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Original Article

Association between vegetables consumption and the risk of age-related cataract: a meta-analysis

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Abstract: Background: Quantification of the association between the consumption of vegetables and risk of age-related cataract is still conflicting. We therefore conducted a meta-analysis to summarize the evidence from epidemiological studies of vegetables consumption with the risk of age-related cataract. Methods: Pertinent studies were identified by searching of PubMed and Web of Science. The random effect model was used to combine the results. Meta-regression and subgroups analyses were used to explore potential sources of between-study heterogeneity. Publication bias was estimated using Egger's regression asymmetry test. Results: Finally, 9 articles involving 6,464 cataract cases and 112,447 participants were included in this meta-analysis. Pooled results suggested that highest vegetables consumption level compared with lowest level was inverse with the risk of age-related cataract [summary relative risk (RR) = 0.723, 95% CI = 0.594-0.879, I^2 = 72.8%]. The associations were also significant in America [summary RR = 0.872, 95% CI = 0.791-0.960] and Europe [summary RR = 0.507, 95% CI = 0.416-0.619], but not in the other population. No publication bias was found. Conclusions: Higher vegetables consumption might be inversely associated with risk of cataract.

Keywords: Vegetables, age-related cataract, meta-analysis

Introduction

Worldwide age-related cataract is the leading cause of low vision and blindness, accounting for almost half of all cases [1]. In Europe, cataract was found to be the principal cause of unilateral visual impairment, accounting for 50-65% of cases, as well as for 5-year incident bilateral visual impairment according to US criteria, accounting for 45% of cases [2]. Thus, identifying modifiable risk factors of cataract is important and may help to establish the preventive measures.

The recent studies had reported that antioxidant vitamins such as vitamin A, vitamin C and vitamin E may play an important role in cataract prevention [3-5]. These antioxidants cannot be synthesized by the body and must be obtained from dietary sources, mainly from vegetables. However, no meta-analysis was performed to assess this association. Up to now, a number of epidemiologic studies have been published to explore the relationship of vegetables with the risk of age-related cataract. However, the results are not consistent. Therefore, we conducted a meta-analysis to assess the cataract risk for the highest vs. lowest categories of vegetables consumption. We also assess the heterogeneity among studies and publication bias.

Methods

Search strategy

Studies were identified by a literature search of PubMed and Web of Knowledge through April 2015 and by hand-searching the reference lists of the computer retrieved articles. The following search terms were used: 'vegetable' or 'diet' combined with 'cataract' or 'lens opacities'. Two investigators searched articles and reviewed of all retrieved studies independently. Disagreements between the two investigators were resolved by consensus with a third reviewer.

