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Original Article

Association of seafood consumption with sleep quality according to high sensitivity C-reactive protein levels in Korean adults

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ABSTRACT

Objective: The consumption of seafood, which is major sources of *n*-3 polyunsaturated fatty acids, such as docosahexaenoic and eicosapentaenoic acids, has been associated with sleep quality. Seafood and its bioactive components may enhance sleep quality by regulating systemic inflammation and neuroendocrine pathways. However, longitudinal studies examining the interplay between seafood consumption, sleep quality, and inflammatory status are lacking. Therefore, in this cohort study of 2332 participants from the Korean Genome and Epidemiology Study, we investigated the potential modulatory role of inflammatory status for the association between seafood consumption and the risk of poor sleep quality.

Methods and measurements: Dietary intake was assessed using a validated 106-item food frequency questionnaire. High-sensitivity C-reactive protein (hs-CRP) levels were assessed as a marker of systematic inflammatory status. Sleep quality was assessed using Pittsburgh Sleep Quality Index. The hazard ratio (HR) and 95% confidence interval (CI) for the risk of poor sleep quality was estimated using Cox proportional hazards model.

Results: After 6 years of follow-up, 118 and 192 cases of poor sleep quality were documented among men and women, respectively. The greater seafood consumption was significantly associated with lower risk of poor sleep quality. The multivariable-adjusted HR (95% CI) comparing the highest with the lowest tertile of seafood consumption was 0.66 (0.45–0.98) (p-trend = 0.032). This inverse association appeared to be limited to participants with lower levels of hs-CRP.

Conclusion: Our results suggested that the favorable effects of seafood consumption on sleep quality could vary by inflammatory status. Larger cohort studies are warranted to replicate our findings.

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1. Introduction

Poor sleep is emerging as a global major public health concern [1]. Poor sleep has been linked to an increased risk of physical and psychological complications, such as hypertension [2], type 2 diabetes [3], cardiovascular disease [4], depression [5], and cognitive disorders [6] and all-cause and cause-specific mortality [7]. The global pooled prevalence rate of sleep problems during the COVID-19 pandemic was 37.5% of people from all populations [8]. In Korea, according to Korean National Health Insurance claims data, the prevalence of sleep disorders increased from 3,867,975 (7.62%) in 2011 to 7,446,846 (14.41%) in 2020, nearly doubling over 10 years [9]. The causes of poor sleep are multifactorial, encompassing genetic predispositions, environmental influences, and behavioral components [10]. Among these, specific lifestyle factors such as alcohol intake [11], smoking [12], physical activity [13], and diet [14] have been associated with sleep quality, suggesting the potential for identifying modifiable risk factors could inform prevention strategies and guide for future intervention.

Dietary factors may influence the risk of poor sleep quality [14]. In particular, growing evidence suggests a potential association between

Abbreviations: PUFAs, polyunsaturated fatty acids; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; DVS, dietary variety score; CRP, C-reactive protein; (IL)-6, interleukin; TNF-α, tumor necrosis factor-alpha; KoGES, Korean Genome and Epidemiology Study; PSQI, Pittsburgh Sleep Quality Index; SQFFQ, semi-quantitative food frequency questionnaire; hs-CRP, high-sensitivity CRP; BMI, body mass index; HRs, hazard ratios; CIs, confidence intervals; KRW, Korean won; SES, socioeconomic status; CSF, cerebrospinal fluid; ROS, reactive oxygen species; tHcy, total homocysteine; PSG, polysomnography.

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seafood consumption and sleep quality. To date, few cross-sectional studies have reported an inverse association between seafood consumption and poor sleep quality in populations from China [15], Japan [16], and Ecuador [17]. Although the longitudinal evidence on the association between seafood consumption itself and sleep quality, which may help develop a more precise and practical dietary recommendation, is limited, one longitudinal study of older Japanese adults found a cross-lagged positive association between the dietary variety score (DVS)— characterized by the frequent intake of fish/shellfish and seaweed—and sleep quality [18]. In addition, seafood is a major dietary source of *n*-3 polyunsaturated fatty acids (PUFAs), particularly docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) and also constitutes a key component of the Mediterranean diet pattern, both of which have been associated with improvement in sleep quality indices [19] and sleep quality characteristics [20] in a systematic review and meta-analysis of 8 randomized controlled trials [19] and 23 observational studies [20].

