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The association between carotid intima media thickness and individual dietary components and patterns

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Abstract *Aims:* To review: 1) the correlation between individual dietary components and carotid intima media thickness (cIMT); 2) the relationship between dietary patterns and cIMT; 3) the effect of dietary interventions on cIMT progression.
Data synthesis: An electronic search for epidemiological and intervention trials investigating the association between dietary components or patterns of intake and cIMT was performed in PUBMED, EMBASE and the Cochrane Library. Epidemiological data shows that a higher intake of fruit, wholegrains and soluble fibre and lower consumption of saturated fat in favour of polyunsaturated fat is associated with lower cIMT. In people at high risk of cardiovascular disease >93 g/day of fruit is associated with lower cIMT. Lower cIMT has also been observed when >0.79 serves/day of wholegrains and >25 g/day of fibre, predominately in the soluble form is consumed. Saturated fat is positively associated with cIMT, for every 10 g/day increase in saturated fat cIMT is 0.03 mm greater. Olive oil is inversely associated with cIMT, with a benefit seen when >34 g/day is consumed. While there are many epidemiological studies exploring the association between dietary intake and cIMT there are few intervention studies. Intervention studies show that a Mediterranean diet may reduce cIMT progression, especially in those with a higher cIMT.
Conclusions: A Mediterranean style dietary pattern, which is high in fruits, wholegrains, fibre and olive oil and low in saturated fat, may reduce carotid atherosclerosis development and progression. However further research from randomised controlled trials is required to understand the association between diet and cIMT and the underlying mechanisms.

Introduction

In 2008, 17.3 million people died of CVD, representing 30% of all global deaths [1]. Carotid intima media thickness (cIMT) is an early marker of atherosclerosis [2] and a single measurement is a predictor of cardiovascular risk [3] but whether cIMT progression is a predictor of future vascular events remains unclear [3,4]. Although, cIMT does not independently add to traditional cardiovascular risk predictive models such as the Framingham score in healthy populations [5–7], it does in people at intermediate risk of CVD [8]. However, data has been mixed with regard to type 2 diabetes [9–11]. The 2010 ACCF/AHA guidelines for assessment of cardiovascular risk in asymptomatic adults state that there is level B evidence for measuring cIMT in people at risk of CVD [12]. The aim is to review the evidence for dietary intake and cIMT including: 1) the correlation between individual dietary components and cIMT; 2) the relationship between dietary patterns and cIMT; 3) the effect of dietary interventions on cIMT progression.

Methodology

An electronic search was performed in PUBMED, EMBASE and the Cochrane Library for 1) epidemiological studies

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investigating the association between cIMT and individual foods, food groups, food components, nutrients or dietary patterns; 2) controlled and uncontrolled intervention studies aiming to determine the effect of a dietary intervention on cIMT progression. Reference lists of retrieved articles were also searched for relevant articles. No restrictions were placed on publication date. Studies were limited to those published in English. Studies of vitamin, mineral and food extract supplementation while not the focus of this review, were included to help explain the mechanisms behind the observed effect. Studies including lifestyle modification (e.g. exercise or stress management) or pharmacological treatment in addition to dietary changes were excluded. If the placebo group was given a dietary intervention the study was not included. Intervention studies where cIMT was not measured at baseline were also excluded.

Fruit

There is a significant body of epidemiological evidence showing that higher intake of fruit is associated with lower cIMT in the people with risk factors for CVD. Observational studies, including people with type 2 diabetes [13,14], men with hypercholesterolaemia [15] and those at high risk of CVD [16] have demonstrated this. In the PREvenci'on con DIeta MEDiterr'anea (PREDIMED) trial there was a significant inverse association between fruit intake and cIMT (p for trend <0.01) after multivariate adjustment [16]. Similarly, in men with hypercholesterolaemia, a 5.5% mean difference in cIMT between the highest (>256 g/day) and lowest quartile of fruit intake (4–97 g/day) was observed. This study reported that for every 1 portion of fruit consumed per day (150 g) cIMT was 2.4% lower [15]. In people with type 2 diabetes, higher fruit consumption (101 g/day) was associated with a 9% lower cIMT compared with an intake <80 g/day, after multivariate adjustment [14]. A Chinese study of people with type 2 diabetes also showed that the highest tertile of fruit intake (92.6 g/day) had a significantly lower mean maximum cIMT than the lowest tertile (14.5 g/day) of consumption (0.97 ± 0.02 vs. 1.08 ± 0.03 mm; $p = 0.046$) [13]. This epidemiological data indicates that daily fruit intake should be at least 93 g, and preferably up to 256 g to see a cardiovascular benefit.