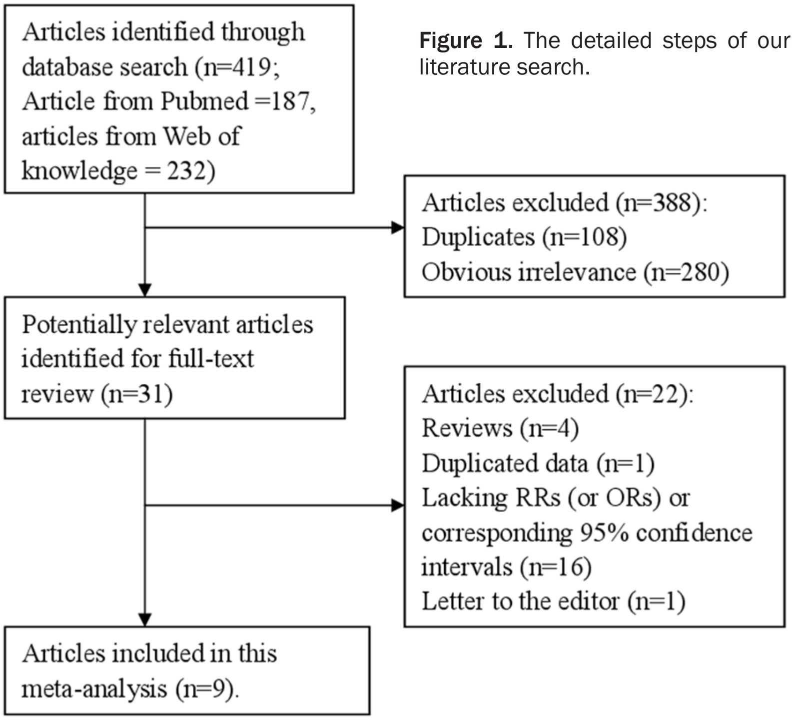

Figure 1. The detailed steps of our literature search.

Inclusion criteria

For inclusion, studies had to fulfill the following criteria: (1) have a prospective or case-control or cross-sectional design; (2) the exposure of interest was vegetables; (3) the outcome of interest was age-related cataract; (4) the subtype cataract was as an independent study when the total cataract was not observed; and (5) the relative risk (RR) with 95% confidence interval (CI) for vegetables consumption with risk of age-related cataract was provided. Accordingly, the following exclusion criteria were also used: (1) reviews and (2) repeated or overlapped publications.

Data extraction

The following data were collected from all studies independently by two investigators: the design type (case-control study, cohort study, cross-sectional study), the first author's last name, publication year, age range, location where the study was performed, sample size and number of cases, variables adjusted for in the analysis, RR (OR) estimates with corresponding 95% CI for the highest versus lowest categories of vegetables. For studies that reported results from various covariate analyses, we abstracted the estimates based on the model that included the most potential confounders. If there was disagreement between the two investigators about eligibility of the data, it was resolved by consensus with a third reviewer.

Statistical analysis

The pooled measure was calculated as the inverse variance-weighted mean of the natural logarithm of multivariate adjusted RR with 95% CI for vegetables consumption and age-related cataract risk. Random-effects model was used to combine study-specific RR (95% CI), which considers both within-study and between-study variation [6]. The Q test and I^2 of Higgins & Thompson [7] were used to assess heterogeneity among included studies. I^2 describes the proportion of total variation attributable to between-study heterogeneity as opposed to random error or chance, and I^2 values of 0, 25, 50 and 75% represent no, low, moderate and high heterogeneity, respectively [8]. Meta-regression with restricted maximum likelihood estimation was performed to assess the potentially important covariate exerting substantial impact on between-study heterogeneity [9]. Publication bias was estimated using Egger's regression asymmetry test [10]. A study of influence analysis [11] was conducted to describe how robust the pooled estimator is to removal of individual studies. An individual study is suspected of excessive influence, if the point estimate of its omitted analysis lies outside the 95% CI of the combined analysis. All the statistical analyses were performed with STATA version 10.0 (Stata Corporation, College Station, TX, USA). Two-tailed $P \leq 0.05$ was accepted as statistically significant.

Results

Search results and study characteristics

The search strategy identified 187 articles from Pubmed and 232 from the Web of Knowledge, and 31 articles were reviewed in full after reviewing the title/abstract. Twenty-two of

Table 1. Characteristics of studies on vegetables consumption and age-related cataract risk

