Higher frequency of dairy intake is associated with a reduced risk of breast cancer: Results from a case-control study in Northern and Eastern China

LIXIANG YU[1,2], LIYUAN LIU[1,2], FEI WANG[1,2], FEI ZHOU[1,2], YUJUAN XIANG[1,2], SHUYA HUANG[1,2], GENGSHEN YIN[1,2], YINGJIE ZHUO[1,2], ZHONGBING MA[1,2], QIANG ZHANG[1,2] and ZHIGANG YU[1-3]

[1]Department of Breast Surgery, The Second Hospital of Shandong University;
[2]Institute of Translational Medicine of Breast Disease Prevention and Treatment, Shandong University, Jinan, Shandong 250033; [3]Suzhou Institute, Shandong University, Suzhou, Jiangsu 215123, P.R. China

Abstract. The association between dairy intake and breast cancer risk has not been well investigated, especially in the Chinese population. This study aimed to examine the association between the weekly frequency of dairy intake and the risk of breast cancer among women in Northern and Eastern China, and to investigate whether the association varied by hormone receptor status. A total of 1,286 cases of breast cancer and 1,461 controls were enrolled in this study. Dairy intake was obtained using a food-frequency questionnaire (FFQ). Frequency of dairy intake per week was divided into four categories (<1 day/week, 1-2 days/week, 3-4 days/week and 5-7 days/week). Unconditional multivariate logistic regression analysis was used to estimate odds ratios (ORs) and 95% confidence intervals (95% CI). Stratified analyses were performed by residence, age, and education level. Separate analyses were also conducted for different estrogen receptor (ER) and progesterone receptor (PR) status. This analysis revealed that weekly frequency of dairy intake was strongly inversely associated with breast cancer risk, with an adjusted OR for intake 5-7 days/week of 0.53 (95% CI=0.39-0.72, P<0.001 for trend). In the stratified analyses, women who consumed dairy 5-7 days/week had a lower risk of breast cancer in urban areas (OR=0.45, 95% CI=0.30-0.66, P<0.001 for trend), in the group 45-59 years old (OR=0.39, 95% CI=0.26-0.60, P<0.001 for trend), and in the group educated to senior high school or above (OR=0.39, 95% CI=0.25-0.59, P<0.001 for trend). There was an inverse association between the weekly frequency of dairy intake and the risk of ER[+], PR[+], and ER[+]PR[+] breast cancer (all P<0.001 for trend). These results indicated that the weekly frequency of dairy intake was inversely associated with the risk of breast cancer among women in Northern and Eastern China.

Introduction

Worldwide, breast cancer is the most common cancer among women, with 1.67 million people diagnosed with breast cancer in 2012 (1). Although the incidence of breast cancer in China is historically low, it has been increasing twice as fast as that of the global rate in recent years (2-4). Breast cancer is a hormone-related malignancy; evidence suggests that hormone-related factors, such as obesity, parity, and the use of exogenous hormones, may affect the risk of breast cancer by increasing systemic exposure to hormones, which are modified by different hormone receptor status (5). Dairy may influence the risk of breast cancer through its effects on hormone levels (6), and it has been suggested that the correlation between dairy intake and the risk of breast cancer varies with hormone receptor status (7,8).

With the rapid development of China's economy, the average intake of dairy products in China has gradually increased (9), and it is important to study the associations between dairy intake and breast cancer risk in Chinese women. Despite numerous studies evaluating the relationship between dairy intake and the risk of breast cancer in recent decades, the results have been non-conclusive (10-12). A previous pooling analysis from eight prospective cohort studies failed to detect significant associations between dairy intake and breast cancer risk (13); however, two recent meta-analyses suggested that compared with low dairy consumption, high dairy intake was associated with a reduced risk of breast cancer (12,14). Dairy intake is likely to vary among different populations with varying geography, culture, socioeconomic status, and lifestyle habits. Nevertheless, most studies have been conducted in the United States or Northern Europe, with only two case-control studies reported in China (7,15). Therefore, the relationship between dairy intake and the risk of breast cancer in Chinese women requires further exploration.

