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Original Article

Fruit consumption and the risk of age-related cataract: a meta-analysis

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Abstract: The quantification association of fruit consumption and age-related cataract risk was still not clear. Therefore, we conducted a meta-analysis from epidemiological studies to summarize the relationship of fruit consumption with the risk of age-related cataract. PubMed and Web of Science were used to search pertinent studies. 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. Nine articles involving 6,464 cataract cases and 112,447 participants met inclusion criteria. A random effect model suggested that highest fruit consumption level could protect the age-related cataract [summary relative risk (RR) = 0.804 95% CI = 0.655-0.986, I^2 = 67.1%]. When compared with the lowest level of fruit consumption, the associations were also significant in Europe [summary RR = 0.603, 95% CI = 0.448-0.812, I^2 = 20.8%], but not in America [summary RR = 0.936, 95% CI = 0.808-1.086, I^2 = 42.4%] or the other population [summary RR = 0.373, 95% CI = 0.108-1.287, I^2 = 59.0%]. No publication bias was found. In summary, higher fruit consumption might decrease the risk of age-related cataract, especially in Europe.

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

Introduction

Worldwide, the prevalence of moderate to severe visual impairment and blindness is 285 millions [1]. More than 40% of low vision and blindness was caused by age-related cataract throughout the world, and the majority of people blind from cataract were found in the developing world [2]. Besides, the number of people blind from cataract is increasing due to changes in the demographic structure of populations, especially the increased life expectancy [3]. Thus, it is important to identify the protective factors for age-related cataract and may help to enhance the quality of life for older people.

Many studies had suggested that lutein and zeaxanthin or antioxidant vitamins, which are highly concentrated in fruits, may play an important role in cataract prevention [4-6]. Up to now, some researchers have done a lot of research on fruit consumption and age-related cataract risk and a number of epidemiologic studies have been published on this field. However, the results are not consistent. Therefore, we conducted a meta-analysis to summarize the relationship between the highest vs. lowest level of fruit intake and the cataract risk.

Materials and methods

Search strategy

Studies were identified by searching PubMed and Web of Knowledge up to October 2015 and by hand-searching the reference lists of included articles. The following search terms were used: 'fruit' or 'diet' combined with 'lens opacities' or 'cataract'. Two investigators performed the searching articles and reviewed the relevant references independently. The solution on final study selection was resolved by consensus with a third reviewer.

Inclusion criteria

For inclusion, study inclusion criteria were as follows: (1) have a prospective or case-control or cross-sectional design; (2) studies reporting any one of our major outcomes were included;

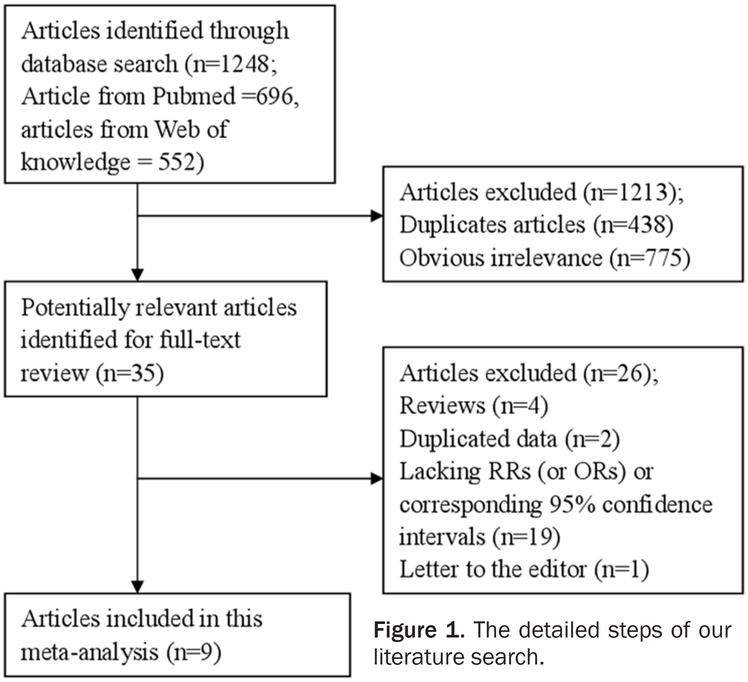

Figure 1. The detailed steps of our literature search.

(3) the relative risk (RR) with 95% confidence interval (CI) for highest fruit consumption versus lowest category with risk of age-related cataract was provided; and (4) the studies were written in English.

