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Review Article

Systematic review and meta-analysis suggest that dietary cholesterol intake increases risk of breast cancer



Changkun Li, Li Yang, Dongfeng Zhang, Wenjie Jiang*

Department of Epidemiology and Health Statistics, the Medical College of Qingdao University, No. 38 Dengzhou Rd, Qingdao, Shandong 266021, People's Republic of China

ARTICLE INFO

Article history:

Received 9 November 2015

Revised 7 April 2016

Accepted 23 April 2016

Keywords:

Dietary cholesterol

Breast cancer

Fat intake

Meta-analysis

Review

ABSTRACT

Several epidemiological investigations have been conducted to evaluate the relationship between dietary cholesterol intake and risk of breast cancer, but the results are inconsistent. This meta-analysis was performed to summarize the evidence from observational studies to test the hypothesis that dietary cholesterol intake increases the risk of breast cancer. PubMed, EMBASE, Web of Science, and China National Knowledge Infrastructure were searched for relevant articles published up to July 2015. Pooled relative risks were calculated with random effects model. Dose-response relationship was assessed by restricted cubic spline model. Overall, 9 articles involving 6 cohort studies and 3 case-control studies were included in this study. The pooled relative risk with 95% confidence intervals of breast cancer for the highest vs lowest category of dietary cholesterol intake was 1.29 (1.06–1.56). For dose-response analysis, a nonlinear relationship was found between dietary cholesterol and breast cancer, and the association became statistically significant when the cholesterol intake was greater than 370 mg/d. Results from this meta-analysis indicated that dietary cholesterol was associated with an increased risk of breast cancer.

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1. Introduction

Breast cancer is the second most common cancer in women worldwide, with about 1.7 million new cases diagnosed yearly, and remains the leading cause of cancer death among women in both the developed and developing world. Reproductive, hormonal factors and unhealthy lifestyles are considered as risk factors of breast cancer [1]. Furthermore, observational studies have indicated that obesity, as a potentially modifiable

risk factor, could increase the risk of breast cancer in women [2–4]. Because obesity is primarily diet induced and a comorbidity of hypercholesterolemia, a Western diet which is rich in fat and cholesterol may increase the risk of breast cancer [5,6]. Since the 1980s, many epidemiological studies have investigated the relation of high-fat/high-cholesterol diet and the risk of breast cancer. Although a pooled analysis of 7 cohort studies in 1996 showed no evidence of an association between total dietary cholesterol intake and the risk of breast cancer, recent

Abbreviations: 27HC, 27-hydroxycholesterol; BMI, body mass index; CI, confidence interval; RR, relative risk.

* Corresponding author. Tel: +86 532 82991712; fax: +86 532 83801449.

E-mail address: wenjie-jiang@126.com (W. Jiang).

