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Meta-analyses

Effect of nut consumption on vascular endothelial function: A systematic review and meta-analysis of randomized controlled trials

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SUMMARY

Objective: nut consumption has consistently been found to be associated with a reduced risk of cardiovascular diseases (CVD) and mortality in prospective studies. However, its effect on endothelial function, a prognostic marker of CVD, is still controversial in clinical trials. This meta-analysis of randomized controlled trials (RCTs) aimed to quantitatively assess the effect of nuts on vascular endothelial function.

Methods: Major electronic databases were searched for published RCTs that reported the effect of nuts on flow mediated dilation (FMD) as a measurement of endothelial function in the adult population (age eighteen years or over). We calculated the pooled estimates of weighted mean differences (WMDs) and their 95% confidence intervals (CIs) by using random-effects models.

Results: A total of nine papers (10 trials) involving 374 participants were included. The pooled estimates found that nut consumption significantly improved FMD (WMD: 0.41%; 95% CI: 0.18%, 0.63%; $P = 0.001$). Moderate and marginally significant heterogeneity was observed among the studies ($I^2 = 39.5\%$, $P = 0.094$). Subgroup analyses indicated that walnuts significantly improved FMD (WMD: 0.39%; 95% CI: 0.16%, 0.63%; $P = 0.001$). In addition, nut consumption had a significant effect on FMD in the trials with study duration <18 weeks, nut dose <67 g/d, or subjects with baseline FMD ≥8.6%.

Conclusions: Nut consumption significantly improved endothelial function. However, the beneficial effect was limited to walnuts. More studies examining the effect of other nuts on endothelial function are needed in the future.

1. Introduction

Epidemiological studies have observed that consumption of nuts is associated with a reduced risk of type 2 diabetes, cardiovascular disease (CVD) and mortality [1,2]. Nuts are rich in unsaturated fatty acids [3] and are rich sources of bioactive compounds with potential benefits for CVD prevention, such as dietary fiber, vitamin E, folic acid, flavonoids, and polyphenols [4]. Nuts also contain considerable amounts of L-arginine, which is the precursor amino acid of nitric oxide (NO). Among the different types of nuts, walnuts have been found to be particularly beneficial. In comparison with other nuts, walnuts have a higher content of α—linolenic acid (ALA), a plant n-3 fatty acid, which might have additional anti-atherogenic effects [5]. Healthy diets which are rich in a variety of nuts, for example, a Mediterranean diet, have been found to reduce the risk factors of CVD, including lipids, inflammation, and blood pressure in previous clinical trials [6,7]. Two meta-analyses found that, compared with control diets, walnut-rich diets reduced the levels of low-density lipoprotein cholesterol (LDL-C) and total cholesterol in previous randomized controlled trials (RCTs) [8,9].

Endothelial dysfunction is an event in the early-stage of atherosclerosis and an independent predictor of future CVD events [10]. Endothelial function can be evaluated non-invasively by several methods, such as peripheral artery tonometry, or brachial

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artery ultrasound. In most studies, flow-mediated dilation (FMD) measured by brachial artery ultrasound has been widely used and found to be sensitive and accurate in measuring endothelial function [11]. Experimental studies found that vasodilation could be improved by dietary interventions, for example, fish oil n-3 fatty acid, flavonoids, polyphenols, and L-arginine [12]. The effect of nuts, including walnuts, almonds, pistachios, and hazelnut, which are rich in these compounds, on endothelial function has been investigated in previous clinical trials [13–28]. However, the results have not been consistent, likely due to the relatively small sample sizes, different duration, and types and doses of nut interventions of these trials. Therefore, the precise effect of nut intake on endothelial function has not been well established. In the present study, a meta-analysis of RCTs was performed to comprehensively assess the evidence and quantitatively estimate the effect of nut consumption on endothelial function measured by FMD.

2. Materials and methods

2.1. Data sources and search strategy

We performed a systematic review and meta-analysis of the RCTs following the PRISMA criteria guidelines [29] (Fig. 1). Relevant articles were identified by searching the major electronic databases, including PubMed (www.ncbi.nlm.nih.gov/pubmed), Cochrane database (http://www.cochrane.org), Embase (www.embase.com), and Google Scholar (www.scholar.google.com) through July 2016, with no language restriction. Three groups of keywords were used in the literature search: first group: “nut”, “almond”, “pistachio”, “hazelnut”, “walnut”, “cashew”, “ macadamia”, “pecan”, “peanut”, or “soy nut”; second group: “endothelial”, “endothelium”, “FMD”, or “flow-mediated dilatation”; and third group: “-randomized”, “intervention”, “controlled trial”, “random”, and “placebo”. The first keyword group was combined with both the second and the third groups to search relevant studies.