In addition, emerging evidence suggests that inflammation plays a key role in regulating sleep quality. Poor sleep quality was found to be positively correlated with systematic inflammatory markers, such as C-reactive protein (CRP), interleukin (IL)-6, and tumor necrosis factor-alpha (TNF-α) [21]. Seafood and its bioactive constituents, *n*-3 polyunsaturated fatty acids (PUFAs), were potentially suggested to exert a beneficial effect on sleep quality through their anti-inflammatory properties and neuroendocrine regulation [22–24]. Regarding these results, it can be speculated that inflammatory status may partially modulate the association between seafood consumption and sleep quality. However, to our knowledge, no study has yet examined whether the association of seafood consumption with sleep quality varies by inflammatory status.

Therefore, we hypothesized that seafood consumption may exert heterogeneous effect on sleep quality by inflammatory status. This study aimed to investigate the role of inflammatory status as a modulator of longitudinal association between seafood consumption and the poor sleep quality, using hs-CRP as an inflammatory indicator.

2. Material and methods

2.1. Study population

Study participants in the present study were drawn from the large, community-based cohort of the Korean Genome and Epidemiology Study (KoGES), which was established to identify risk factors for common chronic diseases in the Korean population [25]. Briefly, a total of 10,030 participants aged 40–69 years residing in Ansan and Ansung were initially enrolled in 2001–2002 (1st wave) and have been followed up biennially since then [25]. In the present study, we defined the 4th wave (2007–2008)—which corresponds to the 3rd follow-up examination and included 6688 of the original KoGES participants—as the baseline, because sleep quality was first assessed at this time point. The end of follow-up was set at the 6th follow-up examination (2013–2014). Among the 6688 participants at the 3rd follow-up, those with poor sleep quality at baseline (n = 335) were excluded, allowing us to investigate the longitudinal association between seafood consumption and incident poor sleep quality. We also excluded participants who had reported implausible total energy intakes (<500 or >4000 kcal/day, n = 490), had never participated in the follow-up examinations (n = 309), had missing information on covariates (n = 102), and did not complete the sleep quality questionnaire at baseline (n = 3120). Consequently, our final analytic sample included 2332 participants (1240 men and 1092 women) (Fig. 1).

2.2. Ethical approval

This study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human participants were approved by the Institutional Review Board of Ewha Womans University (No. 202403-0030-01). All participants provided written informed consent.

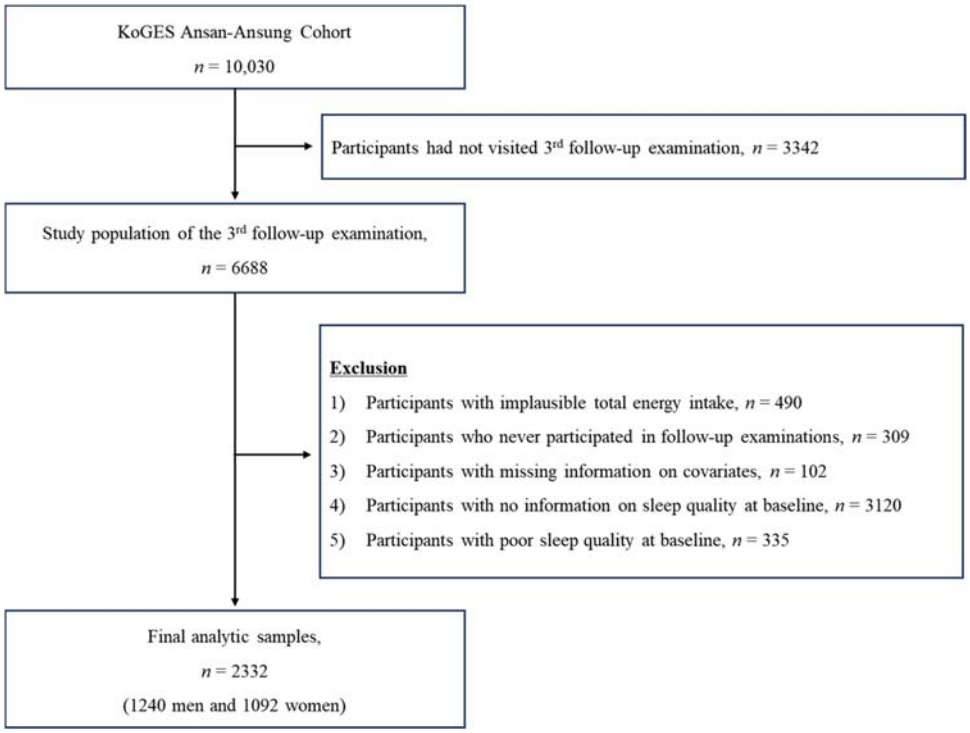


Fig. 1. Study population flowchart.

