Dietary Patterns and Breast Cancer Risk: A KCPS-II Cohort Study

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Abstract

Background: There have been inconsistencies in the evidence for a role of dietary risk factors in the development of breast cancer. In this study, we used a large-scale cohort (Korean Cancer Prevention Study-II [KCPS-II]) to examine the association between dietary patterns and breast cancer risk in Korean women.

Methods: The dietary patterns of 14,807 women from the KCPS-II were derived by factor analysis and 135 cases of breast cancer were diagnosed during the follow-up period. Cox proportional models were used to estimate the hazard ratios (HR) and 95% confidence intervals (CI) for the risk of breast cancer.

Results: The following three major dietary factors were identified: “Korean dietary pattern” (high intake of Kimchi, vegetables, and rice); “Sweet dietary pattern” (high intake of soda and sugar); and “Western-like dietary pattern” (high intake of dairy products, eggs, oil, fruits, and bread). After adjusting for potential confounders, neither the Korean (HR for the highest compared with the lowest tertile, 1.04; 95% CI 0.53–2.06) nor the Sweet dietary patterns were associated with the risk of breast cancer. In contrast, the Western-like dietary pattern was found to be significantly associated with an increased risk of breast cancer with an HR (95% CI) of 1.01 (0.65–1.60) for the second tertile and 1.61 (1.04–2.50) for the third tertile as compared with the lowest tertile. After stratifying by menopausal status, these effects were only statistically significant among premenopausal women for the third tertile, compared with those in the bottom tertile (HR 1.69; 95% CI 1.06–2.68; $p = 0.028$). No significant association was observed between the Korean or Sweet dietary pattern and breast cancer among either pre- or postmenopausal women.

Conclusions: Our findings revealed that a greater consumption of a Western-like diet was associated with an increased breast cancer risk and consequently offer a potential prevention strategy for Korean women.

Background

Breast cancer is one of the leading causes of death in women globally [1]. It was among the most commonly diagnosed types of cancer in Korean women: 22,300 new cases were reported by the Korea Central Cancer Registry in 2017 [2]. The age-specific incidence rate has been steadily increasing from 21.4 per 100,000 in 1999 to 55.6 per 100,000 in 2017 [2].

Although several epidemiologic studies have examined the association between nutrient intake and breast cancer risk [3], their results have been inconsistent [4-6]. Therefore, researchers have recently recognized the importance of identifying dietary patterns, following a holistic approach, rather than individual nutrients, in their contribution to chronic disease [7]; not only are such patterns practical tools for developing dietary recommendations but also a valuable method to determine risk factors and prevent disease simultaneously [8]. Recently, prospective epidemiologic studies have examined associations between certain dietary patterns and breast cancer risk [9-13]. However, most studies have been conducted in European populations, and only few studies have investigated this relationship in Asian populations [14, 15]. In addition, Zhang et al. [16] reported that a diet high in vegetables, fruits, and

soy could decrease the breast cancer risk, while Cui et al. [17] reported that this was not true for a vegetable-soy pattern, suggesting an inconsistency in results. Thus, this study aimed to identify dietary patterns and examine their association with the risk of developing breast cancer using a large-scale cohort study (Korean Cancer Prevention Study-II [KCPS-II]).

Methods

Study population

The KCPS-II is a prospective cohort study initiated in April 2004 supported by the Seoul city government as a part of the Korean Metabolic Syndrome Research Initiative study [18]. Participants received routine health assessments at 18 health promotion centers across South Korea. The number of retrospectively enrolled KCPS-II participants based on health examination records between 1994 and 2005 is 270,514; data from 192,358 participants was prospectively collected between 2004 and 2013. After excluding participants with missing information on lifestyle and dietary habits, as well as those who were male or had a history of breast cancer, a total of 14,807 participants were included for final analyses (Figure 1).

Our health examinations included questions on lifestyle, family, and personal medical history in addition to an assessment of anthropometric and clinical factors. General demographic and lifestyle variables including age, sex, education level, smoking status, and alcohol intake were collected by a standardized questionnaire; we also deployed a short version of the food-frequency questionnaire (FFQ). The Severance Medical Ethics Committee approved the study (no. 4-2011-0277), and all participants provided written, informed consent prior to participation.