Accordingly, study exclusion criteria were as follows: (1) publication type is reviews or letter to the editor; (2) repeated or overlapped publications; (3) lacking RRs (or ORs) or corresponding 95% CIs.

Data extraction

Data were extracted from all included studies independently by two investigators using standardized data extraction tables: first author's name, publication year, study design type, age range, the country where the study performed, sample size and cases number, variables adjusted, RRs (or ORs) estimates with corresponding 95% CI for the highest versus lowest categories of fruit. The extracted data was checked by the third researchers.

Statistical analysis

Relative risk (RR) with 95% confidence interval (CI) was used to pool the outcomes of fruit consumption and age-related cataract risk. We used random-effects model for meta-analysis to combine study-specific RR (95% CI) [7]. Heterogeneity among included studies was assessed by the I^2 of Higgins & Thompson [8]. 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 [9]. We used meta-regression to assess the potentially important covariate exerting substantial impact on between-study heterogeneity [10]. Egger's regression asymmetry test [11] was used to visually examine publication bias at outcome level. A study of influence analysis [12] was conducted to describe how robust the pooled estimator is to removal of individual studies. The individual study is thought to produce excessive influence, if the point estimate lies outside the 95% CI of the combined analysis. We used STATA version 10.0 (Stata Corporation, College Station, TX, USA) for the meta-analysis. $P \leq 0.05$ (two-tailed) was accepted as statistically significant for computed effects.

Results

Search results and study characteristics

Six hundred ninety-six articles from PubMed and 552 from the Web of Knowledge were selected by our search strategy. After reviewing the title/abstract, 35 articles were reviewed in full, and 26 of which were subsequently excluded for various reasons. Ultimately, 9 articles [13-21] involving 6,464 cataract cases and 112,447 participants met inclusion criteria. Among these studies, five studies were in cohort design, 3 in case-control design and 1 in cross-sectional design. Four studies were carried out in America, 3 in Europe, 2 in other continents. The flow diagram for our literature search is shown in **Figure 1**. The characteristics of included studies are listed in **Table 1**.

High versus low analyses

For overall meta-analyses were to comparing highest fruit level versus lowest level and sub-

Table 1. Characteristics of studies on fruit 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
Tavani et al. (1996)	Italy	Case-control	207 (25-80)	0.9 (0.5-1.6)	Adjusted for age, sex, education, smoking status, diabetes, body mass index, and calorie intake.
Brown et al. (1999)	United States	Cohort	824 (45-75)	0.87 (0.68-1.11)	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.
Lyle et al. (1999)	United States	Cohort	246 (43-84)	1.8 (1.0-3.3)	Adjusted for age, energy intake, and pack-years of smoking.
Ojofeitimi et al. (1999)	Nigeria	Case-control	31 (20-70)	0.17 (0.02-0.34)	Adjusted for age and sex.
Christen et al. (2005)	United States	Cohort	2067 (≥45)	0.89 (0.75-1.06)	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)	0.93 (0.80-1.08)	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.
Tan et al. (2008)	Australia	Cohort	312 (≥49)	0.62 (0.28-1.37)	Adjusted for age, sex, hypertension, smoking, diabetes, education, use of inhaled steroids, and use of vitamin C supplements.
Pastor-Valero et al. (2013)	Spain	Cross-sectional	433 (≥65)	0.56 (0.31-1.03)	Adjusted for sex, age, energy intake, marital status, smoking, alcohol consumption, physical activity, use of supplement, energy intake, obesity and history of diabetes.
Theodoropoulou et al. (2014)	Greece	Case-control	314 (45-85)	0.53 (0.39-0.72)	Adjusted for age, sex, body mass index, years of education, smoking habits and duration of smoking, and total energy intake.

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

Subgroups	Cases	Studies	RR (95% CI)	I^2 (%)	$P_{heterogeneity}$
All studies	6464	9	0.804 (0.655-0.986)	67.1	0.002
Study design					
Cohort	5479	5	0.924 (0.800-1.067)	35.1	0.187
Case-control	552	3	0.553 (0.304-1.004)	62.9	0.068
Cross-sectional	433	1	--	--	--
Geographic locations					
Europe	954	3	0.603 (0.448-0.812)	20.8	0.283
America	5167	4	0.936 (0.808-1.086)	42.4	0.157
Others	343	2	0.373 (0.108-1.287)	59.0	0.118