2.3. Sleep quality assessment

Sleep quality was assessed between the baseline and 6th follow-up examination using the Pittsburgh Sleep Quality Index (PSQI) questionnaire, which evaluates the previous month's sleep quality and patterns [26]. The PSQI has widely been used in the general population, and its reliability and validity have been reported elsewhere [26]. The PSQI comprises 19 individual items used to derive the following seven component scores: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, sleep medication usage, and daytime dysfunction. Each component is scored on a 0–3 scale, and the total score is calculated by summing the scores of all components. High scores reflect poor sleep quality. In this study, poor sleep quality was defined as a total PSQI score >8.5, which was identified as the optimal cutoff for achieving higher sensitivity and specificity in distinguishing the poor and good sleepers in a previous study of Korean population [27].

2.4. Food and nutrient intake assessment

A validated, semi-quantitative food frequency questionnaire (SQFFQ), which includes 106 food items developed for the KoGES, was used to obtain dietary information [28]. For validation, FFQ was administered twice at 1-year interval (FFQ1 at the beginning and FFQ2 at the end of the study) and diet records were collected for 3 days during each of the four seasons from December 2002 to May 2004. The median Spearman correlation coefficients between the two FFQs 1 year apart were 0.45 for all nutrient intakes and 0.39 for nutrient densities [28]. Consumption of food, particularly regarding the participants' dietary intake over the preceding year, was assessed at the cohort's second follow-up examination. Participants' average frequency of each food item was assessed using a 9-point scale with the following response options: "never or barely," "once a month," "twice or three times a month," "once or twice a week," "three or four times a week," "five or six times a week," "once a day," "twice a day," or "three times a day." Further, the average portion size was assessed on a 3-point scale: "small (half the size of a medium)," "medium (equivalent to one serving of the corresponding food item)," or "large (1.5 times the size of a medium)." Seasonal fruit consumption was divided into four categories (3, 6, 9, and 12 months).The average daily intake (grams per day) of each food item is calculated by multiplying the reported consumption frequency (times per day) of intake by its corresponding portion size per intake (grams per time). Nutrient values were derived from the food database of the Computer Aided Nutritional Analysis program (version 3.0; Korean Nutrition Society, Seoul, Korea) [29] and the Korean food composition table provided by the Rural Development Administration [30].

Specifically for the study, seafood consumption was determined based on summing the average daily intake of 17 seafood items, including fish, shellfish, and seaweed (Table S1). As a result of data availability, seafood consumption was adjusted for total energy intake according to the nutrient density method and calculated in grams per 1000 kilocalories per day [31]. Then, participants were divided into three groups based on seafood consumption tertiles.

2.5. Measurement and definition of inflammatory status

High-sensitivity CRP (hs-CRP) is a well-established marker of systematic inflammation status that has been validated for its predictive value in assessing numerous adverse disease conditions [32]. In our study, hs-CRP was measured using the immunoradiometric assay (ADVIA 1650; Siemens, USA) at baseline. The participants were divided into low and high inflammatory groups based on the median hs-CRP level (men, ≥0.72 mg/L; women, ≥0.61 mg/L) in our samples, which has been shown to be a potent predictor of inflammatory predicting adverse outcomes in Asian populations [33,34], who generally exhibit lower hs-CRP levels, compared to Western population [35].

2.6. Data collection

Participants' baseline sociodemographic and lifestyle data were collected using questionnaires. Anthropometric measurements were conducted by trained researchers. The body mass index (BMI) was calculated as follows: weight (kg) divided by height squared (m^2).

2.7. Statistical analysis

Baseline characteristics are presented as the mean ± standard error for continuous variables and as numbers (percentages) for categorical variables according to tertiles of seafood consumption. A generalized linear model was used to compare the mean values of baseline characteristics and analyze linear trends across seafood-consumption tertiles. The Chi-square test was used to examine differences in the distribution of study participants' general characteristics. Cox proportional hazard regression models—adjusted for potential confounders—were used to estimate the multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for poor sleep quality according to seafood-consumption tertile. Person-years were computed for each participant from the study baseline to the date of poor sleep quality onset or the end of the follow-up. In multivariable-adjusted analyses, we included confounding factors potentially associated with seafood consumption and sleep quality as follows: age (continuous), BMI (continuous), alcohol consumption (current drinker, non-current drinker) [11], smoking status (current smoker, non-current smoker) [12], physical activity (<30 min/day, ≥30 min/day) [13], monthly income (<200 million Korean won [KRW], ≥200 million KRW) [36], marital status (married, other), fruit and vegetable consumption (continuous) [37]. Additionally, we adjusted for menopausal status (premenopausal, menopausal) in women. The intake of seafood was adjusted for total energy intake by density methods (g/1000 kcal). A test for trend was conducted by treating the median value of seafood consumption within seafood tertile categories as a continuous variable. To determine whether the association between seafood consumption and the risk of poor sleep quality is modulated by inflammatory status, we conducted analyses stratified by hs-CRP level. All analyses were performed using SAS (version 9.4; SAS Institute Inc., Cary, NC, USA). Statistical significance was set at $p < 0.05$.