Assessment of dietary intake and risk factors

A brief dietary assessment evaluated and validated in a previous study was used for estimating dietary patterns [19]. This assessment comprised a short version of the FFQ, which is suitable to identify relationships between dietary intake and disease risk [20]. It consists of 17 food items based on seven food groups: (1) fish, meat, eggs, and soybean products; (2) milk and dairy products; (3) vegetables; (4) fruits; (5) cereals and potatoes; (6) sugars and candies; and (7) fats and oil. Daily nutrient intakes were calculated based on food consumption: participants were asked to fill out the frequency of their current intake of each food item according to four categories (0: never, 0.5: often, 1.0: regular, 1.5: always sufficient). According to the food exchange list for Korea, portion sizes were estimated. Each participant's age, regular exercise habit (yes, no), alcohol intake (never, ex-drinkers, current drinkers), smoking status (never, ex-smokers, current smokers), menopausal status (yes, no), age at menarche, and the presence of family history of cancer (no, yes) were obtained using the questionnaire. The body mass index (kg/m^2) was calculated by dividing the body weight (kg) by the square of height (m).

Statistical analysis

General characteristics of study participants stratified by breast cancer incidence outcome were compared using Student's t-test and chi-square test. Cox proportional hazards model with person-years was used to evaluate the hazard ratio (HR) and 95% confidence interval (CI) of breast cancer risk for each three dietary factors. Principal factor analysis was used to cluster factors, followed by orthogonal (varimax) rotation to assist in interpretation of the factors (PROC FACTOR and VARIMAX options). The principal factor analysis requires the number of clusters to be specified in advance and generates mutually exclusive clusters by comparing Euclidean distances between each subject and each cluster center in an interactive process using a K-means method [19]. Food groups with an absolute loading greater than 0.3 on a given factor were considered to contribute importantly to that factor. We determined three factors based on a combination of eigenvalues, the scree plot test, and our derived factors. The final number of clusters was selected as 3-cluster by comparing between cluster variance and within-cluster variance ratios.

Results

The results derived from the factor loading matrix for major dietary patterns are depicted in Table 1. We extracted three major dietary factors from the KCPS-II cohort. Based on the predominant food groups, we labeled these three factors the "Korean dietary pattern," the "Sweet dietary pattern," and the "Western-like dietary pattern." The Korean pattern comprised a high content of meat, fish, tofu, herbs, vegetables, Kimchi, rice, bread, and noodles; the Sweet dietary pattern contained two food groups that consisted of sugar (honey) and soda; the Western-like pattern featured a high load of eggs, milk, dairy products, oil, bread, snacks, and fruits. The total variances of the Korean, Sweet, and Western-like dietary patterns were 1.9%, 1.6%, and 1.6%, respectively.

Table 2 summarizes the general characteristics of study participants stratified by breast cancer incidence. Among the total of 14,807 women included for final analysis, 135 were diagnosed with breast cancer during a mean follow-up of 8.15 years. Education, height, and smoking status showed statistically significant differences between non-breast cancer and breast cancer patients. Table 3 shows HRs between the three dietary patterns and breast cancer risk in multivariate analysis. The Western-like dietary pattern was significantly associated with an increased risk of breast cancer by HR (95% CI), which was 1.01 (0.65–1.60) for the second tertile and 1.61 (1.04–2.50) for the third tertile compared with the bottom tertile. However, the Korean and Sweet dietary patterns showed no statistically significant association with breast cancer risk in multivariate analysis.

Multivariable HRs of breast cancer according to menopausal status are shown in Table 4. In premenopausal women, multivariate HRs for the Western-like pattern were significantly associated with an increased risk of breast cancer; when comparing the highest with the lowest tertile of the Western-like dietary pattern, the HR was 1.69 (95% CI 1.06–2.68). However, this pattern showed no statistically significant association with breast cancer risk among postmenopausal women. In addition, the Korean and Sweet dietary patterns were not associated with the risk of breast cancer after adjusting for lifestyle

factors (smoking status, exercise, and alcohol drinking), total calorie intake, and age among either pre- or postmenopausal women.

