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Consumption of fruit and vegetable and risk of coronary heart disease: A meta-analysis of prospective cohort studies

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ABSTRACT

Background: Observational studies suggest that an association between fruit and vegetable consumption and coronary heart disease (CHD). However, the results are inconsistent. We conducted a meta-analysis to evaluate the relationship of fruit and vegetable consumption with CHD risk and quality the dose–response relationship between them.

Methods: Relevant prospective studies were identified by a search of PubMed, Embase and Web of Science databases to July 2014. A random-effects model was used to calculate the pooled relative risk (RR) and 95% confidence intervals (CI).

Results: Twenty-three studies involving 937,665 participants and 18,047 patients with CHD were included. Compared with the lowest consumption levels of total fruit and vegetable, fruit and vegetable, the RR of CHD was 0.84 (95% CI, 0.79–0.90), 0.86 (95% CI, 0.82–0.91), 0.87 (95% CI, 0.81–0.93), respectively. The dose–response analysis indicated that, the RR of CHD was 0.88 (95% CI: 0.85–0.91) per 477 g/day of total fruit and vegetable consumption, 0.84 (95% CI: 0.75–0.93) per 300 g/day of fruit intake and 0.82 (95% CI: 0.73–0.92) per 400 g/day of vegetable consumption. A nonlinear association of CHD risk with fruit or vegetable consumption separately was found (P for nonlinearity <0.001). In the subgroup analysis of location, a significant inverse association was observed in Western populations, but not in Asian populations.

Conclusions: This meta-analysis indicates that total fruit and vegetable, fruit and vegetable consumption, are significantly associated with a lower risk of CHD. The significant inverse association was found in Western populations, but not in Asian populations, which warrants further research.

1. Introduction

Coronary heart disease (CHD) is a major cause of disease burden in both developed and developing nations. It is the leading cause of death and permanent disability, with heavy economic and social costs owing to functional impairments [1,2]. Therefore the primary prevention of CHD is an important public health and clinical medicine priority.

Foods and nutrients are important, which are one of the main determinants of CHD. Of foods and nutrients, the role of fruit and vegetable has been of increasing interest since they are a good source of micronutrients, macronutrients and fiber requirements without adding substantially to total energy intake [3]. Fruits and vegetables are rich in antioxidant vitamins, minerals (e.g., potassium and magnesium), dietary fiber, and phytochemicals [4]. Controlled trials have shown that fruit and vegetable consumption has beneficial effects on several risk factors of CHD, including lipid levels [5], inflammation [6], and blood pressure [7].

A meta-analysis [8] in 2007 concluded that fruit and vegetable intake >5 servings/day was associated with lower risk of CHD. However, there are some limitations in the review. Firstly, the meta-analysis only included twelve studies. Since then, a number of additional studies have been published. Secondly, it did not assess the potential dose–response relationship. Thirdly, several issues emerging from the inconsistent results of later studies still warranted to be demonstrated, including whether it was total fruit and vegetable consumption that prevent the risk of CHD, fruit or vegetable separately, and whether the associations were consistent in both sexes and different ethnic backgrounds, respectively [9], and what levels of consumption of fruit

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and vegetable that had the greatest protection remained unclear [10]. To investigate these key issues, we conducted a meta-analysis on all published prospective cohort studies to investigate the association between consumption of fruit and vegetable and risk of CHD and quantify the dose–response relationship of fruit and vegetable consumption with CHD risk.

2. Methods

We conducted this systematic review following the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines [11].

2.1. Search strategy

We performed a comprehensive search of Pubmed, Embase and Web of Science databases from their inception through July 2014 for prospective cohort studies published in peer-reviewed journals describing an association between fruit and vegetable consumption and risk of CHD. Search terms included fruits, vegetables, diet, cardiovascular disease, ischemic heart disease, myocardial infarction, coronary disease, heart disease, sudden cardiac death, cohort studies, prospective studies and follow-up studies. The search was restricted to human studies. No restrictions were imposed on language of publications. We also reviewed references from retrieved articles to identify additional studies. One investigator (YG) screened the titles and abstracts of all identified articles; two investigators (YG and XYT) assessed the eligibility of full-texts of potentially relevant articles.

2.2. Study selection

Studies were included in this meta-analysis if they met the following criteria: (1) the study was a prospective cohort study; (2) the exposure of interest was fruit or vegetable consumption; (3) the outcome of interest was risk of CHD; and (4) the study reported risk estimates with corresponding 95% CI for the association between fruit and vegetables and CHD or provided corresponding data to calculate the variance. If duplicate publications from the same study were identified, we included the result with the largest number of cases from the study.

2.3. Data extraction

Two investigators (YG and XYT) independently extracted the data by using a standardized electronic format, including the name of first author, publication year, study location, sample size, sex, age range or mean age at entry, length of follow-up, number of cases, method of assessment of exposure, outcome measurements, relative risks (RRs) with corresponding 95% CIs for all categories of fruit and vegetable consumption, and covariates included in the adjusted models. We extracted risk estimates with the most adjustment (when available). For dose–response analysis, when studies reported the consumption in servings or times per day or week or month, we standardized all data into g per day, using standard units of 106 g for total fruit and vegetable [12,13], 80 g for fruit and 77 g for vegetable [8]. Differences in data extraction between the two investigators were resolved by discussion with the third investigator (ZXL).

