

Milk and yogurt intake and breast cancer risk

A meta-analysis

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Abstract

Different patterns of milk and breast cancer rates across countries suggest that several components of milk could affect breast cancer risk. However, the components of diet are complex including milk that could potentially influence risk. Some milk products such as whole milk and cheese have a high fat content which may increase risk. Moreover, milk products may contain pesticides which have carcinogenic potential. In contrast, some contents of milk such as calcium and vitamin D have been hypothesized to reduce breast cancer risk. Therefore, we performed this meta-analysis to derive a more precise estimation of the association between dairy food intake and breast cancer risk. Using the data from 8 available publications, we examined low-fat/skim milk, whole milk, and yogurt in relation to risk of breast cancer by meta-analysis. Pooled odds ratio (OR) with 95% confidence interval (CI) was used to assess the association. However the results of all milk models and the available epidemiologic evidence do not support a strong association between the consumption of milk or milk products and breast cancer risk. Further studies with larger participants worldwide are needed to validate the relationship of dairy food intake and breast cancer.

Abbreviations: CI = confidence interval, EPIC = European Prospective Investigation into Cancer and Nutrition, OR = odds ratio, RR = relative risk.

Keywords: breast cancer, low-fat/skim milk, meta-analysis, whole milk, yogurt

1. Introduction

Breast cancer is the most common cancer type in women worldwide and is the main cause of cancer mortality in females in the world.^[1,2] Both breast cancer incidence and mortality rates have been increasing over the past 30 years for our limited understanding of breast cancer.^[3] The incidence of breast cancer is influenced by many factors such as exogenous hormone intake, diet, and alcohol. The association between dairy intake and breast risk has been analyzed in many epidemiological studies. A previous meta-analysis of 10 studies published from 1981 to 1990 reported a modest increase in breast cancer risk with higher milk consumption.^[4] However, inverse results were found in some recent studies.^[5–7] In addition, another review including 36 case-control and 10 cohort studies which analyzed the relationship of milk and milk products intakes and breast cancer suggested that the epidemiologic evidence does not support a significant relevance of milk or milk products and breast

cancer.^[8] Therefore, an available data analysis is needed to provide consistent evidence for an association between milk and milk products and breast cancer risk.

The purpose of this study is to assess the connection of intakes of milk and milk products (yogurt) and risk of breast cancer by a meta-analysis of case-control studies. This analysis was based on separately ingredients of milk, including low-fat/skim milk, whole milk, and yogurt. We based on the previous meta-analysis and extend more case-control studies to identify the relationship of milk or milk products intakes with breast cancer incidence.

2. Material and methods

2.1. Publication search

We searched the available studies in PubMed and Chinese biomedicine databases for related articles published in any language to June 2, 2009. For the computer searches we used the key words as follows: “dairy products” or “milk” combined with “breast cancer”. Case-control studies containing available data which showed the relationship of milk (low-fat/skim milk and whole milk) or yogurt intakes and incidence or mortality from breast cancer were selected. All results of these studies must be shown as an odds ratio (OR) or a relative risk (RR) and 95% confidence interval (CI).

2.2. Data extraction and classification

Study characteristics data showed the first author, publication year, location of the study, year of data collection, measure of exposure and range of exposure, odds ratio, and risk estimates with corresponding 95% CI.

2.3. Statistical analysis

The measure of effect is the OR and the corresponding 95% CI. We listed all results as OR for simplicity and quantified

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associations of milk and milk products intakes with breast cancer risk using random-effects models^[9] of OR comparing the highest with the lowest category. The summary OR estimates were obtained from random effects models^[9] which applied to the study-specific dose-response slopes.

The publication bias was assessed by an Egger linear regression asymmetry test and Begg-adjusted rank correlation test (funnel plot method) ($P < .05$ considered representative of statistical significance).^[10] All meta-analyses were carried out using Stata software (version 9.0; Stata Corporation, College Station, TX).

