Clinical Nutrition 34 (2015) 635–641

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Meta-analyses

Egg consumption is associated with increased risk of ovarian cancer: Evidence from a meta-analysis of observational studies

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ARTICLE INFO

Article history:
Received 14 March 2014
Accepted 18 July 2014

Keywords:
Ovarian cancer
Egg
Dietary
Epidemiology
Meta-analysis

SUMMARY

Background: The findings of epidemiologic studies on the association between egg consumption and ovarian cancer risk remain conflicting. The aim of this meta-analysis was to investigate whether an association exists between egg intake and ovarian cancer risk in epidemiologic studies.
Methods: A literature search was carried out using PUBMED, EMBASE, and Cochrane Library Central database for all medical literature published in English-language journals up to August 2013. Before meta-analysis, between-study heterogeneity and publication bias were assessed using adequate statistical tests. Fixed-effect and random-effect models were used to estimate summary relative risks (RR) and the corresponding 95% confidence intervals (CIs). Subgroup analyses and sensitivity analysis were also performed.
Results: A total of 12 eligible studies (six case-control studies and six cohort studies) were included, involving 629,453 subjects and 3728 ovarian cancer cases. We found that high egg intake (comparing the highest with the lowest category) was associated with a significant increased risk of ovarian cancer (RR = 1.21, 95% CI [1.06, 1.38]). When we examined whether the associations differed by study type, statistically significant effect of egg intake on ovarian cancer was observed among case-control studies (RR = 1.22, 95% CI [1.03, 1.43]), but not among cohort studies (RR = 1.20, 95% CI [0.97, 1.48]).
Conclusions: Our findings suggest that egg consumption may increase ovarian cancer risk. Additional studies, especially large prospective cohort studies, are warranted to confirm the findings.

1. Introduction

Ovarian cancer is the sixth leading cause of cancer and the seventh most common cause of cancer death among women worldwide, however, the rates vary substantially by country [1]. The majority of cases are diagnosed with ovarian cancer at later stages [2]. Due to the current lack of availability of good screening methods for ovarian cancer and low survival rates among women diagnosed with disease at an advanced stage [3], identification of potentially modifiable factors contributing to its cause may help reduce the burden of this disease. Although the associations between oral contraceptive use, parity, and family history and ovarian cancer risk are well defined [4,5], the role of other factors, such as diet, remains controversial.

The association between egg consumption and ovarian cancer risk has received much attention since 1980s. Several observational studies had examined the impact of egg consumption on the development of ovarian cancer [6–17], however, their findings were controversial. The possible mechanism that may explain a possible detrimental effect of egg intake upon ovarian cancer risk involves the high cholesterol content of eggs, which could increase the formation of secondary bile acids in both humans and animals [18,19]. Previous meta-analyses have investigated the association between egg intake and the risk of several cancers [20–24]. However, to date, no quantitative assessment has been reported concerning the association between egg consumption and the risk of ovarian cancer. Hence, we performed a meta-analysis of observational studies to evaluate the effect of egg consumption on the risk of developing ovarian cancer.

2. Materials and methods

2.1. Data sources and searches

The present meta-analysis was conducted following the Preferred Reporting Items for Systematic reviews and Meta-

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http://dx.doi.org/10.1016/j.clnu.2014.07.009

Analyses guidelines (PRISMA) [25], and the meta-analysis of observational studies in epidemiology (MOOSE) guidelines [26]. A literature search was carried out using Pubmed, Embase, and Cochrane Library Central database for all medical literature published in English-language journals up to August 2013. Search terms included: "egg" or "diet" or "dietary" and "ovarian" or "ovary" and "cancer" or "neoplasm" or "malignancy". The reference lists of each comparative study included in this meta-analysis and previous reviews were manually examined to identify additional relevant studies.

2.2. Study selection criteria

Two reviewers independently selected eligible case-control and cohort studies that investigated egg intake and ovarian cancer risk. Disagreement between the two reviewers was settled by discussing with the third reviewer. Inclusion criteria were: (i) used a case-control or cohort study design; (ii) evaluated the association between egg intake and ovarian cancer risk; (iii) presented odds ratio (OR), relative risk (RR), or hazard ratio (HR) estimates with its 95% confidence interval (CI). When there were multiple publications from the same population, only data from the most recent report were included in the meta-analysis and the remaining were excluded.

2.3. Data extraction

The following data was collected by two reviewers independently using a purpose-designed form: name of first author, publishing time, country of the population studied, study design, study period, number of cancer cases and subjects, dietary assessment method, control source, the study-specific adjusted ORs, RRs, or HRs with their 95% CIs for the highest category of egg consumption versus the lowest, confounding factors for matching or adjustments.