3. Results

3.1. Baseline characteristics

Over a 6-year follow-up period, 118 and 192 cases of poor sleep quality were reported among men and women, respectively. Table 1 presents the baseline characteristics of the participants according to seafood consumption tertile. In both men and women, no significant differences in the baseline hs-CRP level and PSQI score were noted among the groups. In addition, participants exhibiting higher seafood consumption had higher socioeconomic status (SES) in terms of household income ($p < 0.01$). Among men, participants displaying greater seafood consumption had a higher mean BMI and a larger proportion of current drinkers and smokers ($p < 0.01$). Among women, higher seafood consumption was associated with younger age, greater physical activity, and the married status ($p < 0.01$).

3.2. Dietary intake

Table 2 displays food consumption (g/1000 kcal) according to seafood consumption tertile. Seafood consumption was positively associated with most food groups, such as meats, eggs, and plant-based foods (all p-trend <0.05) in both men and women. Among women, participants exhibiting higher seafood consumption showed a higher consumption of milk and dairy products (p-trend = 0.040). However, it

Table 1
General characteristics according to seafood consumption.

	Seafood consumption			
	Tertile 1	Tertile 2	Tertile 3	*P*-value[†]
Men				
No. of participants	413	414	413	
Energy-adjusted seafood consumption, median	10.19	18.53	31.88	
Hs-CRP (mg/L)	1.5 ± 0.2	1.5 ± 0.2	1.5 ± 0.2	0.869
Age (years)	65.37 ± 0.37	64.94 ± 0.34	64.75 ± 0.33	0.435
BMI (kg/m^2)	24.31 ± 0.13	24.48 ± 0.13	25.13 ± 0.13	<0.001
Baseline PSQI score	4.16 ± 0.09	4.46 ± 0.10	4.21 ± 0.10	0.057
Current drinker	281 (68.0)	293 (70.8)	319 (77.2)	0.010
Current smoker	100 (24.2)	113 (27.3)	140 (33.9)	0.007
Physical activity, ≥30 min	156 (37.8)	155 (37.4)	156 (37.8)	0.994
Monthly income, ≥2 million KRW	314 (76.0)	321 (77.5)	349 (84.5)	0.006
Marital status, married	401 (97.1)	403 (97.3)	408 (98.8)	0.209
Women				
No. of participants	364	364	364	
Energy-adjusted seafood consumption, median	10.04	18.35	31.91	
Hs-CRP (mg/L)	1.3 ± 0.1	1.3 ± 0.2	1.5 ± 0.3	0.743
Age (years)	65.97 ± 0.41	64.54 ± 0.35	64.29 ± 0.34	0.002
BMI (kg/m^2)	24.56 ± 0.16	24.43 ± 0.16	24.52 ± 0.16	0.839
Baseline PSQI score	4.53 ± 0.10	4.50 ± 0.10	4.50 ± 0.10	0.979
Current drinker	101 (27.8)	107 (29.4)	107 (29.4)	0.852
Current smoker	3 (0.8)	9 (2.5)	4 (1.1)	0.140
Physical activity, ≥30 min	83 (22.8)	97 (26.7)	125 (34.3)	0.002
Monthly income, ≥2 million KRW	221 (60.7)	259 (71.2)	253 (69.5)	0.006
Marital status, married	299 (82.1)	327 (89.8)	329 (90.4)	0.001
Menopausal status, menopause	231 (63.5)	224 (61.5)	208 (57.1)	0.202

Hs-CRP, High-Sensitivity C-Reactive Protein; PSQI, Pittsburgh Sleep Quality Index; BMI, body mass index; KRW, Korean won.
Values are expressed as the mean ± SE for continuous variables and numbers (percentages) for categorical variables.
[†] *P*-values were obtained from the general linear models for continuous variables and the Chi-square test for categorical variables.