Discussion

In our study we identified three major dietary patterns: Korean, Sweet, and Western-like. We found that a higher consumption of a Western-like diet was significantly associated with an increased risk of developing breast cancer. However, there were no associations between the Korean or the Sweet dietary pattern and breast cancer risk among Korean women.

Previous cohort studies on the association between dietary patterns and breast cancer risk have been predominantly conducted in European populations [9, 21, 22] and the results have been inconsistent. A recent meta-analysis suggested that a Western-like diet may be associated with an increased risk of breast cancer, whereas and a reduced risk could be attributed to a prudent dietary pattern [23]. However, another systematic review and meta-analysis found no evidence of an association between Western dietary patterns and breast cancer risk [24]. Dietary patterns are likely to vary among different populations due to cultural preferences, geographic characterization, socioeconomic status, and accessibility [25]. Besides, heterogeneity in components of dietary patterns and deviations in measurement methods between studies could have contributed to these inconsistent findings. In our study, we identified a Western-like dietary pattern, characterized by a high intake of dairy products, oil, bread, and fruit in Korean women, and high consumption according to this pattern was significantly associated with the risk of breast cancer. Based on our previous cohort study [19], the consumption of Korean traditional foods, such as vegetables and cereals, has decreased, whereas a new dietary pattern has emerged among Korean adults, whereby the intake of dairy products and fruits has increased. In the past, the traditional ingredients of a Korean diet consisted of grains, including rice and bean-based soup, as the main protein source. However, according to the statistics of Korea National Health and Nutrition Examination Survey (2010) [26], less than 40% of the protein intake is derived from animal sources. This may be influenced by Western-style breakfasts, which mainly consist of dairy products and eggs. It is important to note that the Western-like dietary pattern identified in our study differs from that in others in several aspects. Although among European populations this diet is characterized by a high intake of red and processed meats [24, 27], which may contain pro-carcinogenic factors, such as heterocyclic amines and N-nitroso compounds, the major components of the Western-like dietary pattern in this study were eggs, oil, bread, and dairy products. This pattern is consistent with that found in our previous study, in that the Western and “New” diets were characterized by a high consumption of eggs, oil, soda, fruits, dairy products, and potatoes using factor analysis in Korean women [19]. Thus, the current Korean diet has dramatically shifted from the traditional foods to a more Western-like dietary pattern, which along with the economic development and globalization supports our observations [28].

In addition, most prospective studies found significant associations between Western dietary patterns and breast cancer risk among postmenopausal [9, 10, 13, 29], but not premenopausal women, although the etiology is still unclear. In contrast, in the current study, stratified-analyses showed that the positive

association between a Western-like dietary pattern and breast cancer risk was statistically significant among premenopausal, but not postmenopausal women. Given one of the obvious differences between pre- and postmenopausal women, the elevated levels of estrogen may be one plausible explanation for the impact a Western-like dietary pattern has on the risk of developing breast cancer. A migration study of Asian-American women suggested that the dietary habits in early adult life may strongly affect breast cancer risk [30]. Further studies are needed to clarify the mechanism regarding the effect of menopausal status on breast cancer risk.

Although many epidemiologic studies investigating the association between vegetable intake and breast cancer risk yielded inconsistent results, prudent dietary patterns characterized by an intake of vegetables and fruits have been assumed to decrease the breast cancer risk due to anti-oxidative effects [31]. However, in this study, we found no significant association between the Korean dietary pattern, which was mainly characterized by high intake of Kimchi (spicy cabbage), rice, and vegetables, and breast cancer risk. This is in line with a prospective study among Japanese women, which identified three dietary patterns: “vegetable pattern” (vegetables, potatoes, seaweed, tofu, fruits, fresh fish, eggs, and miso soup); “animal food pattern” (meat, deep-fried foods, fried vegetables, fish paste, and salt-preserved fish); and “dairy product pattern” (milk, dairy products, fruits, coffee, and tea) [32]. The authors found that the animal food pattern was significantly associated with a decreased risk of breast cancer morbidity, whereas no significant association was observed between the vegetable and dairy product dietary patterns and breast cancer risk [15]. Furthermore, the World Cancer Research Fund also reported that no statistically significant association was found between vegetables (including fruits) and breast cancer [33]. However, a study examining Singapore Chinese women demonstrated that there was a dose-dependent trend of decreasing breast cancer risk for the vegetable-fruit-soy dietary pattern only among postmenopausal women [14]. Diversities exist among cooking methods or types of vegetables among each country, which may account for the differences observed between the various studies.

