Thrombosis Research 134 (2014) 790–794

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Regular Article

Nut consumption and the risk of coronary artery disease: A dose–response meta-analysis of 13 prospective studies

Ling Ma, Fei Wang, Wenyun Guo, Hongning Yang, Yan Liu, Weize Zhang *

Department of Cardiology, Lanzhou General Hospital of Lanzhou Military Region, Lanzhou, Gansu 730050, China

ARTICLE INFO

Article history:
Received 20 March 2014
Received in revised form 7 June 2014
Accepted 30 June 2014
Available online 5 July 2014

Keywords:
Nut consumption
Coronary artery disease
Dose–response meta-analysis

ABSTRACT

Introduction: Epidemiological studies evaluating the association of nut with risk of coronary artery disease (CAD) have produced inconsistent results. We conducted a meta-analysis to summarize the evidence from prospective cohort studies regarding the association between nut consumption and risk of CAD.
Materials and methods: Pertinent studies were identified by searching Web of Knowledge, Pubmed and Wan Fang Med Online up to January 2014. Random-effect model was used to combine the results. Dose–response relationship was assessed by restricted cubic spline. Publication bias was estimated using Begg' funnel plot and Egger's regression asymmetry test.
Results: Nine articles with 13 prospective studies involving 6,127 CAD cases and 347,477 participants were included in this meta-analysis. Pooled results suggested that highest nut consumption amount versus lowest amount was significantly associated with the risk of CAD [summary relative risk (RR) = 0.660, 95%CI = 0.581-0.748, I^2 = 39.6%]. Linear dose–response relationship was found between nut consumption and CAD risk, and the risk of CAD decreased by 5% for every 1 serving/week increase intake of nut. A protective effect for CAD was found when consumed more than 2 servings/week of nut. The RR of CAD was 0.96 (0.89-1.02), 0.91 (0.82-0.99), 0.85 (0.77-0.95), 0.80 (0.72-0.89), 0.75 (0.65- 0.85) and 0.70 (0.58-0.83) for 1, 2, 3, 4, 5 and 6 servings/week of nut consumption, respectively.
Conclusions: Our analysis indicated that nut consumption has a protective effect on CAD.

Introduction

Coronary artery disease (CAD) is the leading cause of death in industrialized countries [1], accounting for up to 40% of all lethal events [2], and it is expected to be the leading cause of disease burden worldwide by 2020 [3]. Despite being high in fat and relatively energy dense, higher intake of nuts has been associated with several health benefits, including reduced risk of cardiovascular disease (CVD) [4]. Nut consumption was also inversely associated with total and cause-specific mortality [5]. Beneficial health effects have been attributed to the macronutrient and micronutrient profiles of nuts [6]. In the United States, nut consumption has been declining steadily since the mid-1980s, perhaps because of increased concern about the effect of dietary fat on health [6]. However, nuts are an important part of the Mediterranean diet, which is now recognized as a healthy diet because mortality rates from coronary heart disease (CHD) and cancer were extremely low in traditional Mediterranean populations [7]. Up to date, a number of epidemiologic studies have been published to explore the relationship between nut consumption and CAD. However, the results are not consistent. Therefore, we conducted a meta-analysis to (1) first assess the CAD risk for the highest vs. lowest amount of nut consumption; (2) assess the dose–response association between CAD risk and nut consumption; (3) assess the heterogeneity among studies and publication bias.

Materials and Methods

Literature Search and Selection

We performed a literature search up to January 2014 using the databases of PubMed, Web of Knowledge and Wan Fang Med Online. The following search terms were used: [coronary artery disease (CAD) OR cardiovascular disease (CVD) OR myocardial infarction (MI) OR coronary heart disease (CHD) OR ischemic heart disease (IHD)] AND (nut OR diet OR lifestyle) and restricting studies conducted in humans. Moreover, we reviewed the reference lists from retrieved articles to search for further relevant studies.

Two investigators independently reviewed all identified studies, and studies were included if they met the following criteria: (1) using a prospective design; (2) the exposure of interest was nut; (3) the outcomes of interest were CAD or CHD or MI or CVD or IHD; (4) relative risk (RR) with 95 % confidence interval (CI) was provided; and (5) for dose–response analysis, the nut consumption for each category must

* Corresponding author. Tel./fax: +86 13919241762.
E-mail address: zhangzwz@medmail.com.cn (W. Zhang).

http://dx.doi.org/10.1016/j.thromres.2014.06.017
0049-3848/

also be provided (or data available to calculate them). If data were duplicated in more than one study, we included the study with the largest number of cases.

Data Extraction

The following data were extracted from each study by two investigators: the first author's last name, year of publication, geographic locations, sample source, the age range of study participants, duration of follow-up, the number of cases and participants (person-years), definition of cases and RR (95%CI) for each category of nut consumption were also extracted. From each study, we extracted the RR that reflected the greatest degree of control for 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

Pooled measure was calculated as the inverse variance-weighted mean of the logarithm of RR with 95% CI, to assess the strength of association between nut consumption and the risk of CAD. Random-effects model was used to combine study-specific RR (95%CI), which considers both within-study and between-study variation [8]. The I^2 was used to assess heterogeneity, and I^2 values of 0, 25, 50 and 75% represent no, low, moderate and high heterogeneity [9], respectively. Meta-regression with restricted maximum likelihood estimation was performed to assess the potentially important covariates that might exert substantial impact on between-study heterogeneity [10], and to examine the statistical significance of the difference in RR in subgroup analysis [11]. Publication bias was evaluated using Begg' funnel plot [12] and Egger regression asymmetry test [13]. A study of influence analysis [14] was conducted to describe how robust the pooled estimator is to removal of individual studies.

