Clinical Nutrition 35 (2016) 109–116

Contents lists available at ScienceDirect

Clinical Nutrition

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

Meta-analyses

Association of carotenoids with risk of gastric cancer: A meta-analysis

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ARTICLE INFO

Article history:
Received 16 August 2014
Accepted 5 February 2015

Keywords:
Diet
Stomach cancer
Cancer prevention
Epidemiology

SUMMARY

Background & aims: Prior studies on carotenoids and gastric cancer risk have generated inconsistent results. We performed a meta-analysis of observational studies to summarize the evidence regarding the relation of carotenoids and gastric cancer risk.

Methods: A comprehensive search was performed to identify all observational studies providing quantitative estimates between gastric cancer risk and carotenoids. The fixed or random effect model was selected based on the homogeneity test among studies in the highest vs. lowest categorical analyses.

Results: 13 published case–control studies with 14 results including 3919 cases and 7400 controls, and 8 cohort studies involving 1972 cases of gastric cancer and 96,691participants, met the inclusion criteria. For case–control studies, only intake of β-carotene and α-carotene were significantly associated with a reduced gastric cancer risk. The summary OR(95%CI) for β-carotene, α-carotene, lycopene and lutein were 0.52(0.46–0.59), 0.59(0.37–0.92), 0.88(0.55–1.41) and 0.85(0.56–1.30) respectively. In contrast, the summary RR(95%CI) for β-carotene, α-carotene, lycopene and lutein were 0.72(0.50–1.03), 0.79(0.58–1.07), 0.80(0.60–1.07) and 0.95(0.77–1.18), respectively.

Conclusion: Although data from case–control studies suggested that β-carotene, α-carotene were inversely associated with risk of gastric cancer, there was no conclusive evidence on this association because of inconsistencies between case–control and cohort studies.

1. Introduction

Gastric cancer is a very common disease worldwide and the second most frequent cause of cancer death, affecting about 1 million people per year, which is an enormous public health problem [1]. Thus, there is an urgent need to develop more primary prevention strategies for this disease. Although many risk factors have been suggested the causative and protective agents for gastric cancer remain to be clarified. Dietary factors are believed to play an important role in the prevention of gastric cancer, among which dietary carotenoids has received considerable interest [2–4]. Dietary antioxidants can inhibit the process of nitrosation and are believed to exert protective effects on gastric cancer [5,6].

Numerous epidemiologic studies have been reported regarding the association between dietary carotenoids intake or serum level of carotenoids and gastric cancer risk, however, the results are conflicting. Studies vary by design, for example, in most [7,8]but not all [9]case–control studies, higher intakes of β-carotene have been associated with a reduced risk of gastric cancer. However, the results for plasma carotenoids have been inconsistent in cohort studies of gastric cancer. Several [3,10], but not all [2]studies of plasma or serum concentrations of carotenoids and gastric cancer reported non-significant associations. To clarify these findings we conducted a meta-analysis of epidemiological studies of carotenoids and gastric cancer risk by summarizing the separate results of published case–control studies and cohort studies, respectively.

2. Methods

2.1. Search strategy

A comprehensive search was performed for relevant articles through Oct. 2013 using the following databases: (1) PubMed; (2) Web of Science (ISI); (3) China Biology Medical literature database (CBM); (4) Database of Chinese Scientific and Technical Periodicals (VIP); and (5) China National Knowledge Infrastructure (CNKI). Search terms included 'carotenoids', "α -carotene", "β-carotene", "β-cryptoxanthin", "lutein/+zeaxanthin", "lycopene", and "gastric,

Abbreviations: OR, odds ratio; RR, relative risk; CI, confidence interval.

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http://dx.doi.org/10.1016/j.clnu.2015.02.003