First author, year	Country	Study design	Cases, age	RR (95% CI) for highest versus lowest category	Adjustment for covariates
Brown et al. 1999	United States	Cohort	824, 45-75	0.77 (0.61-0.97)	Adjusted for age, time period, diagnosis of diabetes, cigarette smoking, BMI, area of US residence, aspirin use, energy intake, physical activity, alcohol intake, routine eye exams, and profession
Christen et al. 2005	United States	Cohort	2067, ≥45	0.88 (0.74-1.04)	Adjusted for age, randomized treatment assignment, smoking, alcohol use, history of diabetes, history of hypertension, history of hypercholesterolemia, BMI, physical activity, parental history of myocardial infarction, menopausal status, postmenopausal hormone use, use of multivitamins or vitamin C supplements, total energy intake, and history of an eye exam in the past 2 y in Cox proportional hazards regression models
Christen et al. 2008	United States	Cohort	2030, ≥45	0.92 (0.80-1.06)	Adjusted for age, randomized treatment assignment, smoking, alcohol use, BMI, exercise, postmenopausal hormone use, history of hypertension, history of hypercholesterolemia, history of diabetes, family history of myocardial infarction before the age of 60, history of eye exam in the last 2 years
Lyle et al. 1999	United States	Cohort	246, 43-84	0.7 (0.4-1.2)	Adjusted for age, energy intake, and pack-years of smoking
Ojofeitimi et al. 1999	Nigeria	Case-control	31, 20-70	0.75 (0.39-1.11)	Adjusted for age and sex
Pastor-Valero et al. 2013	Spain	Cross-sectional	433, ≥65	0.54 (0.30-0.98)	Adjusted for sex, age, energy intake, marital status, smoking, alcohol consumption, physical activity, use of supplement, energy intake, obesity and history of diabetes
Tan et al. 2008	Australia	Cohort	312, ≥49	0.80 (0.34-1.89)	Adjusted for age, sex, hypertension, smoking, diabetes, education, use of inhaled steroids, and use of vitamin C supplements
Tavani et al. 1996	Italy	Case-control	207, 25-80	0.7 (0.4-1.1)	Adjusted for age, sex, education, smoking status, diabetes, body mass index, and calorie intake
Theodoropoulou et al. 2014	Greece	Case-control	314, 45-85	0.47 (0.38-0.59)	Adjusted for age, sex, body mass index, years of education, smoking habits and duration of smoking, and total energy intake

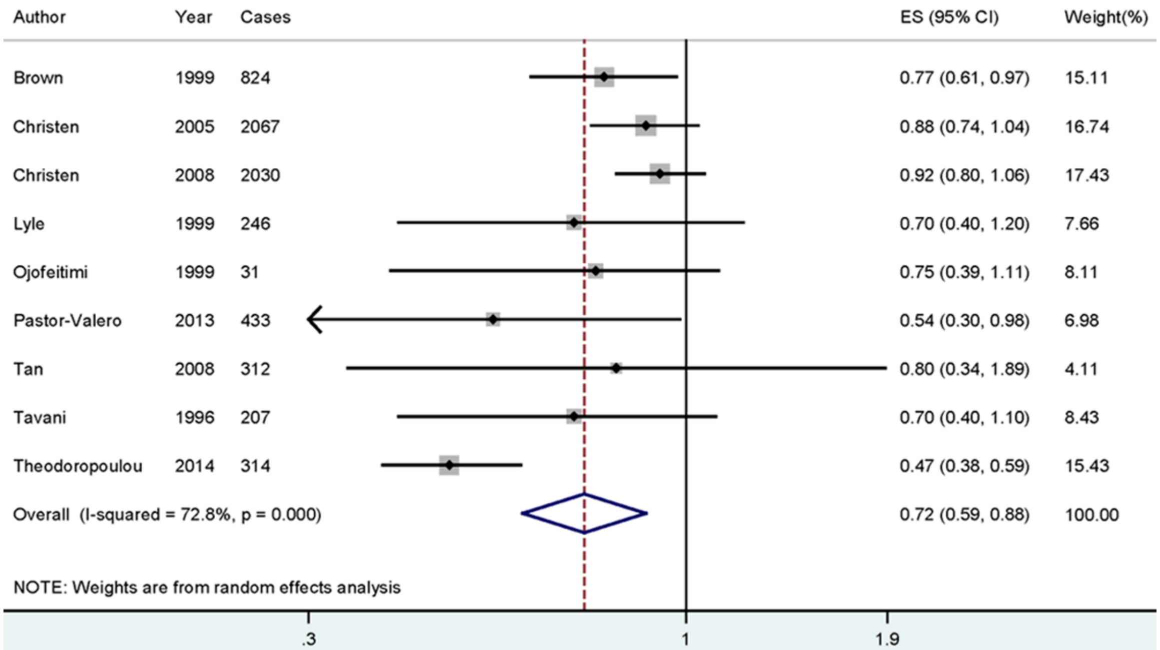

Figure 2. The multivariate-adjusted risk of age-related cataract for the highest versus lowest categories of vegetables consumption.