2.4. Statistical analysis

The study-specific adjusted RRs were used as the common measure of association across studies. Because the absolute risk of ovarian cancer is low in humans, the ORs in case-control studies should approximate the RRs or HRs; therefore, we reported all results as RRs for simplicity. Heterogeneity was assessed using the Cochran Q and I^2 statistics. For the Q statistic, a P value<0.10 was considered statistically significant for heterogeneity; for the I^2 statistic, heterogeneity was interpreted as absent (I^2: 0%–25%), low (I^2: 25.1%–50%), moderate (I^2: 50.1%–75%), or high (I^2: 75.1%–100%) [27]. Subgroup analyses were carried out according to (i) study design (cohort studies versus case-control studies), (ii) geographic location (Europe versus North America versus Asia), (iii) control source (population-based versus hospital-based), (iv) number of adjustment factors ($n \geq 9$ versus $n \leq 8$), adjustment for smoking status (yes, no), adjustment for alcohol intake (yes, no), adjustment for BMI (yes, no), adjustment for oral contraceptive use (yes, no), adjustment for family history of ovarian cancer (yes, no), adjustment for parity (yes, no), adjustment for total energy intake (yes, no). Pooled RR estimates and corresponding 95% CIs were calculated using the inverse variance method. When substantial heterogeneity was detected ($I^2 \geq 50\%$), the summary estimate based on the random-effect model (DerSimonian-Laird method) [28] was reported, which assumes that the studies included in the meta-analysis had varying effect sizes. Otherwise, the summary estimate based on the fixed-effect model (the inverse variance method) [29] was reported, which assumes that the studies included in the meta-analysis had the same effect size. We carried out sensitivity analysis by excluding one study at a time to explore whether the results were strongly influenced by a specific study. Cumulative meta-analysis was also performed to identify the change in trend of reporting risk over time. In cumulative meta-analysis, studies were chronologically ordered by publication year, then the pooled RRs were obtained at the end of each year. Publication bias was assessed using Begg and Mazumdar adjusted rank correlation test and the Egger regression asymmetry test [30,31]. All analyses were performed using Stata version 11.0 (StataCorp, College Station, TX).

3. Results

3.1. Search results and characteristics of studies included in the meta-analysis

The process of study selection was shown in Fig. 1. The primary literature search identified 5654 citations. On the basis of the titles and abstracts, we identified 33 full-text articles. After further evaluation, 18 studies were excluded for lack of available data, and three studies were excluded for they were from the same population. At last, a total of 12 eligible studies published between 1984 and 2007 were identified, including six case-control studies [6,7,10,11,14,17] and six cohort studies [8,9,12,13,15,16] (Baseline data and other details of included studies are shown in Table 1). A total of 629,453 subjects, including 3728 ovarian cancer cases were involved. Of the 12 included studies, three studies were conducted in Europe [7,11,15], three studies in Asia [10,12,13], five studies in North America [6,8,14,16,17], and one study in Australia [9]. Most

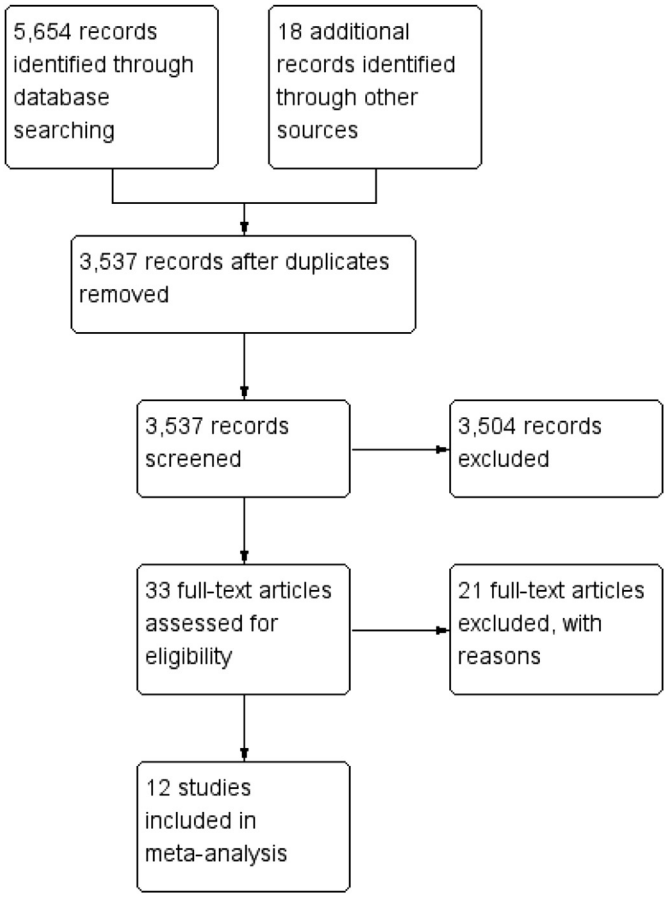

Fig. 1. Flow diagram of screened, excluded, and analysed publications.