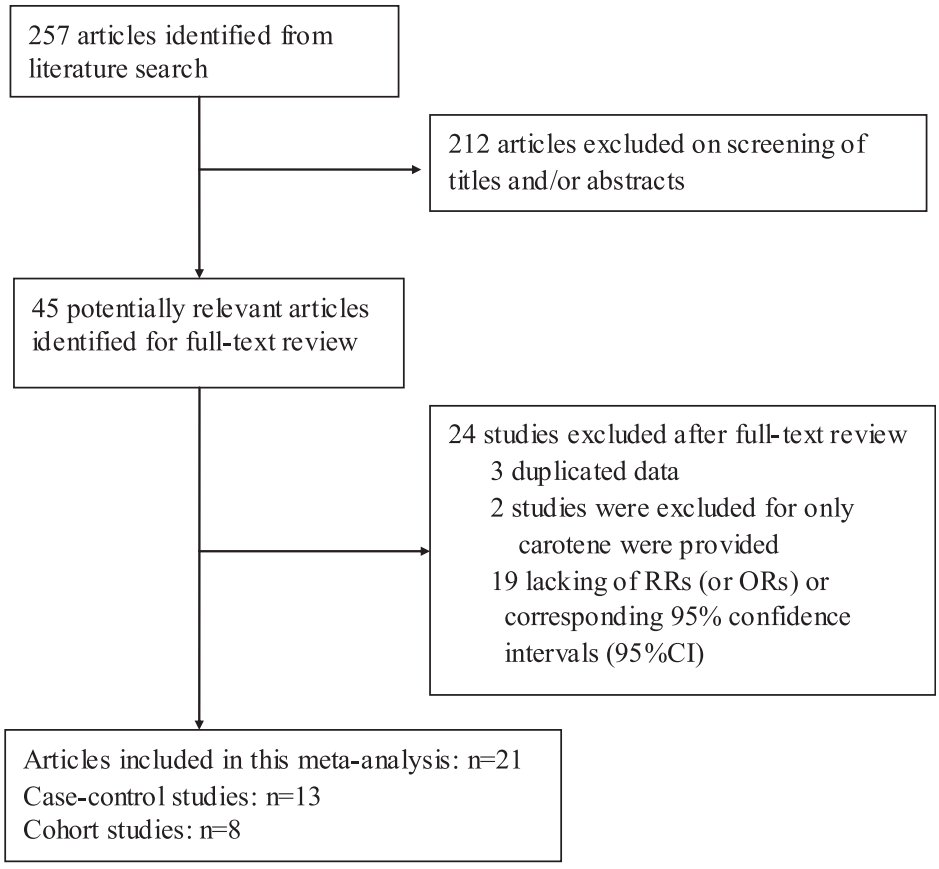

Fig. 1. Flow diagram of study selection.

stomach cancer, and/or carcinoma and/or neoplasm". Moreover, we identified studies not captured by our database by reviewing reference lists from retrieved articles to search for further relevant articles. We followed standard criteria for conducting meta-analyses and reporting the results [11].

2.2. Eligibility criteria

Each identified study was independently reviewed by two investigators to determine whether an individual study was eligible for inclusion in this meta-analysis. The inclusion criteria are as follows: (1) case–control or cohort study; (2) the exposure of interest was intake of carotenoids (β-carotene,α-carotene, lycopene or other carotenoids) or blood (plasma or serum) levels of carotenoids; (3) the outcome of interest was gastric cancer; and (4) odds ratio (OR) or relative risk (RR) estimates with 95%confidence intervals (CIs) were reported. If data were duplicated in more than 1 study, we included the study with the largest number of cases.

2.3. Data extraction and quality assessment

The following data were collected from all studies: the first author's name, year of publication, country where the study was performed, sex, number of cases or controls (participants for cohort studies), variables adjusted for in the analysis, as well as multivariate adjusted RRs(ORs for case–control studies) and 95% CIs for each category of carotenoids. For studies that reported results from various covariates 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 article, it was resolved by consensus with a third reviewer.

To assess the study quality, an evaluation system based on the Newcastle-Ottawa Scale [12] was adopted. The included studies were judged on 3 aspects: the selection of study populations, the comparability of the populations, and ascertainment of exposure (including the dietary change) or the outcomes of interest for case–control or cohort studies, respectively. The full score was 10 stars, and a high-quality study was defined as a study with 7 or more stars.

2.4. Statistical analysis

Pooled measure was calculated as the inverse variance-weighted mean of the natural logarithm of multivariate adjusted RRs with 95% CIs to assess the association of carotenoids consumption with gastric cancer. The Q test and I^2 of Higgins and Thompson were used to assess heterogeneity among studies [13]. I^2describes the proportion of total variation attributable to between-study heterogeneity as opposed to random error or chance. In the presence of substantial heterogeneity (I^2>50%) [14], the DerSimonian and Laird random effect model (REM) was adopted as the pooling method; otherwise, the fixed effect model (FEM) was used as the pooling method. The 'leave one out' sensitive analysis [15] was carried out using I^2>50% as the criteria to evaluate the key studies with substantial impact on between-study heterogeneity. Influence analyses were conducted [16] that 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% CIs of the