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Original research

Consumption of citrus and cruciferous vegetables with incident type 2 diabetes mellitus based on a meta-analysis of prospective study[☆]



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ABSTRACT

Background: Observational studies and meta-analyses suggested that increased total fruits and vegetables consumption have a protective role in incidence of type 2 diabetes mellitus (T2DM). However, we still don't know whether the subtypes, such as citrus fruits and cruciferous vegetables (CV), have a preventive role.

Methods: We systematically searched the MEDLINE and EMBASE databases up to December 31, 2014. Summary relative risks (SRRs) and 95% confidence intervals (CIs) were calculated using random-effects models.

Results: Seven distinct prospective cohort studies (five articles) were identified for this study. A total of 16,544 incident cases of type 2 diabetes were ascertained among 306,723 participants with follow-up periods ranging from 4.6 to 24 years. Based on four prospective cohort studies, we found that overall, consumption of CV had a protective role in the T2DM incidence (highest vs. lowest analysis: SRR = 0.84, 95% CI: 0.73 to 0.96), with evidence of significant heterogeneity ($P = 0.09$, $I^2 = 54.4\%$). This association was independent of the main risk factors for cardiovascular disease: smoking, alcohol use, BMI, and physical activity etc. Consumption of citrus fruits did not have a protective role in the T2DM development (highest vs. lowest analysis: SRR = 1.02, 95% CI: 0.96 to 1.08), with no evidence of significant heterogeneity ($P = 0.49$, $I^2 = 0$).

Conclusions: Higher consumption of CV, but not citrus fruits, is associated with a significantly decreased risk of type 2 diabetes. Further large prospective studies are needed to elucidate both relationships.

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1. Introduction

Over the past two decades, the prevalence of type 2 diabetes mellitus (T2DM) has been elevated markedly worldwide [1].

Studies have shown that increased exercise, quit smoking, weight lost among obese individuals, adoption of a diet rich in fiber may reduce the incidence of T2DM [2,3].

Dietary factors are potential risk factors, but the relationship between fruit and vegetable intake and incidence

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of T2DM is not fully understood. Although a meta-analysis published in 2010, which included six prospective cohort studies, reported that greater intake of fruits was not associated with risk of T2DM [Summary relative risk (SRR)=0.93, 95% confidence interval (CI): 0.83 to 1.01] [4], the updated two meta-analyses, which included 10 prospective cohort studies, found a protective role for fruit intake [5,6]. Furthermore, a significantly inverse association between citrus fruits consumption and risk of T2DM was observed among one cohort of Chinese women with intermediate levels of citrus consumption (10.0–25.2 g/day) as compared to low citrus consumption, but no significant association was found for a high intake (median, 44.4 g/day) [7]. Others, studies from USA and Europe found a non-significant association between citrus consumption and risk of T2DM [8–10]. Likewise, mixed results were reported for the association between CV consumption and T2DM [7,8,9,10]. Like other fruits, both citrus fruits and CV contain many nutrients, such as carotenoids, polyphenols, flavonoids, limonoids, folic acid, and dietary fiber, which are believed to delay the digestion and absorption of carbohydrates and suppress postprandial glycemia, oxidative stress, and low-grade inflammation [10]. Importantly, CVs are unique in that they are rich sources of glucosinolates [11,12], the precursors of isothiocyanates and indole-3-carbinol [13,14]. Researches have observed a protective role of isothiocyanate in the development of DM via improved glucose tolerance and insulin signaling [15]. In addition, researches [16,17] have indicated that extract of citrus fruits has hypoglycemic effects in the diabetic experimental models.

In this meta-analysis, we focused on only prospective cohort studies due to the following: (1) no systematic reviews and meta-analyses have looked at the effects of intake of citrus fruits and CV on the overall risk of T2DM. (2) Both case-control and cross-sectional designs are subjected to the selection and recall bias, and the prospective evidences on these associations have been reported with inconsistent results [7–10,18]. (3) Only several clinical trials investigate the effects of intakes of citrus [19] and CV [20,21] on the development of complications in patients with T2DM, but not the development of T2DM. Therefore, to better characterize this issue, we conducted a meta-analysis of prospective cohort studies to evaluate such relationships following the meta-analysis of observational studies in epidemiology (MOOSE) [22].

2. Methods

2.1. Search strategy

For this meta-analysis, searches were performed electronically through the MEDLINE and EMBASE database for prospective cohort studies examining the association between citrus fruits and CV intake and risk of T2DM. We supplemented this search by hand-searching the reference lists of the retrieved articles. The search strategy used the following terms of Medical Subject Headings or keywords: (1) fruit OR citrus OR grapefruit OR orange OR tangerine OR lemon OR lime OR cruciferous vegetables OR brassica OR broccoli OR cauliflower OR cabbage; (2) diabetes OR hyper glucose OR hyperglycemia OR NIDDM; (3) risk OR incidence OR prevalence.

Searches included the earliest available online indexing year up to December 31, 2014, with no language restrictions. Two investigators (J.X.J. and Z.L.N.) did this literature search.

2.2. Study selection

Two researchers (J.X.J. and Z.L.N.) independently reviewed all potentially relevant articles to determine whether an article met the general inclusion criteria, and any discrepancy was solved by consultation of a third investigator (S.S.Q.). To be included, studies had to: (1) have a prospective cohort design; (2) evaluate the association between citrus fruits and/or CV consumption and the development of T2DM; (3) point estimates of relative risk (RR) with 95% CIs or standard errors available or derivable; and 4) report the associations at least adjusted by age. Studies on pregnant women or children (≤ 18 y) were excluded. Animal studies, in vitro researches, case reports, ecological studies and reviews were not considered eligible. We also excluded studies which reported risk association for type 1 diabetes. If data were duplicated in more than one studies, we included the most recent or informative ones.

2.3. Data extraction

Two researchers (J.X.J. and Z.L.N.) extracted the following information independently and in duplicate: basic information (author, publication year), study characteristics (name of the study, study design, country, duration of follow-up, and number of participants and incident cases), participant characteristics (age and sex), exposure (intake levels for each category) and dietary assessment method, outcome (type 2 diabetes) ascertainment, analytic comparison, RR estimates and 95% CIs for each incremental category of intake, and covariates included in the models. From each study, we extracted the risk estimates adjusted for the greatest number of potential confounders, as suggested by Chene et al. [23]. For one study [18] that included data from three cohorts, we considered the analysis for each cohort as an independent report and extracted data separately.

2.4. Quality assessment for individual studies

The quality of each study was evaluated according to the Newcastle–Ottawa quality assessment scale (NOS) [24], which assigns a maximum of 9 points for quality assessment. NOS use three quality parameters for cohort studies: selection (4 points), comparability (2 points), and outcome (3 points) assessment. A total score of ≥ 7 points is indicative of high-quality studies; score of ≤ 6 points of low-quality studies. Studies that could not be evaluated by NOS because of insufficient information were considered to be low-quality studies. Two reviewers (J.X.J. and Z.L.N.) carried out the quality assessment independently.

2.5. Statistical analysis

We used the method of a random-effects model to calculate the summary RR estimations and 95% CIs of T2DM for the highest vs. lowest level of intake. This method was developed

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