Table 2
Food consumption according to seafood consumption.

	Seafood consumption			
Food consumption (g/1000 kcal/d)	Tertile 1	Tertile 2	Tertile 3	*P*-trend[†]
Men				
Grains	426.02 ± 3.29	401.56 ± 3.14	372.08 ± 3.33	<0.001
Potatoes	5.91 ± 0.38	6.70 ± 0.32	7.13 ± 0.38	0.020
Sweet foods and sugars	7.27 ± 0.29	6.44 ± 0.25	6.38 ± 0.29	0.036
Legumes	13.47 ± 0.49	14.91 ± 0.47	16.37 ± 0.46	<0.001
Nuts and seeds	0.42 ± 0.06	0.57 ± 0.05	0.73 ± 0.06	<0.001
Fruits	102.62 ± 3.48	113.67 ± 3.32	129.62 ± 4.43	<0.001
Vegetables	29.37 ± 0.79	37.94 ± 0.93	46.31 ± 1.06	<0.001
Mushrooms	3.19 ± 0.15	3.93 ± 0.19	5.25 ± 0.28	<0.001
Meats	21.31 ± 0.72	27.37 ± 0.84	31.87 ± 0.93	<0.001
Eggs	5.87 ± 0.31	6.66 ± 0.36	7.76 ± 0.39	<0.001
Fish and shellfish	9.05 ± 0.16	18.03 ± 0.14	35.18 ± 0.66	<0.001
Seaweeds	0.53 ± 0.02	0.65 ± 0.02	0.83 ± 0.03	<0.001
Milk and dairy products	60.74 ± 3.04	58.65 ± 2.92	60.59 ± 2.82	0.969
Women				
Grains	420.68 ± 3.73	390.37 ± 3.74	352.63 ± 4.15	<0.001
Potatoes	9.37 ± 0.48	10.78 ± 0.57	11.78 ± 0.56	0.002
Sweet foods and sugars	5.96 ± 0.34	5.65 ± 0.3	5.41 ± 0.28	0.219
Legumes	13.47 ± 0.70	16.46 ± 0.58	18.49 ± 0.60	<0.001
Nuts and seeds	0.55 ± 0.10	0.62 ± 0.07	0.86 ± 0.11	0.018
Fruits	148.20 ± 4.71	175.98 ± 5.72	198.19 ± 5.82	<0.001
Vegetables	36.90 ± 1.09	45.56 ± 1.14	59.33 ± 1.68	<0.001
Mushrooms	4.23 ± 0.33	5.06 ± 0.26	6.63 ± 0.32	<0.001
Meats	15.11 ± 0.65	17.41 ± 0.65	21.37 ± 0.78	<0.001
Eggs	5.92 ± 0.34	7.26 ± 0.38	7.35 ± 0.35	0.010
Fish and shellfish	8.74 ± 0.18	17.83 ± 0.14	35.82 ± 0.90	<0.001
Seaweeds	0.68 ± 0.03	0.95 ± 0.04	1.10 ± 0.05	<0.001
Milk and dairy products	77.74 ± 3.86	84.47 ± 3.75	89.12 ± 3.83	0.040

Values are expressed as the mean ± SE.
[†] *P*-values for trends were calculated by treating the median value of each tertile as a continuous variable in the general linear model.

was negatively associated with grain intake in both sexes (p-trend <0.001). Among men, participants exhibiting higher seafood consumption demonstrated a lower consumption of sweet foods and sugars (p-trend = 0.036). Nutrient intake according to seafood consumption is described in the Table S2.

3.3. Association between seafood consumption and the risk of poor sleep quality

After adjusting for potential confounders, seafood consumption was inversely associated with the risk of poor sleep quality among women. Further, a graded decrease in the HR for incident poor sleep quality was observed as seafood consumption increased (Table 3). Compared with participants in the lowest seafood consumption tertile, those in the highest yielded an HR and 95% CI of 0.66 (0.45–0.98) for poor sleep quality (p-trend = 0.032). Among men, seafood consumption was not significantly associated with the risk of poor sleep quality. The coefficients for all of the variables in the models are described in the Table S3-1 and 3-2.

3.4. Association between seafood consumption and the risk of poor sleep quality according to baseline hs-CRP level

In the inflammatory status-stratified analysis, the inverse association formerly observed in the main analysis appeared to be limited to participants with low hs-CRP levels (Table 4). An inverse association between seafood consumption and poor sleep quality was observed only among female participants with low hs-CRP levels (adjusted HR = 0.49; 95% CI: 0.28–0.86, p-trend = 0.015). No association was noted among male participants. The coefficients for all of the variables in the models are described in the Table S4-1 and 4-2.