Correspondence to: Professor Zhigang Yu, Department of Breast Surgery, The Second Hospital of Shandong University, 247 Beiyuan Street, Tianqiao, Jinan, Shandong 250033, P.R. China
E-mail: yuzhigang@sdu.edu.cn

In order to better understand the characteristics and risk factors for breast cancer in Chinese women, a large case-control study including 21 hospitals in Northern and Eastern China was conducted between April 2012 and April 2013. Using data from a food-frequency questionnaire (FFQ), we aimed to find the relationship between the frequency of dairy intake and breast cancer risk in Chinese women, and whether the association varied by hormone receptor status was also investigated.

Patients and methods

Study population. The detailed study methods for this case-control study have been described in previous studies (16,17). The target population was female outpatients with breast cancer aged 25-70 years from 21 hospitals in 11 provinces in Northern and Eastern China, from April 2012 to April 2013. Eligibility criteria for the case group were as follows: Newly diagnosed breast cancer (histologically confirmed), Han ethnic group, and females aged 25-70 years. Women who had recurrent or metastatic breast cancer and/or complications of other malignant tumors confirmed by clinical or pathological diagnosis were excluded from this group. The inclusion criteria for the control group were: Han ethnic group, having regular physical examinations or hospitalized at the same hospital with a similar visiting period (± 2 months), being of 1:1 matched age with the cases (± 3 years), negative physical examination results, negative ultrasound scans of breast and/or mammographic screening results, and no evidence or history of cancer. Patients who had neoplastic disease at any other site or other major chronic disease were excluded from the study.

Data collection. All participants completed face-to-face interviews based on a self-designed structured questionnaire after diagnosis, including basic demographic characteristics, reproductive factors, family history of breast cancer, and lifestyle habits, as described in a previous study (16). Dairy intake was obtained using a FFQ, which had also been used in a previous cross-sectional epidemiological survey (18). Participants were asked to recall their usual frequency of dairy intake per week in the 1-year period before diagnosis. The frequency of dairy intake per week was divided into four categories (<1 day/week, 1-2 days/week, 3-4 days/week, and 5-7 days/week). Medical and pathology records from the hospital where the patient was originally diagnosed were reviewed to obtain information on estrogen receptor (ER) and progesterone receptor (PR) status and other pathological results. Both ER and PR status were determined using immunohistochemical staining. Briefly, tissue specimens were sliced into 3-μm sections. Then, sections were deparaffinized with xylene, rehydrated through a graded alcohol series. After antigen retrieval and blocking the endogenous peroxidase, the sections were stained with antibodies to ER (1:100 dilution; cat. no. Kit-0012) and PR (1:100 dilution; cat. no. Kit-0013) (both Maxim Biotech Inc., Fuzhou, China) according to the manufacturer's instructions. Following incubation, the secondary antibody horseradish peroxidase-conjugated goat anti-rabbit IgG (1:50 dilution; cat. no. A0208; Beyotime Institute of Biotechnology, Haimen, China) was added to the samples. Color reactions were visualized using 3,3'-diaminobenzidine. ER and PR expression was scored by two pathologists. Cell nuclei exhibiting brown staining were classified as positive cells. The proportion of stained cells for each tumor was recorded. Positivity was defined as ≥1% of tumor cells with positive staining, according to the American Society of Clinical Oncology (ASCO)/College of American Pathologists (2010) recommendations. All participating hospitals had national quality certifications for pathological diagnosis.

There were 1,489 case-control sets that met the inclusion criteria. After excluding participants with inadequate information (case group: 173 without hormone status information and 30 without dairy information; control group: 28 without dairy information), 1,286 cases and 1,461 controls were included in this study. All participants provided written informed consent and the study was approved by the Institutional Review Board at the Second Hospital of Shandong University.

Quality control. Interviewers were selected from medical professionals or medical post-graduates. All interviewer candidates were required to complete standardized training and were certified to conduct independent surveys. To minimize recall bias, several similar questions were asked in different sections of the questionnaire. The questionnaires and forms were coded twice and were double-entered by different clerks. Inconsistent records were manually checked and corrected. EpiData 3.1 software (EpiData Association, Odense, Denmark) to check the logic and reasonable range of responses throughout the questionnaire to identify contradictory responses was also used.