The beneficial effect fruit exerts on cIMT is not fully understood. Fruit is a good source of vitamins, potassium and soluble fibre which may be involved in the observed effect. Fruit also contains carotenoids and phytochemicals including polyphenols which may have an antioxidant effect [17–19]. These antioxidants may reduce oxidative damage to blood vessels and therefore slow atherosclerosis development [20]. Inverse associations between flavonoids [21] and pomegranate juice [22], which contain potent antioxidants, and cIMT have been observed. Investigation of the effect of carotenoids, including α-carotene, β-carotene, lutein, zeaxanthin, β-crytoxanthine, on cIMT has yielded mixed results [23]. However, there is significant evidence of an inverse association between serum/plasma lycopene concentration and cIMT [24–28].

A number of studies have shown an inverse association between fibre from fruit and cIMT [16,29,30]. In the PREDIMED trial energy adjusted fibre intake >35 g/day was associated with a 0.051 mm lower cIMT compared with <25 g/day fibre ($p = 0.02$) after full multivariate adjustment [16]. Fruit was the only major source of fibre significantly associated with cIMT after adjustment for confounding factors; no significant association was observed for vegetables, legumes or cereals. This finding is consistent with data from the Los Angeles Atherosclerosis Study where pectin was the only type of fibre inversely associated with cIMT progression [29]. These epidemiological studies indicate that a fibre intake of at least 25 g/day and up to 35 g/day may be required to slow intima media thickening. Soluble fibre may be protective against intimal thickening due to its beneficial effect on blood lipids [29]. A meta-analysis of 67 controlled clinical trials showed soluble fibre reduced total cholesterol and LDL cholesterol [31]. However, there is no consistent evidence that either soluble or insoluble fibre is more strongly associated with a reduced risk of cardiovascular end points. The majority of studies show that both types are inversely associated with cardiovascular risk [32], although, it has been shown that insoluble fibre does not lower lipid levels [33].

Wholegrains

In the Multi-Ethnic Study of Atherosclerosis (MESA) study no relationship was found between intake of wholegrains (mean 0.54 serves/day) and common or internal cIMT [34]. Conversely, in the Insulin Resistance Atherosclerosis Study (IRAS), common cIMT ($\beta = -0.043 + 0.013$; $p = 0.005$) and internal cIMT ($\beta = -0.049 + 0.023$; $p = 0.05$) were independently and inversely associated with wholegrain intake (median 0.79 serves/day), after multivariate adjustment [30]. Epidemiological data shows that wholegrain intake is inversely associated with CVD [35]. The beneficial components of wholegrains include fibre, magnesium, folate, vitamin B6 and vitamin E [36]. These constituents may act by improving insulin sensitivity [37,38], lowering body weight and central adiposity [37].

Vegetables

To date there have been no published studies which have shown a statistically significant relationship between vegetable intake and cIMT. Zhu et al. [14], Buil-Cosiales et al. [16], Chan et al. [13] and Ellingsen et al. [15] have all reported no statistically significant association between vegetable intake and cIMT. However, vegetable intake has been shown to be inversely associated with CVD. In a meta-analysis for each additional portion of vegetables consumed per day the risk of coronary heart disease was 11% lower (95% CI 0.83–0.95; $p < 0.0023$) [39].

Plant sterols

Plant sterol consumption of 2.15 g/day has been shown to reduce LDL cholesterol by 8.8% [40]. There has been