2.4. Quality assessment

We assessed the methodological quality of study by using an assessment tool with reference to MOOSE [11] and STROBE [14]. The scoring system was a maximum of 5 points (1 point for appropriate inclusion and exclusion criteria; 1 point if the fruit and vegetable consumption assessment was validated; 1 point if the consumption of fruit and vegetable was appropriately categorized; 1 point if the ascertainment of outcome was confirmed according to the accepted clinical criteria and not based on self-report; 1 point for the controlled of confounders). The scores from 0 to 3 were considered as lower study quality, and scores from 4 to 5 were considered as higher study quality. Each study was rated independently by two investigators (YG and XYT).

2.5. Statistical analysis

RRs were considered as the common measure of the association between fruit and vegetable consumption and CHD risk. We preferentially pooled multivariable adjusted RRs' estimates where such estimates were available. When adjusted estimates were unavailable (one study), we pooled the unadjusted estimates. A random effects model was used to calculate summary RRs and 95% CIs for the highest versus the lowest level of consumption of fruit and vegetable and for the dose–response analysis [15]. For two studies [16,17] that included data from multiple cohorts, we considered the analysis for each cohort as an independent report. One study [18] respectively reported the risk estimates of fruit and vegetable intake and CHD by smoking status (never smokers, former smokers and current smokers), and was considered as three independent reports. Any studies that expressed data separately for fatal CHD and nonfatal MI or for men and women, the analysis for each sex or subtype of CHD was also treated as an independent report.

For the dose–response analysis, we used the method described by Greenland and Longnecker [19] to calculate the trend from the correlated estimates for log relative risk across categories of fruit and vegetable consumption. The amount of fruit and vegetable consumption, the distributions of cases and person years, and RRs and 95% CI were extracted according to the method. If the person years were not available for each category of fruit and vegetable intake, but reported the total number of cases/person-years, we estimated the distribution. If consumption of fruit and vegetable was analyzed by quartiles (and could be approximated), e.g., the total number of person years was divided by 4 when the data were analyzed by quartiles in order to derive the number of person-years in each quartile [20].

The median or mean fruit and vegetable consumption in each category was assigned to the corresponding dose of consumption. The midpoint of the upper and lower boundaries was considered the dose of each category if the median or the mean intake per category was not available. When the lower boundary for the lowest category was not provided, the assigned median value was half of the upper boundary of that category. If the highest category was open-ended, we assumed that the median value of the category was the cut-off point plus a 25% increment.

We presented the dose–response results in the forest plots for a 477, 300 and 400 g/day increment for total fruit and vegetable, fruit and vegetable on the basis of intakes associated with the lowest risk in observational studies [21] and the dietary targets set by advocacy organization [22]. Additionally, we used restricted cubic splines with 4 knots at percentiles 5%, 35%, 65%, and 95% to test for nonlinearity in the association between fruit and vegetable consumption and CHD risk.

Statistical heterogeneity across studies was assessed by using the I^2 statistic (ranging from 0% to 100%). I^2 values of 25%, 50%, and 75% represent cut-off points for low, moderate, and high degrees of heterogeneity, respectively [23,24]. Subgroup analyses were conducted to explore the potential sources of heterogeneity among studies, and the differences among groups were tested by using meta-regression. Sensitivity analyses were performed to evaluate the effect of removing a single study from the analysis on pool risk estimates. The Begg's test [25] and Egger's test [26] were used to assess the potential publication bias. All statistical analyses were conducted with STATA version 12.0 (StataCorp, College Station, Texas, USA). P values were two tailed with a significance level of 0.05.

3. Results

3.1. Literature search

The results of literature research and selection were shown in Fig. 1. We identified 408 articles from the PubMed, 564 articles from the Embase and 332 articles from the Web of Science. After the initial screening, based on titles and abstracts, 452 articles remained for further full-text assessment. After retrieving the full-text review of the remaining 26 articles for detailed evaluation, three articles were excluded because they were duplicate publications. Finally, 23 prospective cohort studies [16–18,27–46] comprising 25 independent cohorts were included in this meta-analysis.

3.2. Study characteristics

Characteristics of the included studies are presented in Supplemental Table 1. These studies involving 937,665 participants and 18,047 patients with CHD were published between 1992 and 2014 during follow-up periods ranging from 5 to 37 years. Nine studies [16,33,34,36,37,39,40,44,46] were from the United States, 9 studies [18,27,29–31,35,38,41,42] were from Europe, and 5 studies [17,28,32,43,45] were from Asia (China and Japan). 14 studies [16,17,27–29,32,35–37,41–44,46] included both men and women, 5 studies [18,30,34,38,40] men only and 4 studies [31,33,39,45] women only. The dietary intake was assessed by food frequency questionnaires (FFQ) in all studies, except for 5 studies (3-day food record [46], dietary history interview [42], 7-day diet record [34], 7-day household inventory [35], 24-hour recall [29]). The scores from our assessment of study quality ranged from 3 to 5 scores. The average score was 4.6.

3.3. Association between total fruit and vegetable consumption and risk of CHD

Twelve studies [16–18,27–31,34,36,37,39] with 16 reports investigated the relationship between the highest versus the lowest categories of total fruit and vegetable consumption levels and CHD risk. The RRs of CHD for the highest versus the lowest total fruit and vegetable consumption categories were shown in Fig. 2. Of the 16 reports, 5 showed