Statistical analysis. The percentage of variables was used to compare the distribution in each group, and significant differences in categorical variables were determined using the Chi-Square test. Unconditional multivariate logistic regression analysis was used to estimate the odds ratios (ORs) and 95% confidence intervals (95% CIs) of dairy intake, using intake of <1 day/week as the reference. According to the literature, the following variables of breast cancer risk factors were included as covariates: Residence (urban, rural), age (25-44, 45-59, 60-70 years), education (junior high school or lower, senior high school or above), family monthly income (<5,000, ≥5,000 RMB), body mass index (BMI) (<24.0, ≥24.0 kg/m^2), age of menarche (≤12, 13-14, 15-16, ≥17 years), number of births (0, 1, 2, ≥3), age at first childbirth (<20, 20-24, 25-29, 30-35, ≥35 years), breast-feeding (no, yes), menopausal status (premenopausal, postmenopausal), family history of breast cancer in first-degree relatives (no, yes), cigarette smoking (never, sometimes, often), alcohol drinking (never, sometimes, often), and physical activity (never, sometimes, often). Tests for trend were performed by treating the categorical variables as continuous variables in the models. Since the concept of healthy eating was likely to vary among populations with differing levels of urbanization, ages, and education, stratified analyses were performed by residence, age, and education level. Separate analyses were also conducted by different hormone receptor status (ER$^+$, ER$^-$, PR$^+$, PR$^-$, ER$^+$PR$^+$, and ER$^-$PR$^-$), and the Wald test was used to evaluate heterogeneity across cancer subtypes. All data analyses were performed using SPSS software (version 16.0; SPSS Inc., Chicago, IL, USA). All statistical tests were two sided, and P<0.05 was considered to indicate statistical significance.

Table I. Characteristics of case and control groups.

Variables	Control (%)	Case (%)	χ^2	P-value
Residence			47.14	<0.001
Rural	510 (37.14)	617 (50.53)		
Urban	863 (62.86)	604 (49.47)		
Age, years			4.58	0.101
25-44	588 (40.25)	467 (36.31)		
45-59	751 (51.40)	700 (54.43)		
60-70	122 (8.35)	119 (9.25)		
Education			42.98	<0.001
Junior high school or lower	578 (40.93)	669 (53.65)		
Senior high school or above	834 (59.07)	578 (46.35)		
Monthly family income, RMB			28.03	<0.001
<5,000	946 (66.71)	954 (76.02)		
≥5,000	472 (33.29)	301 (23.98)		
BMI			1.59	0.207
<24	687 (50.29)	576 (47.80)		
≥24	679 (49.71)	629 (52.20)		
Age of menarche, years			9.40	0.024
≤12	116 (8.06)	103 (8.17)		
13-14	669 (46.49)	571 (45.32)		
15-16	459 (31.90)	364 (28.89)		
≥17	195 (13.55)	222 (17.62)		
Number of births			56.73	<0.001
0	40 (2.78)	27 (2.13)		
1	871 (60.44)	613 (48.38)		
2	419 (29.08)	439 (34.65)		
≥3	111 (7.70)	188 (14.84)		
Age at first childbirth, years[a]			4.13	0.389
<20	31 (2.27)	40 (3.31)		
20-24	584 (42.75)	530 (43.91)		
25-29	679 (49.71)	577 (47.80)		
30-35	61 (4.47)	54 (4.47)		
≥35	11 (0.81)	6 (0.50)		
Breast-feeding			0.67	0.412
No	111 (7.94)	109 (8.83)		
Yes	1,287 (92.06)	1,126 (91.17)		
Menopausal status			8.61	0.003
Premenopausal	988 (70.42)	813 (65.09)		
Postmenopausal	415 (29.58)	436 (34.91)		
History of breast cancer in first-degree relatives			3.25	0.072
No	1,368 (97.30)	1,190 (96.05)		
Yes	38 (2.70)	49 (3.95)		
Cigarette smoking			5.91	0.052
Never	1,427 (97.87)	1,238 (96.42)		
Sometimes	17 (1.17)	21 (1.64)		
Often	14 (0.96)	25 (1.95)		
Alcohol drinking			2.57	0.277
Never	1,278 (87.59)	1,096 (85.65)		
Sometimes	169 (11.58)	171 (13.35)		
Often	12 (0.82)	14 (1.09)		

Table I. Continued.