<http://dx.doi.org/10.1016/j.nutres.2016.04.009>

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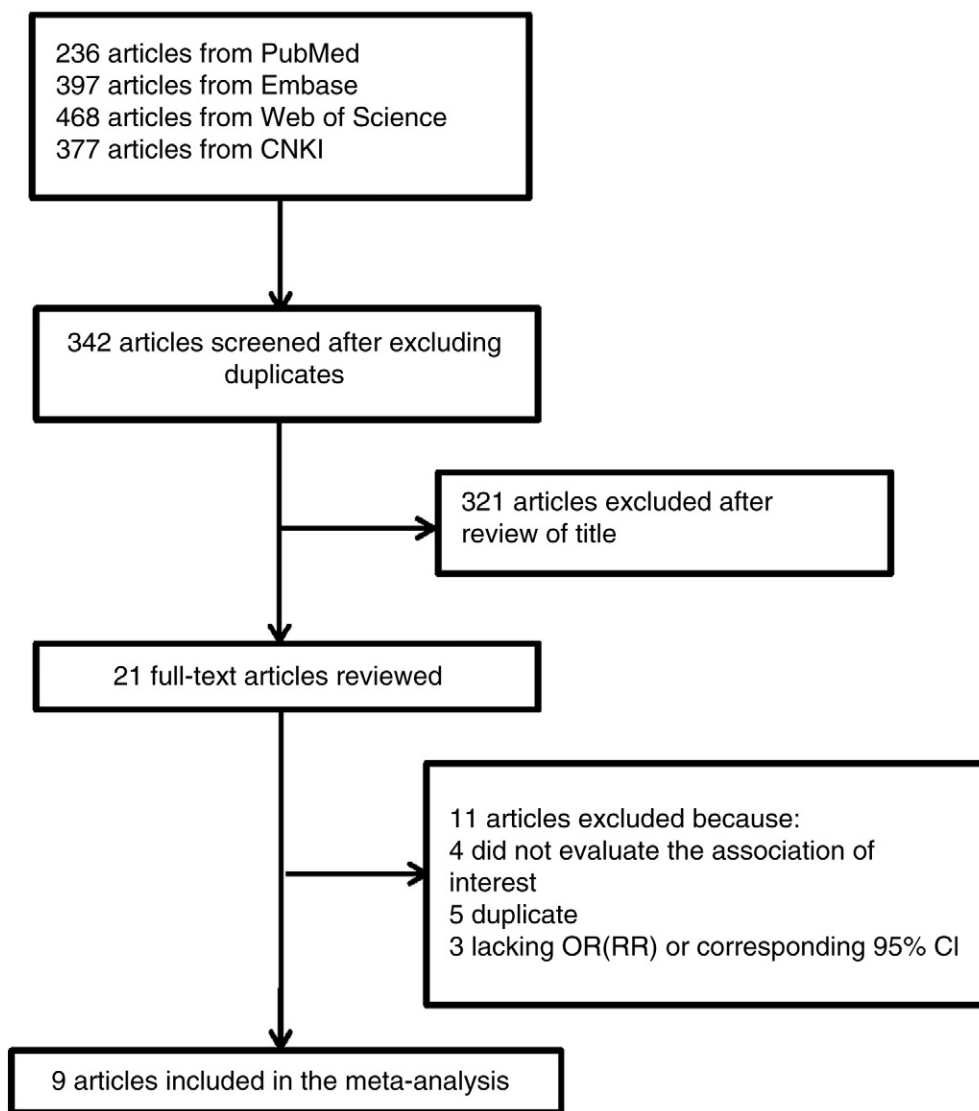


Fig. 1 – Flowchart of detailed steps of selection of studies.

studies from animal models found a link between high-fat/high-cholesterol diet and the development of breast cancer [7–9], and results from in vitro and in vivo studies indicated that 27-hydroxycholesterol (27HC), a cholesterol metabolite, could induce breast cancer [10]. However, recent epidemiologic evidence from cohort studies [11,12] and case-control studies [13–15] are inconsistent. In addition, the dose-response relationship of fat and cholesterol with breast cancer, which is the strong evidence for a causal relationship, is unknown.

To our best knowledge, no meta-analysis of dietary cholesterol intake and breast cancer has been published. Therefore, we reviewed observational studies including cohort studies [11,12,16–19] and case-control studies [13–15] to (1) first assess the breast cancer risk for the highest vs lowest dietary cholesterol consumption and then explore the potential dose-response relationship, (2) assess the potential between-study heterogeneity, and (3) investigate the potential publication bias. The hypothesis that dietary cholesterol intake could increase the risk of breast cancer was tested in

this study. The findings of the study might be meaningful for the possible prevention of breast cancer.

2. Methods and materials

2.1. Literature search strategy

A comprehensive literature search up to July 2015 was performed for pertinent available articles from the following databases: PubMed, EMBASE, Web of Science, and China National Knowledge Infrastructure. The following search terms were used without limitations: *breast cancer OR breast neoplasm OR breast carcinoma OR breast tumor* and *dietary cholesterol OR cholesterol intake OR cholesterol consumption OR fat intake*. Moreover, we also reviewed the reference lists of reviews and relevant articles to identify additional studies not captured by our database searches.

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