Our study has some limitations. First, breast cancer is a heterogeneous disease, and several studies have suggested that risk factors for breast cancer may differ in their association depending on tumor receptor status [13, 34]. Nevertheless, we were unable to consider the hormone receptor status since we had no data on the participants’ molecular subtype. Second, we used a shorter version of the FFQ at baseline, such that we could not consider the possibility that secular transitions in dietary patterns may have occurred during follow-up. Third, we could not exclude the possibility of errors in measuring dietary intake. The diet assessment tool included a limited number of food items, although the tool was validated and the correlation with 3-day diet records confirmed.

Conclusions

Our study found that a Western-like dietary pattern, characterized by high consumption of eggs, oil, dairy products, fruits, and bread, was associated with an increased risk of breast cancer among premenopausal women. In contrast, the Korean and Sweet dietary patterns were not associated with breast cancer risk. Large scale prospective studies in Asian women are needed to confirm our findings.

Abbreviations

CI: Confidence interval; HR: Hazard ratio; FFQ: food-frequency questionnaire; KCPS-II: Korean Cancer Prevention Study-II

Declarations

Ethics approval and consent to participate: The Severance Medical Ethics Committee approved the study (no. 4-2011-0277), and all participants provided written, informed consent prior to participation.

Consent for publication: Not applicable

Availability of data and materials: The datasets analyzed during the current study are not publicly available due to protection of participant privacy and confidentiality, and institution's policy, but may be made available in an anonymized form via the corresponding author on reasonable request after approval of institution.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions: S.H.J conceived the study and interpreted the data. J.Y.L. and H.I.C performed the main data analyses and drafted the initial manuscript. All authors were involved in the data generation or provision and read and approved the final manuscript.

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Tables

Table 1. Factor loading matrix for the three major dietary patterns (N=14,807)

Food group	Korean	Sweet	Western-like
Meat, fish, tofu	0.62407		
Egg			0.68750
Milk, dietary products			0.47546
Herbs, vegetables	0.65056		
Kimchi	0.73593		
Rice, bread, noodles	0.69294		
OIL			0.66155
Sugar, honey		0.83046	
Soda		0.82371	
Bread, snack			0.40228
Fruit			0.43916
Variance explained by each factor	1.9108947	1.6446474	1.5862974

*Factor loading scores less than 0.3 are not shown.

Table 2. General characteristics of study participants

	No breast cancer N=14,672	Incident breast cancer N=135	P value
	Mean (SD)	Mean (SD)	
Age (year)	46.39 (11.07)	46.97 (8.96)	0.4691
Education (year)	13.2 (3.51)	14.0 (3.25)	0.0083
Height (cm)	157.93 (5.49)	158.91 (5.66)	0.0456
Body Mass Index (kg/m^2)	23.04 (3.09)	22.79 (2.88)	0.3618
Family history of breast cancer (%)	3.21	0.00	0.5929
Age in years at menarche (year)	14.90 (1.86)	14.74 (1.99)	0.4662
Menopausal status (%)	6.70	8.15	0.5033
Alcohol amount (g)	5.16 (19.92)	7.79 (24.92)	0.2612
Smoking status (yes/no,%)	4.58	8.15	0.0491
Alcohol drinking (yes/no,%)	38.92	40.74	0.6654
Use of oral contraceptives (%)	17.77	22.81	0.3233
Total energy intake (kcal)	1,728 (311)	1,718 (303)	0.7153
Follow-up (years)	8.43 (4.73)	6.69 (4.51)	<.0001