Variables	Control (%)	Case (%)	χ^2	P-value
Physical activity			5.59	0.061
Never	410 (28.20)	364 (28.44)		
Sometimes	663 (45.60)	534 (41.72)		
Often	381 (26.20)	382 (29.84)		
Hormone receptor status			-	-
ER$^+$	-	977 (75.97)		
ER$^-$	-	309 (24.03)		
PR$^+$	-	888 (69.05)		
PR$^-$	-	398 (30.95)		
ER$^+$PR$^+$	-	868 (67.50)		
ER$^-$PR$^-$	-	289 (22.47)		

[a]limited to participants who had children. BMI, body mass index; ER, estrogen receptor; PR, progesterone receptor.
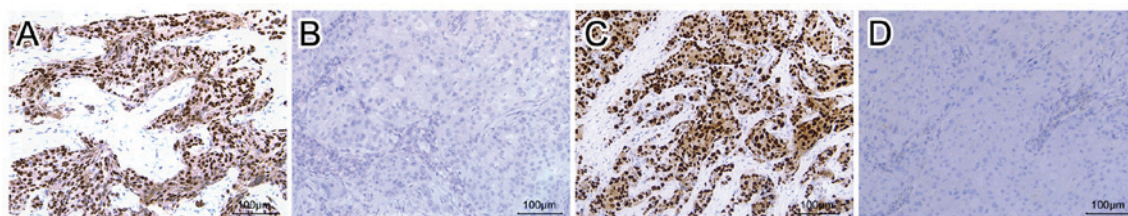

Figure 1. Schematic representation of the expression of ER and PR in breast cancer tissues by immunohistochemical staining (magnification, x200). Cells exhibiting brown staining were classified as positive cells. The positive cells were counted and the positive rate was calculated. Positive expression of ER and PR was defined as ≥1% of tumor cells with positive staining, and negative expression was defined as <1% of tumor cells with positive staining. (A) ER$^+$, (B) ER$^-$, (C) PR$^+$ and (D) PR$^-$. ER, estrogen receptor; PR, progesterone receptor.

Results

Overall descriptive characteristics. A total of 1,286 cases of breast cancer and 1,461 controls were enrolled in this study. Among 1,286 cases of breast cancer, 977 (75.97%) cases were ER$^+$ breast cancer, 888 (69.05%) cases were PR$^+$, 868 (67.50%) cases were ER$^+$PR$^+$, and 289 (22.47%) cases were ER$^-$PR$^-$. Since there was limited data for ER$^+$PR$^-$ (109 cases, 8.48%) and ER$^-$PR$^+$ (20 cases, 1.56%) breast cancer, no further analysis was conducted. The schematic representation of positive or negative expression of ER and PR by immunohistochemical staining is presented in Fig. 1. Basic demographic information of the case and control groups is presented in Table I. In this analysis, there was no significant difference in age, BMI, age at first childbirth, breast-feeding, family history of breast cancer in first-degree relatives, cigarette smoking, alcohol drinking, and physical activity between case and control groups (all P>0.05). The case group had a higher proportion of participants from a rural population, and also had lower education levels and family income (all P<0.001). The data also indicated that the case group had an earlier age of menarche, greater number of births, and a higher proportion of postmenopausal participants (all P<0.05) (Table I).

Weekly frequency of dairy intake and risk of breast cancer in different subgroups. The relationships between the weekly frequency of dairy intake and the risk of breast cancer combined in different subgroups are presented in Table II. The weekly frequency of dairy intake was significantly and inversely associated with breast cancer risk. Compared with women who consumed dairy <1 day/week, women who consumed dairy 3-4 days/week had a 31% reduction in breast cancer (OR=0.69, 95% CI=0.53-0.90), and those who consumed dairy 5-7 days/week had a 47% reduction in breast cancer (OR=0.53, 95% CI=0.39-0.72, P<0.001 for trend). In the stratified analyses, women who consumed dairy 5-7 days/week had a lower risk of breast cancer in urban areas (OR=0.45, 95% CI=0.30-0.66, P<0.001 for trend), in the group 45-59 years old (OR=0.39, 95% CI=0.26-0.60, P<0.001 for trend) and in the group with a senior high school education or above (OR=0.39, 95% CI=0.25-0.59, P<0.001 for trend). No significant associations were found for weekly frequency of dairy intake and breast cancer risk for those in rural areas, those aged 60-70 years old, and in those with a junior high school education or lower (all P>0.05 for trend; Table II).

