoid overconsumption of omega-6 fatty acids.

Conflict of Interest

The authors state no conflict of interest.

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Dr. Kyujo Lee and Mr. Kyeong-Rae Kim equally contributed to both writing the article and statistical analysis as co-first author.

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