these 31 articles were subsequently excluded from the meta-analysis for various reasons. Hence, 9 articles [12-20] (5 cohort studies, 3 case-control studies and 1 cross-sectional study) involving 6,464 cataract cases and 112,447 participants were used in this meta-analysis. The detailed steps of our literature search are shown in **Figure 1**. The characteristics of these studies are presented in **Table 1**. Four studies were carried out in United States, 1 in Nigeria, 1 in Australia, 1 in Greece, 1 in Spain and 1 in Italy.

High versus low analyses

Three of included studies reported an inverse association between vegetables consumption and age-related cataract risk, while no significant association was reported in 6 studies. Our pooled results suggested that highest vegetables level versus lowest level was significantly associated with the risk of cataract [summary RR = 0.723, 95% CI = 0.594-0.879, I^2 = 72.8%] (**Figure 2**).

In stratified analysis by study design, the associations were also found both in the cohort studies [summary RR = 0.871, 95% CI = 0.791-0.959] and in the case-control studies [summary RR = 0.583, 95% CI = 0.420-0.809]. In subgroup analyses for geographic locations, highest vegetables level versus lowest level was significantly associated with the risk of age-related cataract in America [summary RR = 0.872, 95% CI = 0.791-0.960] and in Europe [summary RR = 0.507, 95% CI = 0.416-0.619], but not in the other countries. The details results are summarized in **Table 2**.

Sources of heterogeneity and meta-regression

As seen in **Figure 2**, evidence of heterogeneity (I^2 = 72.8%, $P_{heterogeneity}$ = 0.000) was found in the pooled results. In order to explore the moderate to high between-study heterogeneity founded in several analyses, univariate meta-regression with the covariates of publication year, location where the study was conducted, study design, number of cases and source of controls was performed. Geographic locations was found contributing significantly to the between-study heterogeneity overall (P = 0.02). No significant findings were found in the other analysis.

Influence analysis and publication bias

Influence analysis showed that no individual study had excessive influence on the association of vegetables consumption and cataract

Table 2. Summary risk estimates of the association between vegetables consumption and age-related cataract risk

Sub-groups	Cases	Studies	RR (95% CI)	I^2 (%)	$P_{heterogeneity}$
All studies	6464	9	0.723 (0.594-0.879)	72.8	0.000
Study design					
Cohort	5479	5	0.871 (0.791-0.959)	0.0	0.676
Case-control	552	3	0.583 (0.420-0.809)	18.4	0.135
Cross-sectional	433	1	--	--	--
Geographic locations					
America	5167	4	0.872 (0.791-0.960)	0.0	0.515
Europe	954	3	0.507 (0.416-0.619)	2.9	0.357
Others	343	2	0.763 (0.488-1.193)	0.0	0.900