4. Discussion

This prospective Korean population study examined the heterogeneous effect of seafood consumption on sleep quality with inflammatory status. After multivariable adjustments, we observed a lower risk of poor sleep quality among female participants who consumed more seafood. Moreover, only participants with low hs-CRP levels exhibited the beneficial effects of consuming seafood on sleep quality.

In our study, participants with higher seafood consumption had higher SES in terms of household income in both men and women. Previous studies have suggested that SES—as assessed based on income

Table 3
Hazard ratios and 95% confidence intervals for the risk of poor sleep quality according to seafood consumption.

	Seafood consumption			
	Tertile 1	Tertile 2	Tertile 3	*P*-trend
Men				
No. of cases	28	50	40	
Person-year	2,213.49	2,193.37	2,205.77	
Model 1*	1 (reference)	1.76 (1.10–2.79)	1.40 (0.87–2.27)	0.323
Model 2†	1 (reference)	1.89 (1.18–3.03)	1.67 (0.99–2.81)	0.112
Women				
No. of cases	74	69	49	
Person-year	1,806.09	1,875.05	1,925.01	
Model 1	1 (reference)	0.86 (0.62–1.20)	0.60 (0.42–0.86)	0.004
Model 2	1 (reference)	0.94 (0.67–1.32)	0.66 (0.45–0.98)	0.032

HR, hazard ratio; CI, confidence interval.
* Model 1 was unadjusted.
† Model 2 for men was adjusted for age, BMI, current drinker, current smoker, physical activity, monthly income, marital status, fruit intake, and vegetable intake. Model 2 for women was adjusted for age, BMI, current drinker, current smoker, physical activity, monthly income, marital status, menopausal status, fruit intake, and vegetable intake.

Table 4
Association of seafood consumption with the risk of poor sleep quality according to hs-CRP level.

	Seafood consumption			
	Tertile 1	Tertile 2	Tertile 3	*P*-trend
Men				
Low hs-CRP level (<0.72 mg/L)				
No. of cases	15	23	18	
Person-year	1,102.98	1,104.35	1,124.79	
Model 1*	1 (reference)	1.52 (0.79−2.92)	1.15 (0.58−2.28)	0.834
Model 2†	1 (reference)	1.67 (0.85−3.27)	1.49 (0.71−3.18)	0.337
High hs-CRP level (≥0.72 mg/L)				
No. of cases	13	27	22	
Person-year	1,103.43	1,096.10	1,080.98	
Model 1	1 (reference)	2.01 (1.04−3.90)	1.69 (0.85−3.35)	0.269
Model 2	1 (reference)	2.13 (1.08−4.19)	1.85 (0.88−3.88)	0.216
Women				
Low hs-CRP (<0.61 mg/L)				
No. of cases	39	34	22	
Person-year	911.364	952.153	964.855	
Model 1	1 (reference)	0.70 (0.44−1.10)	0.47 (0.28−0.80)	0.006
Model 2	1 (reference)	0.71 (0.44−1.14)	0.49 (0.28−0.86)	0.015
High hs-CRP (≥0.61 mg/L)				
No. of cases	35	35	27	
Person-year	890.984	928.477	958.323	
Model 1	1 (reference)	1.06 (0.66−1.69)	0.75 (0.45−1.23)	0.224
Model 2	1 (reference)	1.21 (0.74−1.97)	0.90 (0.51−1.56)	0.645

HR, hazard ratio; CI, confidence interval; hs-CRP, high-sensitivity C-reactive protein.
The p-interaction was tested using the cross-product term between seafood consumption and hs-CRP.
* Model 1 was unadjusted.
† Model 2 for men was adjusted for age, BMI, current drinker, current smoker, physical activity, monthly income, marital status, fruit intake, and vegetable intake. Model 2 for women was adjusted for age, BMI, current drinker, current smoker, physical activity, monthly income, marital status, menopausal status, fruit intake, and vegetable intake.

level, education, and occupation—is closely related to diet quality [38,39]. A study analyzing the data of 511 participants from a large-scale online experiment reported that people of a lower SES tended to consume more unhealthy snacks, potentially equating to a 15–22% increase in energy intake [40]. A systematic review of the determinants of seafood consumption revealed a positive association between a higher income level and greater seafood consumption [36]. Considering that the influence of socioeconomic and demographic factors may result in different eating behaviors, thus affecting sleep quality, we adjusted for relevant confounders.