Weekly frequency of dairy intake and risk of breast cancer in different hormone receptor status cases. When stratified by different hormone receptor subtypes (ER$^+$, ER$^-$, PR$^+$, PR$^-$, ER$^+$PR$^+$, and ER$^-$PR$^-$), there was an inverse association between the weekly frequency of dairy intake and the risk of ER$^+$, PR$^+$, and ER$^+$PR$^+$ breast cancer (all P<0.001 for trend).

Table II. Frequency of dairy intake and risk of breast cancer in different subgroups.

Subjects	Dairy intake, days/week				Trend P-value
	<1	1-2	3-4	5-7	
Total					
Controls	332	432	405	292	
Cases	391	434	296	165	
OR (95% CI)[a]	1[b]	0.91 (0.72-1.16)	0.69 (0.53-0.90)	0.53 (0.39-0.72)	<0.001
Residence					
Rural					
Cases	223	225	121	48	
OR (95% CI)[a]	1[b]	1.13 (0.81-1.59)	0.86 (0.58-1.28)	0.67 (0.39-1.16)	0.138
Urban					
Cases	151	189	157	107	
OR (95% CI)[a]	1[b]	0.74 (0.52-1.06)	0.56 (0.39-0.81)	0.45 (0.30-0.66)	<0.001
Age, years					
25-44					
Cases	133	166	113	55	
OR (95% CI)[a]	1[b]	1.03 (0.69-1.53)	0.73 (0.48-1.12)	0.66 (0.40-1.10)	0.043
45-59					
Cases	229	226	153	92	
OR (95% CI)[a]	1[b]	0.82 (0.59-1.13)	0.67 (0.46-0.97)	0.39 (0.26-0.60)	<0.001
60-70					
Cases	29	42	30	18	
OR (95% CI)[a]	1[b]	1.27 (0.47-3.43)	0.89 (0.31-2.50)	1.12 (0.32-3.89)	0.900
Education					
Junior high school or lower					
Cases	260	230	127	52	
OR (95% CI)[a]	1[b]	1.07 (0.78-1.47)	0.83 (0.57-1.20)	0.69 (0.43-1.13)	0.106
Senior high school or above					
Cases	124	195	154	105	
OR (95% CI)[a]	1[b]	0.70 (0.48-1.03)	0.51 (0.34-0.76)	0.39 (0.25-0.59)	<0.001

[a]Adjusted for residence (urban, rural), age (25-44, 45-59, 60-70 years), education (junior high school or lower, senior high school or above), family monthly income (<5,000, ≥50,00 RMB), body mass index (<24.0, ≥24.0 kg/m^2), age of menarche (≤12, 13-14, 15-16, ≥17 years), number of births (0, 1, 2, ≥3), age at first childbirth (<20, 20-24, 25-29, 30-35, ≥35 years), breast-feeding (no, yes), menopausal status (premenopausal, postmenopausal), family history of breast cancer in first degree relatives (no, yes), cigarette smoking (never, sometimes, often), alcohol drinking (never, sometimes, often) and physical activity (never, sometimes, often). For the stratified analyses, the stratification variable was excluded from the model. [b]Reference for calculating OR. OR, odds ratio; CI, confidence interval.

No significant associations were found between weekly dairy intake and the risk of ER⁻, PR⁻, and ER⁻PR⁻ breast cancer (all P>0.05 for trend). In addition, no statistically significant heterogeneity was found in the risk estimates for the frequency of dairy intake between the different hormone receptor subtypes (all P>0.05 for heterogeneity; Table III).

Discussion

In the present case-control study, the weekly frequency of dairy intake had a strong inverse association with the risk of breast cancer overall, especially among women in urban areas, women with a senior high school education or above, and women aged 45-59 years old in Northern and Eastern China. When analyses were performed by different hormone receptor status, significantly inverse associations were found between the weekly frequency of dairy intake and the risk of hormone receptor-positive (ER⁺, PR⁺, and ER⁺PR⁺) breast cancer, but not for hormone receptor-negative breast cancer. However, this conclusion should be considered with caution. It is important to take into account that there were fewer documented receptor-negative breast cancers, and that the Wald test revealed no detected differences between positive and negative receptor breast cancers.