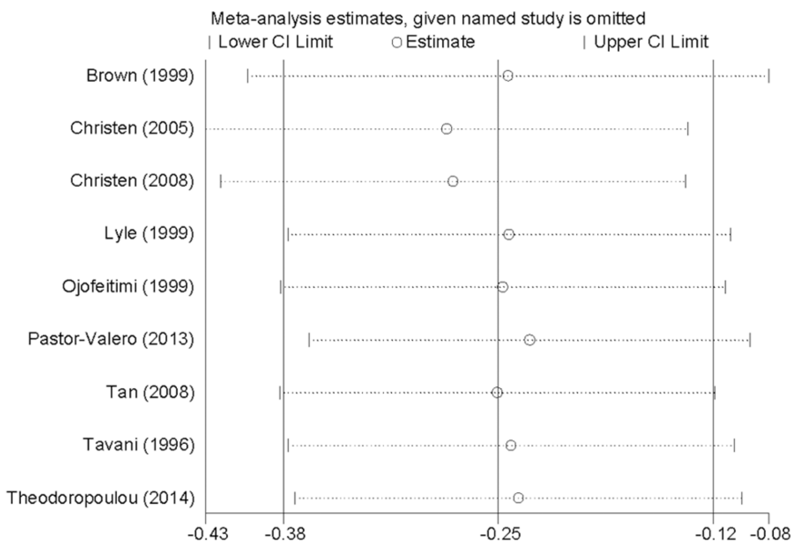

Figure 3. Analysis of influence of individual study on the pooled estimate in vegetables consumption and cataract risk. Open circle, the pooled RR, given named study is omitted. Horizontal lines represent the 95% CIs.

risk (**Figure 3**). Egger's test ($P = 0.345$) showed no evidence of significant publication bias between vegetables consumption and cataract risk.

Discussion

The findings from this meta-analysis indicate that higher vegetables consumption is associated with a reduced risk of cataract, especially in America and Europe. Inverse associations were also found both in cohort studies and case-control studies.

Antioxidants and dietary fibers might play a key role in the prevention of cataract development [21, 22]. The protective effects of vegetables and fruit are thought to be mediated by multiple components, including beta-carotene, fiber, vitamins, alpha-tocopherol, retinoids, phytoestrogens and folate [23]. These components are involved in numerous biological processes that may alter cataract risk, including the normal synthesis and methylation of DNA, and protection against oxidative stress and DNA damage [24].

Munafo and Flint reported that between-study heterogeneity is common in meta-analyses [25]. Exploring potential sources of between-study heterogeneity is therefore an essential component of meta-analysis. We found a high degree of heterogeneity ($I^2 = 72.8\%$, $P_{heterogeneity} = 0.000$) in our pooled results. This might have arisen from publication year, location where the study was conducted, study design and number of cases. Thus, we used meta-regression to explore the causes of heterogeneity for the above covariates. Geographic locations was found contributing significantly to the between-study heterogeneity overall (P = 0.02). No significant findings were found in the other analysis. We then performed subgroup analyses by the geographic locations. As seen in **Table 2**, the between-study heterogeneity is very low in the subgroup of America, Europe and other populations.

As a meta-analysis of published studies, our findings showed some advantages. First, this is the first comprehensive meta-analysis of vegetables consumption and cataract risk based on high versus low analysis meta-analysis. Second, large number of cases and participants were included, allowing a much greater possibility of reaching reasonable conclusions between vegetables consumption and cataract risk. Third, no significant publication bias was found, indicating that our results are stable. However, there were some limitations in this meta-analysis. First, as a meta-analysis of observational studies, we cannot rule out that individual studies may have failed to control for potential confounders, which may introduce bias in an unpredictable direction. Second, a meta-analysis of observational studies is susceptible to potential bias inherent in the original studies, especially for case-control studies. Overstated association may be expected from the case-control studies because of recall or selection bias, and early symptoms in patients may have resulted in a change in dietary habits. However, the significant associations were found both in the case-control studies and in the cohort studies. Third, we found significant associations between vegetables consumption and age-related cataract risk in the America and Europe, but not in the other populations. Only 1 study came from Nigeria and 1 from Australia, in which we found no significant association, probably due to the little number of studies included. Due to this limitation, the results are applicable to the America and Europe for vegetables and age-related cataract risk, but cannot be extended to the other populations. Fourth, although we combined the results with highest category of vegetables consumption versus lowest category, we did not do a dose-response analysis because of the limited data in the reported articles. Fifth, between-study heterogeneity was found in the pooled analysis in this meta-analysis, but the between-study heterogeneity was successfully explained by the subgroup analysis and meta-regression.

In summary, results from this meta-analysis suggested that higher vegetables consumption might reduce the risk of age-related cataract, especially among America and Europe populations. Since the potential biases and confounders could not be ruled out completely in this meta-analysis, further studies are warranted to confirm this result.

Disclosure of conflict of interest

None.

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