Table 3. Breast cancer risk with multivariable Cox proportional hazard model

Variables		HR (95% CI)	P value
Age	year	1.04 (1.02-1.06)	0.0001
Education	year	1.09 (1.02-1.16)	0.0038
Smoking status	Never smokers	1.0	
	Ex-smokers	0.98 (0.43-2.25)	0.9641
	Current smokers	2.20 (1.16-4.19)	0.0163
Exercise	Yes	1.0	
	No	1.08 (0.76-1.54)	0.6672
Alcohol drinking	Never drinkers	1.0	
	Ex-drinkers	0.48 (0.15-1.52)	0.2121
	Current drinkers	1.18 (0.81-1.72)	0.3964
Dietary patterns			
Korean	Tertile 1	1.0	
	Tertile 2	1.17 (0.73-1.89)	0.5111
	Tertile 3	1.04 (0.53-2.06)	0.9063
Sweet	Tertile 1	1.0	
	Tertile 2	1.11 (0.72-1.71)	0.6286
	Tertile 3	1.13 (0.73-1.75)	0.5849
Western-like	Tertile 1	1.0	
	Tertile 2	1.01 (0.65-1.60)	0.9534
	Tertile 3	1.61 (1.04-2.50)	0.0337
Total calorie (kcal)	Per unit	1.00 (1.00-1.01)	0.8501
Menopause	No	1.0	
	Yes	0.65 (0.35-1.23)	0.1836

*HR: Hazard ratio, CI: Confidence interval

Table 4. Hazard ratio of breast cancer risk by menopausal status

Variables		HR (95% CI)	P value
Pre-menoposal			
Age	Year	1.04 (1.02-1.06)	<.0001
Education	Year	1.09 (1.03-1.17)	0.0060
Smoking status	Never smokers	1.0	
	Ex-smokers	1.02 (0.44-2.34)	0.9654
	Current smokers	2.00 (1.02-3.91)	0.0435
Exercise	Yes	1.0	
	No	1.13 (0.78-1.62)	0.5279
Alcohol drinking	Never drinkers	1.0	
	Ex-drinkers	0.56 (0.18-1.79)	0.3292
	Current drinkers	1.27 (0.86-1.89)	0.2293
Dietary patterns			
Korean	Tertile 1	1.0	
	Tertile 2	1.12 (0.68-1.83)	0.6655
	Tertile 3	0.98 (0.48-1.98)	0.9456
Sweet	Tertile 1	1.0	
	Tertile 2	1.01 (0.64-1.59)	0.9604
	Tertile 3	1.13 (0.72-1.78)	0.5909
Western-like	Tertile 1	1.0	
	Tertile 2	1.09 (0.67-1.75)	0.7373
	Tertile 3	1.69 (1.06-2.68)	0.0280
Total calorie (kcal)	Per unit	1.00 (1.00-1.00)	0.7917
Post-menopausal			
Age	Year	1.03 (0.95-1.11)	0.5169
Education	Year	1.14 (0.93-1.39)	0.2162
Smoking status	Never smokers	1.0	
	Ex-smokers	NE	NE
	Current smokers	14.74 (1.15-189.73)	0.0390
Exercise	Yes	1.0	
	No	0.70 (0.18-2.69)	0.6022
Alcohol drinking	Never drinkers	1.0	
	Ex-drinkers	NE	NE
	Current drinkers	0.38 (0.06-2.24)	0.2850
Dietary patterns			
Korean	Tertile 1	1.0	
	Tertile 2	4.35 (0.42-44.90)	0.2176
	Tertile 3	3.61 (0.21-63.34)	0.3803
Sweet food	Tertile 1	1.0	
	Tertile 2	2.68 (0.64-11.27)	0.1788
	Tertile 3	0.87 (0.14-5.65)	0.8860
Western-like	Tertile 1	1.0	
	Tertile 2	0.68 (0.13-3.56)	0.6444
	Tertile 3	1.34 (0.33-5.42)	0.6814
Total calorie (kcal)	Per unit	1.00 (1.00-1.00)	0.6755