For the dose–response analysis, the method reported by Greenland et al. [15] and Orsini et al. [16] was used to calculate study specific slopes (linear trends) based on the results across categories of nut consumption. The method requires that the distribution of cases and person-years or noncases and the RR with the variance estimates for at least three quantitative exposure categories are known. In the first stage, a restricted cubic spline model with three knots at the 25th, 50th and 75th percentiles of the nut consumption was estimated using generalized least-square regression, taking into account the correlation within each set of published RR. Then the study-specific estimates were combined using the restricted maximum likelihood method in a multivariate random-effects meta-analysis [17]. A P-value for non-linearity was calculated by testing the null hypothesis that the coefficient of the second spline is equal to 0. All statistical analyses were conducted with STATA version 11.0 (StataCorp LP, College Station, Texas, USA). Two-tailed $P \leq 0.05$ was accepted as statistically significant.

Results

Search Results and Study Characteristics

The detailed steps of our literature search are shown in Fig. 1. In our analysis, 9 articles [18–26] with 13 prospective studies involving 6,127 CAD cases and 347,477 participants were used in this meta-analysis. Among the 13 prospective studies, 12 studies reported the result from United States and 1 study from Spain. The duration of follow-up ranged from 4.8 to 26 years, and the study cases ranged from 81 to 1,037. The characteristics of these studies are presented in Table 1.

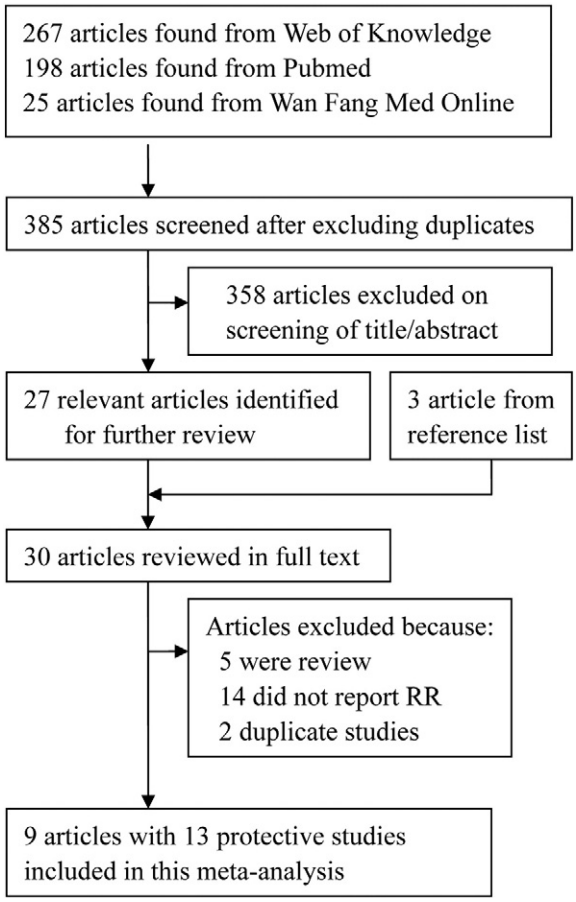

Fig. 1. The flow diagram of screened, excluded, and analyzed publications.

High Versus Low Intake Analyses

Data from 9 articles with 13 prospective studies including 6,127 CAD cases were used in this meta-analysis. Inverse association of nut consumption with risk of CAD was reported in 10 studies, and no significant association was reported in 3 studies. Pooled results suggested that highest nut consumption amount versus lowest amount was significantly associated with the reduced risk of CAD [summary RR = 0.660, 95%CI = 0.581-0.748, I^2 = 39.6%] (Fig. 2). Twelve studies were conduced from United States, and the results was consistent with overall data [summary RR = 0.671, 95%CI = 0.591-0.761, I^2 = 38.8%].

In subgroup analyses for disease outcome, inverse association of nut consumption and risk of CAD were found in CHD [summary RR = 0.657, 95%CI = 0.598-0.721] and CVD [summary RR = 0.516, 95%CI = 0.361-0.739], but not in the MI. When we conducted the subgroup analysis by follow-up duration (<10 years and ≥10 years), significant associations were found both in <10 years follow-up and ≥10 years follow-up. Furthermore, when stratified analysis for number of cases (<500 cases and ≥ 500 cases), the associations were consistent with overall data. The details results are summarized in Table 2.

Dose–response Analysis

For dose–response analysis, data from four articles including seven studies [18,21,22,24] with 4,886 CAD cases were used for the nut consumption and CAD risk. We found no evidence of statistically significant departure from linearity (*P* for nonlinearity = 0.70). The dose–response analysis of nut consumption indicated that an increase in nut consumption of 1serving/week was statistically significantly associated with a 5% decrease in the risk of CAD. A protective effect for