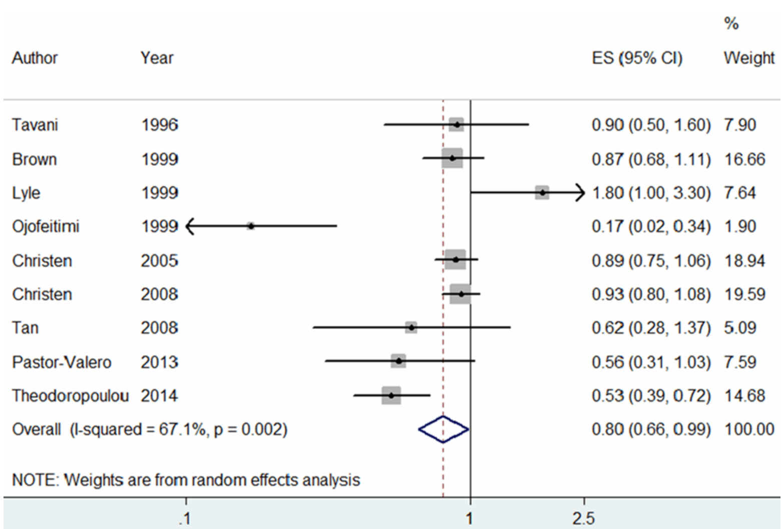

Figure 2. The multivariate-adjusted risk of age-related cataract for the highest versus lowest categories of fruit consumption.

groups analyses were conducted by different study design and geographic locations. The details summary risk estimates are summarized in **Table 2**. Forest plots for fruit consumption and age-related cataract risk in all studies are displayed in **Figure 2**.

Pooled results suggested that highest fruit level versus lowest level was significantly inverse associated with the risk of cataract [summary RR = 0.804 95% CI = 0.655-0.986, I^2 = 67.1%] (**Figure 2**). In subgroup analyses for geographic locations, highest fruit level versus lowest level was significantly inverse associated with the risk of age-related cataract in Europe [summary RR = 0.603, 95% CI = 0.448-0.812, I^2 = 20.8%], but not in America [summary RR = 0.936, 95% CI = 0.808-1.086, I^2 = 42.4%] or the other population [summary RR = 0.373, 95% CI = 0.108-1.287 I^2 = 59.0%]. In stratified analysis by study design, the associations were found neither in the cohort studies [summary RR = 0.924, 95% CI = 0.800-1.067, I^2 = 35.1%] nor in case-control studies [summary RR = 0.553, 95% CI = 0.304-1.004, I^2 = 62.9%].

Sources of heterogeneity and meta-regression

As seen in **Table 2**, evidence of heterogeneity was found in the summary pooled results (I^2 = 67.1% for all studies, $P_{for\ heterogeneity}$ = 0.002). Thus, we conducted univariate meta-regression to explore the reason of causing with the covariates of publication year, cases number, study design and location where the study was conducted. No significant findings were found contributing significantly to the between-study heterogeneity, except the covariates of geographic locations (*P* = 0.017).

Influence analysis and publication bias

Influence analysis did not identify any one individual study that strongly influenced the results of fruit consumption and cataract risk. No evidence of significant publication bias between fruit consumption and cataract risk was confirmed by Egger's test (*P* = 0.306)

Discussion

The findings from the results indicate that higher level fruits intake is being associated with reduced rates of age-related cataract, especially in Europe. A higher level intake of fruit was advocated.

The protection mechanisms that higher fruits intake reduce risk of age-related cataract may have the following several aspects. First of all, lutein and zeaxanthin, which are highly concentrated in fruits, are the predominant carotenoids in the lens [22]. The two substances could protect our eyes from photodamage in vitro [23], and to be associated with reduced risk of cataract. Besides, most fruit are rich in vitamin C, which can explain their protective role in cataract formation [21].

Obvious between-study heterogeneity was found in the process of merging results (I^2 = 67.1%, $P_{for\ \mathrm{heterogeneity}}$ = 0.002). Meta-regression was used to explore the potential covariates that cause between-study heterogeneity. The covariates of geographic locations was found contributing significantly to the high degree heterogeneity (P = 0.017). So, subgroup analysis by the geographic locations was conducted and the heterogeneity was reduced obviously.

The current meta-analysis showed some advantages. First, this is the first comprehensive meta-analysis that combined fruit consumption and age-related cataract risk. Second, a lot of published studies with large number of cases and participants were included, allowing a much greater possibility of reaching reasonable conclusions between fruit consumption and age-related 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, because there were not enough studies to obtain sufficient data, we did not do a dose-response analysis or subgroup analysis about different kinds of fruit.

In summary, our results suggested that higher fruit intake might be associated with reduced rates of age-related cataract, especially in Europe. Further studies are warranted to confirm this result.

Disclosure of conflict of interest

None.

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