*HR: Hazard ratio, CI: Confidence interval

Figures

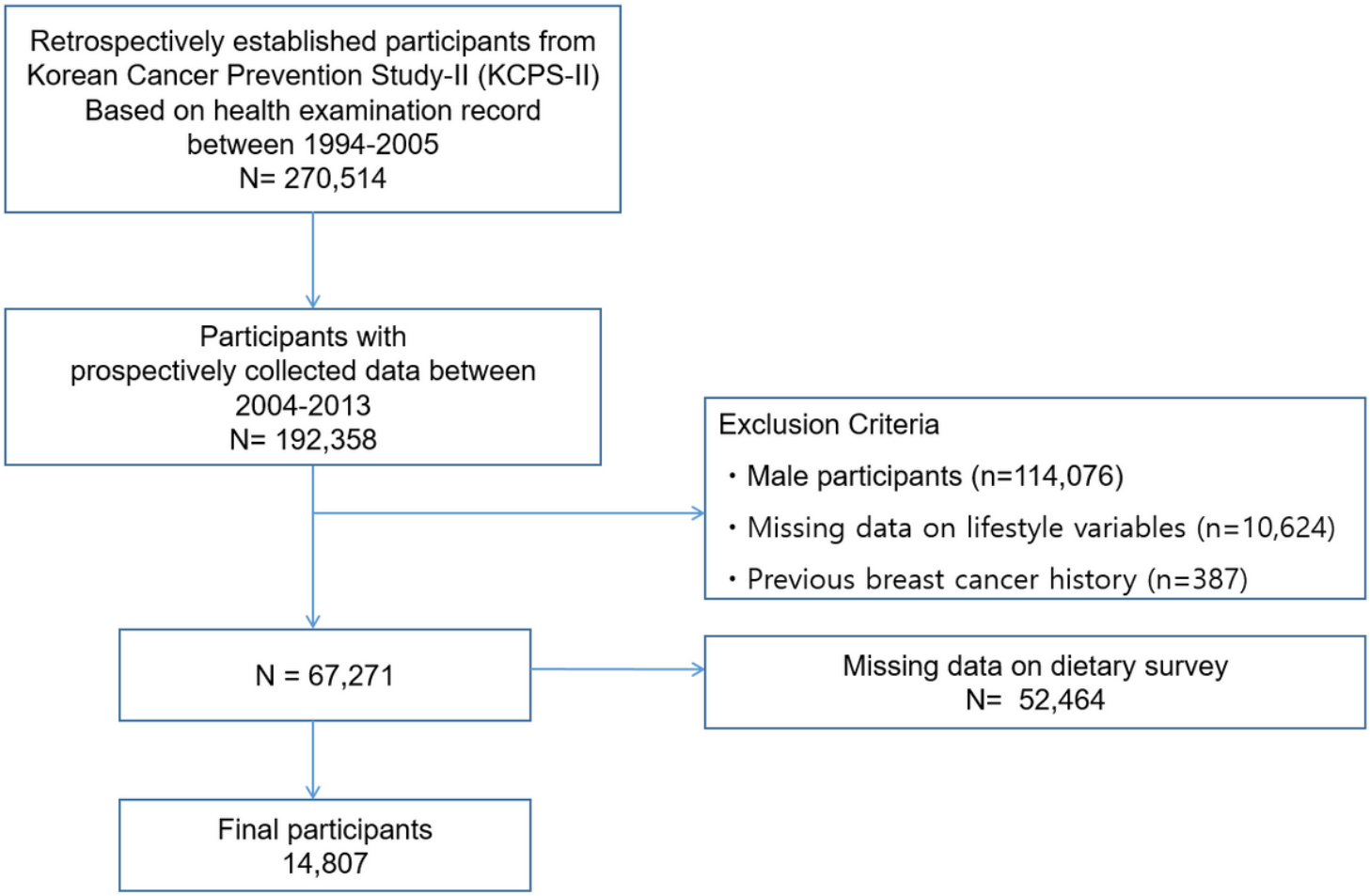

Figure 1

Flow diagram for study participants