Dairy intake has been thought to be associated with the development of breast cancer (19), yet, to date, epidemiological evidence is inconsistent. Several large epidemiologic studies have failed to demonstrate a relationship between dairy intake

Table III. Frequency of dairy intake and risk of breast cancer in different hormone receptor status cases.

Subjects	Dairy intake, days/week				Trend P-value	Heterogeneity P-value[a]
	<1	1-2	3-4	5-7		
Controls	332	432	405	292		
ER[+]						
Cases	313	311	225	128		
OR (95% CI)[b]	1[c]	0.83 (0.64-1.07)	0.66 (0.50-0.87)	0.51 (0.36-0.70)	<0.001	0.158
ER[-]						
Cases	78	123	71	37		
OR (95% CI)[b]	1[c]	1.37 (0.92-2.05)	0.870 (0.55-1.38)	0.68 (0.40-1.15)	0.052	
PR[+]						
Cases	278	290	204	116		
OR (95% CI)[b]	1[c]	0.84 (0.64-1.09)	0.64 (0.48-0.85)	0.49 (0.35-0.68)	<0.001	0.412
PR[-]						
Cases	113	144	92	49		
OR (95% CI)[b]	1[c]	1.18 (0.82-1.69)	0.88 (0.58-1.32)	0.69 (0.43-1.11)	0.066	
ER[+]PR[+]						
Cases	275	282	196	115		
OR (95% CI)[b]	1[c]	0.83 (0.64-1.07)	0.62 (0.46-0.82)	0.49 (0.35-0.69)	<0.001	0.220
ER[-]PR[-]						
Cases	75	115	63	36		
OR (95% CI)[b]	1[c]	1.33 (0.89-2.01)	0.78 (0.48-1.27)	0.71 (0.41-1.22)	0.060	

[a]Heterogeneity between ER[+] and ER[-]; PR[+] and PR[-]; ER[+]PR[+] and ER[-]PR[-]. [b]Adjusted for residence (urban, rural), age (25-44, 45-59, 60-70 years), education (junior high school or lower, senior high school or above), family monthly income (<5,000, ≥5,000 RMB), body mass index (<24.0, ≥24.0 kg/m^2), age of menarche (≤12, 13-14, 15-16, ≥17 years), number of births (0, 1, 2, ≥3), age at first childbirth (<20, 20-24, 25-29, 30-35, ≥35 years), breast-feeding (no, yes), menopausal status (premenopausal, postmenopausal), family history of breast cancer in first degree relatives (no, yes), cigarette smoking (never, sometimes, often), alcohol drinking (never, sometimes, often) and physical activity (never, sometimes, often). [c]Reference for calculating OR. OR, odds ratio; CI, confidence interval; ER, estrogen receptor; PR, progesterone receptor.

and breast cancer (10,12). However, a recent meta-analysis conducted by Zang *et al* (12), including 22 prospective cohort studies (1,566,940 participants) and five case-control studies (33,372 participants), revealed that high and modest dairy intake significantly reduced the risk of breast cancer compared with low dairy consumption. To date, these studies, especially the cohort studies, have mainly been conducted in Western countries. A meta-analysis of five case-control studies from Asia indicated that higher dairy or milk intake was associated with a 27% reduction in breast cancer risk, but only two studies were performed in the Chinese population (8). In the present study, dairy intake was associated with a reduced risk of breast cancer among women in Northern and Eastern China. Dairy foods are rich in vitamin D and calcium, and have been hypothesized to have an anti-carcinogenic effect on cell differentiation, proliferation, and anti-apoptosis (19,20). In the present study, a significant relationship was revealed between dairy intake and the risk of breast cancer among women in urban areas and with an education level of senior high school or above, but not in rural areas and those with a lower education level. This was likely because the concept of healthy eating is associated with urbanization and education levels, and high-quality diets are more often consumed by

urban and better educated people (21,22); these diets include foods such as yogurt, and have had a better effect on breast cancer prevention (23). It was observed that dairy intake was a significant protective factor for breast cancer among women aged 45-59 years old. Research has revealed that the peak of incidence rate of breast cancer in Chinese women is in the group aged 45-59 years (2). The frequency of dairy intake in this group was not more than other groups in the present study and some studies have revealed that this group had the lowest frequency of dairy intake among the Chinese population (9). This was an interesting finding and may indicate that dairy may have a stronger protective effect among women aged 45-59 years old in China. If confirmed, this could have important implications for breast cancer prevention strategies.