A key finding of this study is that seafood consumption was inversely associated with the risk of poor sleep quality among women. To date, only a few cross-sectional studies have directly examined this association, and to our knowledge, our study is the first prospective analyses. An inverse association between seafood consumption and poor sleep quality was reported in China [15], Japan [16], and Ecuador [17]. A nationally representative cross-sectional study of 12,930 US adults reported that lower intakes of seafood and plant proteins were associated with short sleep duration [41]. A cross-sectional study of 1270 Japanese male reported a greater prevalence of having healthier lifestyle behaviors, such as adequate sleep duration and sensation of deep sleep, among those with a higher weekly frequency of fish intake [42]. *N*-3 PUFAs, particularly EPA and DHA in seafoods are recognized as important contributors to the association between seafood consumption and the risk of poor sleep quality. Supplementation with DHA-rich oil improved actigraphic sleep efficiency and latency among healthy adult normal sleepers who did not habitually consume oily fish [43]. In a large, biomarker-based pooling project that included 12 large-scale studies from five nations, individuals with lower concentrations of extremely long-chain *n*-3 PUFAs were more likely to have poor sleep that exceeds the recommended duration [44]. Further, in a nationally representative sample of Americans, those with a considerably short sleep duration exhibited persistently lower levels of EPA, DHA, and total *n*-3 fatty acids than normal sleepers [45]. Regarding the above results, it might be suggested that higher intakes of *N*-3 PUFA, EPA, and DHA among participants with higher seafood consumption could partially explain the inverse association between seafood consumption and poor sleep quality.

In our results, participants with higher seafood consumption showed higher intakes of *N*-3 PUFA, EPA, and DHA, which were considered as the main bioactive components influencing sleep quality. The beneficial effects of seafood and its bioactive constituents on sleep quality may be explained by numerous mechanisms. Neurotransmitter-mediated neuroendocrine regulation plays an important role in the circadian sleep–wake cycle. *N*-3 PUFAs help regulate the production of neurohormones, such as serotonin and melatonin. In particular, the enzymatic transformation of serotonin into melatonin by aralkylamine N-acetyltransferase is supported by DHA [21] via its positive effects on membrane fluidity and serotonin levels in the prefrontal cortex, ultimately modulating the transition between sleep and wakefulness [46,47]. Besides these mechanisms, neuroinflammatory processes have been implicated in the maintenance of circadian function [48]. *N*-3 PUFAs decreased proinflammatory cytokine production, such as TNF-α and IL 1 beta (IL-1β), which are physiologically associated with diverse clinical conditions involving sleep disorders [49]. These anti-inflammatory actions of *n*-3 fatty acids included down-regulated expression of inflammatory cytokine genes and activation of the anti-inflammatory transcription factor [50]. Interconnected with above mechanisms, *n*-3 PUFAs lowered membrane content of arachidonic acid, which was released from the phospholipids through the action of phospholipase A2 enzymes, which are activated by inflammatory stimuli [50].

Besides *n*-3 PUFAs, seafood also represents a rich source of dietary antioxidants, such as vitamins, carotenoids, and flavonoids, which play a key role in the body defense system against reactive oxygen species (ROS) [51]. Fish consumption may contribute to improved sleep quality as oxidative stress, an imbalance between the production and scavenging of ROS by the antioxidant defense system, serves an essential role in sleep problems [52]. Moreover, the hypothalamus, a key brain region responsible for regulating sleep duration, is vulnerable to oxidative damages caused by excessive oxygen levels [53]. Antioxidants derived from fish consumption may exert neuroprotective effects on hypothalamus by mitigating ROS levels and preventing oxidative damage [54], and ultimately enchance sleep quality. Indeed, supporting our speculation, a systematic review of 5 cross-sectional, 1 case-control, and 1 prospective cohort studies reported an inverse association between the dietary total antioxidant capacity with sleep disorders and common mental disorders [55]. A cross-sectional study of women with type 2 diabetes found that those in the highest tertile of the dietary total antioxidant capacity-related score exhibit a 94% and 87% lower risk of poor sleep, compared to those in the lowest tertile [56].