2.2. Study selection

The following inclusion criteria were used: 1) studies were RCTs; 2) the RCTs focused on the effect on endothelial function and used FMD as a measurement of endothelial function; 3) the RCTs examined consumption of nuts, broadly defined as a hard-shelled dry fruit or seed with a separable rind or shell and interior kernel, including walnuts, almonds, pecans, peanuts, hazelnuts, pistachios, cashews, macadamia nuts, and soy nuts; 4) the RCTs explicitly reported baseline and follow-up values of FMD or the mean change between baseline and follow-up for each group, or the mean difference between intervention and control groups;

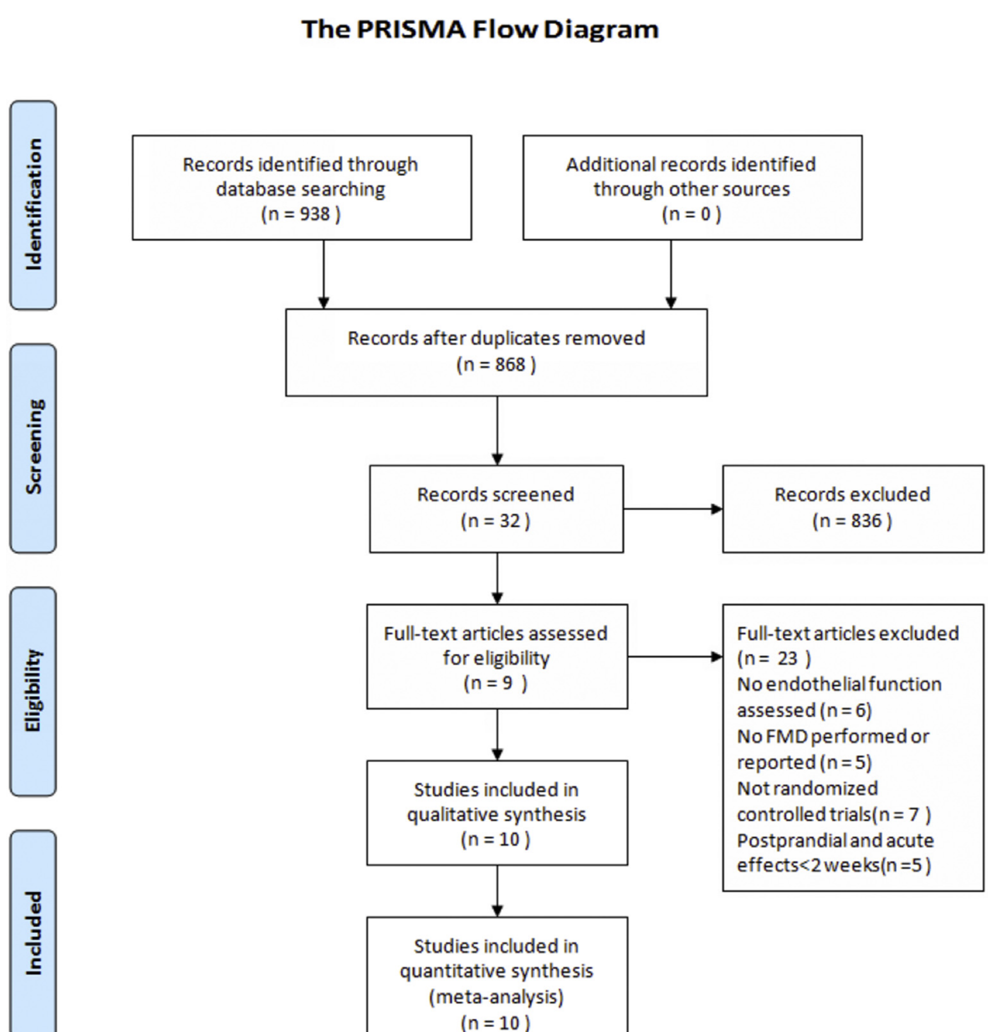

Fig. 1. Flowchart of study selection process.

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