To the best of our knowledge, a limited number of studies have shown the potential relationship between dairy intake and breast cancer by different hormone receptor status. In the Malmo Diet and Cancer cohort, regular milk and yogurt were associated with protective linear risk trends for ER[+]PR[+] breast cancer (23). A population-based case-control study (The Shanghai Breast Cancer Study) conducted by Bao *et al* (7) revealed that milk intake was associated with a reduced risk of ER[+]PR[+] breast cancer, which was similar to the present

findings. However, a cohort study of African-American women found null associations for dairy intake and risk of ER+PR+ breast cancer (11). It had been thought that the risk factors associated with hormone-receptor positive breast cancer mainly involved hormonal mechanisms related to estrogen and progesterone exposure, and Wirfalt *et al* (23) hypothesized that the protective association between fermented milk and ER+PR+ breast cancer possibly implies a hormone-dependent mechanism involving fiber and enterolactone. Enterolactone, a phytoestrogen formed in the gut, could modulate the activity of estrogen receptors and decrease estrogen exposure (24), and lactic acid bacteria from dairy products were involved in stabilizing the gut environment by suppressing pathological bacteria and lowering the pH in the gut, which was important for the production of enterolactone (25). However, the exact mechanism requires more investigation.

There are some limitations in the present study that need to be addressed. First, potential recall bias is one major limitation of this case-control study. The diet of participants from the previous year was used as the surrogate for overall exposure. Second, in this study the data of a previous case-control study was reanalyzed (16). The frequency of dairy intake per week was collected using a questionnaire that considered dietary exposure in the one-year period before the survey, but the dairy subtype and amount consumed were not assessed. Therefore, the association between the amount consumed or different dairy items (e.g., whole milk, low fat milk, yogurt) and breast cancer risk could not be analyzed. It is also important to explore the interaction between dairy intake and protein or lipid intake in breast cancer. However, protein and lipid intake were not collected in this study; thus, the interaction between dairy intake and protein or lipid intake in breast cancer could not be analyzed. Third, the small sample size was also one of the limitations in this study. A breast cancer cohort in China is currently being established by the authors, and the number of samples will be expanded in future research. Finally, significant inverse associations between the weekly frequency of dairy intake and the risk of hormone receptor-positive (ER+, PR+, and ER+PR+) breast cancer was revealed, but not in hormone receptor-negative breast cancer. However, this conclusion should be considered with caution. It is important to take into account that there were fewer receptor-negative breast cancers, and that no differences were detected using the Wald test between positive and negative receptor breast cancers. In the future, we aim to validate the protective effect of dairy intake in this study using a better-designed study.

In summary, it was observed that the weekly frequency of dairy intake was strongly inversely associated with breast cancer risk among women in Northern and Eastern China. Separate analyses by different hormone receptor status revealed that dairy intake was a protective factor for hormone receptor-positive (ER+, PR+, and ER+PR+) breast cancer. However, this conclusion should be considered with caution. The impact of dairy products on breast cancer risk may involve multiple factors, and different dietary components may also interact in the development of breast cancer. Future well-designed epidemiological studies, especially large cohort studies of Chinese women, are required to clarify the relevance of dairy intake to breast cancer risk.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

LY participated in the study design, population survey, and data interpretation, and drafted the manuscript. LL and FW supervised the study and analyzed the data. FZ, YX, SH, GY, YZ, ZM and QZ participated in the population survey and data collection. ZY was the chief designer of this study and wrote the final draft. All authors read and approved the manuscript and agree to be accountable for all aspects of the research in ensuring that the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics approval and consent to participate

All participants provided written informed consent and the study was approved by the Institutional Review Board at the Second Hospital of Shandong University.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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