2.4. Ethical approval

Ethical approval was waived or not necessary. Because we did not make any clinical research in this manuscript, we just collected the data from available publications.

3. Results

3.1. Characteristics of studies for meta-analysis

In this meta-analysis, we examined 8 potential publications on the association between milk intake and breast cancer. Among the 8 studies, 2 were conducted in the United States, 1 each in French, the Netherlands, Norwegian, Finland, and Japan and another was from EPIC (European Prospective Investigation into Cancer and Nutrition). We separate the results by different milk styles, including low-fat/skim milk, whole milk, and yogurt.

3.2. Low-fat/skim milk

The association between low-fat/skim milk intake and breast cancer risk was identified in 3 studies. The intake and range of low-fat/skim milk of each study were listed in Table 1.^[6,11–17] The summary OR was 0.853 (95% CI=0.702–1.037, $P = .110$) (Table 2). The result suggested that no support for a role of low-fat/skim milk in the etiology of breast cancer.

3.3. Whole milk

Results from 8 studies on consumption of whole milk and breast cancer risk were analyzed. The intake and range of whole milk of each study were shown in Table 1. The overall OR was 0.951

Table 2

Summary ORs and 95% CI for breast cancer risk under different milk models.

Milk model	OR (95% CI) <i>P</i>	Begg test <i>P</i> value	Egger test <i>P</i> value
Low-fat/skim milk	0.853 (0.702–1.037).110	.602	.583
Whole milk	0.951 (0.800–1.132).572	.621	.272
Yogurt	0.900 (0.684–1.183).449	.497	.553

CI=confidence interval, OR=odds ratio.

(95% CI=0.800–1.132, $P = .572$) (Table 2). This result indicated that high intakes of whole milk had no effect on breast cancer.

3.4. Yogurt

The meta-analysis of yogurt consumption included 4 studies. The intake and range in each study of yogurt were shown in Table 1. The overall OR for high and low yogurt consumption was 0.900 (95% CI=0.684–1.183, $P = .449$) (Table 2). The result suggested that yogurt intake had no effect on the risk of breast cancer.

3.5. Publication bias

We evaluated publication bias by Egger test and Begg test. The results of the Egger test ($P > .05$), and the Begg test ($P > .05$) provided statistical evidence for funnel plot symmetry in the overall results, suggesting the absence of publication bias (Table 2).

4. Discussion

The published epidemiologic data do not provide consistent evidence for an association between the consumption of milk or milk products and breast cancer risk. However, among these data many factors must be considered. Moreover, assessment of dietary factor in relation to cancer risk is very difficult and affected by many potential biases. Several methods used in epidemiologic studies, such as food frequency questionnaires and diet records or food diaries, have shown only moderate reliability, and some misclassification of intake is also unavoidable.^[18,19] Therefore, different dietary assessment methods may produce different results. It is generally believed that most dietary

Table 1

The distribution and ORs (95% CI) for studies on 3 milk models and breast cancer.