The hs-CRP remains a widely used biomarker of inflammation suggesting that high hs-CRP levels are reflective of systematic and low-grade inflammation [32]. Therefore, we aimed to investigate the role of inflammatory status as a modulator of association between seafood consumption and sleep quality, using hs-CRP as an indicator. Our study revealed a significantly inverse association between seafood consumption and poor sleep quality exclusively among female participants with low hs-CRP levels. To the best of our knowledge, no study has examined the interactive effect of inflammatory status in the association between seafood consumption and sleep quality. Nonetheless, the results of several studies could support our findings, possibly suggesting the heterogeneous effect of *n*-3 PUFAs by inflammatory status. A post-hoc analysis, which investigated whether plasma total homocysteine (tHcy) levels—indicative of the induction of inflammatory determinants—modify the effects of n-3 fatty acid supplementation on cognitive performance and clinical status, revealed that n-3 fatty acid intake potentially improves both cognitive and clinical outcomes in patients with relatively low tHcy levels [57]. In chick embryos, exposure to elevated Hcy levels reduced DHA levels in membranes [58]. Moreover, embryonic exposure to high Hcy levels has been associated with reduced levels of brain phosphatidylcholine, which is a vital carrier molecule of DHA and EPA in the blood and across the blood-brain barrier [58,59]. Additionally, in a clinical randomized trial, participants with high hs-CRP or IL-1ra (high inflammation) levels exhibited a decrease in the effect size of EPA treatment on the Hamilton Depression Rating Scale score compared with those with low levels of these biomarkers [60]. Based on the foregoing findings, inflammatory status potentially modulates the effect of *n*-3 PUFAs. Therefore, in spite of sufficient *n*-3 PUFA intake from seafood, inflammation may impair the maintenance of *n*-3 PUFA levels and formation of their carriers, ultimately aggravating the risk of poor sleep quality in our study.

In this study, an inverse association of seafood consumption with poor sleep quality was observed only in women. No significant differences in the baseline hs-CRP level were noted between men and women, addressing concerns about misinterpretation due to differences in inflammatory background (Table S5). Sex hormones (e.g., estrogen and progesterone) are known to influence the activity of enzymes involved in PUFA synthesis [61]. A meta-analysis revealed lower DHA values in total plasma lipids and phospholipids among men than among women [62]. In addition, an intervention study examining whether women possess higher circulating DHA concentrations than men who consume the same diet demonstrated that DHA levels in plasma cholesteryl esters were higher in women than in men [63]. The effects of sex hormones, presumably estrogens, may induce an increase in DHA concentration in women by regulating DHA biosynthesis. Meanwhile, women had higher mean intakes of *N*-3 PUFAs, EPA and DHA, which were considered as the main bioactive components influencing sleep quality in our study (Table S6). Therefore, it might be suggested that these factors partially contribute to the favorable effects of seafood consumption on sleep quality among women.

A key strength of our study is its prospective study design of 6-year follow-up. Further, to our knowledge, this is the first study to investigate the interaction effects between seafood consumption and the level of hs-

CRP, a marker of inflammatory status, on sleep quality in Korean adults. Finally, we used a validated FFQ for the dietary assessment and could compare the differential association between seafood consumption and sleep quality by sex. Nonetheless, our study also has certain limitations. First, we were unable to evaluate the cumulative average intake of fish consumption over the course of the follow-up period, which may have attenuated the results of our study. Second, regarding the assessment of sleep quality, although the definition of poor sleep quality relied on a self-reported questionnaire, not objective tools such as actigraphy and polysomnography (PSG), the sleep efficiency and sleep latency of the PSG had correlations with the questionnaire component scores that were statistically significant. Finally, we cannot rule out chance or confounding by unmeasured factors such as caffeine intake, psychosocial stress, depression, and chronic disease conditions [64].

5. Conclusions

The consumption of seafood, which comprises fish, shellfish, and seaweed, was associated with a lower risk of poor sleep quality among Korean women. Moreover, this association was exclusively observed among women with low hs-CRP levels, suggesting that inflammatory status potentially modulates the favorable effects of seafood consumption on sleep quality. These findings may provide valuable insights for identifying individuals who are more likely to benefit from consuming seafood. Further investigations through large cohort studies with diverse populations are necessary to replicate our findings.

CRediT authorship contribution statement

Y.K. performed study conceptualization, funding acquisition, and supervision; Y.J. and Y.K. assisted with the study design, data analysis, and investigation; M.K. drafted the manuscript; S.J. and Y.K. critically reviewed and edited the manuscript. All authors have read and approved the final manuscript.

Data share statement

Data described in the manuscript, code book and analytic code will be made available upon request pending approval by the Korea Centers for Disease Control.

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Declaration of competing interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jnha.2025.100611.

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