Milk model	Author	Publication year (years of data collection)	Country	Measure of exposure and range of exposure	OR (95% CI)	References
Low-fat/skim milk	Pala	2009 (1992–2003)	European	> 210 g/d vs never/seldom	0.93 (0.87–1.01)	[11]
	Shin	2002 (1980–1996)	United States	> 1 glasses/d vs < never/seldom	0.72 (0.56–0.91)	[6]
	Männistö	1999 (1990–1995)	Finland	High vs low	0.90 (0.40–2.00)	[12]
Whole milk	Pala	2009 (1992–2003)	European	>150 g/d vs never/seldom	1.06 (0.97–1.15)	[11]
	Kesse-Guyot	2007 (1995–2003)	French	> 248 g/d vs < 25 g/d	0.95 (0.52–1.73)	[13]
	Shin	2002 (1980–1996)	United States	> 1 glasses/d vs never/seldom	0.80 (0.54–1.016)	[6]
	HJARTÅKER	2001 (1991–1992)	Norwegian	High vs low	0.51 (0.27–0.96)	[14]
	Männistö	1999 (1990–1995)	Finland	High vs low	2.20 (1.00–4.90)	[12]
	Byrne	1996 (1982–1984)	United States	> 7 glasses/wk vs < 7 glasses/wk	0.50 (0.10–2.10)	[15]
	Hirose	1995 (1988–1992)	Japan	Daily vs lowest	0.97 (0.79–1.20)	[16]
	van't Veer	1989 (1985–1987)	The Netherlands	> 225 g/d vs never/seldom	0.82 (0.43–1.57)	[17]
Yogurt	Kesse-Guyot	2007 (1995–2003)	French	> 125 g/d vs < 25 g/d	0.79 (0.41–1.53)	[13]
	Shin	2002 (1980–1996)	United States	> 4 servings/wk vs < never/seldom	0.95 (0.66–1.37)	[6]
	Männistö	1999 (1990–1995)	Finland	High vs low	1.20 (0.60–2.40)	[12]
	van't Veer	1989 (1985–1987)	The Netherlands	> 225 g/d vs < never/seldom	0.55 (0.24–1.27)	[17]

factors have relatively small effects on cancer risk and the inevitable misclassification of dietary variables increases the difficulty of detection in risk associated with consumption of milk products.

Consistently, in our meta-analysis no associations with breast cancer risk were identified for intake of low-fat/skim milk, whole milk, and yogurt. Another challenge when evaluating milk and milk products in relation to breast cancer risk is the correlation among nutrients in diet. Persons with high consumption of milk products may likely to consume large amounts of meat or other high fat foods that could also contribute to an increased risk of breast cancer.^[20] Although total energy intake is controlled for, it also difficult to completely separate the effects of milk intake from that of other dietary factors, including intake of various types of fat. Once again, it may be difficult to separate the effects of dairy products from those of other nutrients that alter breast cancer risk.

In addition, average intake varies should be considered between different populations such as a level of consumption that is defined as “low” in one population might be considered “high” in another population. For instance, in a Japanese study, daily intake of milk or milk products was identified as highest exposure category.^[21] While, in a study conducted in the United States, the reference category of the lowest exposure level was reported consuming ≤ 1 serving/d and the highest level was reported > 3 servings/d.^[6] In some cases, the investigators did not report the level of consumption within each quantile, which made it impossible to compare effects at similar levels of consumption across studies. Besides the challenges that are common to many studies of nutritional epidemiology, there are specific challenges related to evaluating milk products. A main hypothesis suggesting that dairy products may reduce breast cancer risk is based on vitamin D content of these products. In the United State, most manufacturers add vitamin D to many products, including milk and margarine. These differences suggest that studies from countries with different regulations and practices regarding vitamin D fortification are not strictly comparable. If vitamin D is the component of milk products that influences breast cancer risk, comparisons should take into account not only the milk products but also the level of vitamin D in milk products.

Generally, the epidemiology studies reviewed do not provide consistent evidence for an association between milk product consumption and breast cancer risk. In addition, some studies also suggest that certain types of fat, growth factors, or environmental contaminants found in milk could increase risk of breast cancer.

Another important question is the cow received bovine growth hormone thus potentially increasing insulin-like growth factors-1 levels in the milk which could in turn stimulate malignant cells to grow more rapidly.^[22] The data should analyze whether the milk was derived from cow’s receiving bovine growth hormone. We reviewed all the source of milk in those studies, but those studies did not mention sources of milk, and did not analyze the composition of milk. Therefore, additional studies that identify the association with certain hormonal and environmental factors may help to further understand the relationship of milk products and breast cancer risk. In conclusion, although several interesting hypotheses link milk product and breast cancer, the available epidemiologic evidence does not support a strong association between the milk/milk products and breast cancer risk.

Author contributions

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