

Letter to the Editor

Low-carbohydrate diets impair flow-mediated dilatation: evidence from a systematic review and meta-analysis

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With great interest, we read the meta-analysis of Bueno *et al.*⁽¹⁾ ‘Very-low-carbohydrate ketogenic diet *v.* low-fat diet for long-term weight loss: a meta-analysis of randomised controlled trials’, published ahead of print in the *British Journal of Nutrition*⁽¹⁾. In their article, the authors compared the effects of very-low-carbohydrate (VLC) diets *v.* low-fat (LF) diets on the biomarkers of obesity and their associated disorders. With respect to different outcomes between both the regimens, VLC diets turned out to be more effective in lowering body weight, TAG levels and diastolic blood pressure and in increasing HDL-cholesterol levels. However, one established risk factor of CVD, *i.e.* LDL-cholesterol, still turned out to be harmfully affected by the VLC regimen, most probably attributable to the larger amounts of saturated fat in the diet⁽¹⁾. In their discussion, the authors stated that future meta-analyses should investigate the impact of low carbohydrates (LC) *v.* LF on other important pathological markers, *e.g.* endothelial function, in order to further assess the safety of LC dietary therapies. This is reasonable, since evidence from prospective cohort studies has shown that endothelial dysfunction represents an independent risk factor for the development of many CVD including atherosclerosis⁽²⁾. We, therefore, carried out a meta-analysis to compare the effects of LC and LF regimens on flow-mediated dilatation (FMD). FMD of the brachial artery is a non-invasive measure of endothelial function, furthermore reflecting the local bioavailability of endothelium-derived vasodilators, especially NO. Inflammation of the endothelium is regarded

to play a major role in the destabilisation of atherosclerotic lesions, therefore paving the way for future CVD events⁽²⁾. A literature search was performed using the electronic databases MEDLINE (until April 2013), EMBASE (until April 2013) and the Cochrane Trial Register (until April 2013), with restrictions to randomised controlled trials, but no restriction to language using the following search terms: low fat diet AND endothelial function and low carbohydrate diet AND endothelial function (Supplementary material, available online). Studies were included in the meta-analysis if they met all of the following criteria: (1) randomised controlled design with a minimum intervention period of 3 weeks; (2) comparing a LC diet ($\leq 45\%$ carbohydrates of total energy content, TEC) with a LF diet ($\leq 30\%$ fat of TEC)⁽³⁾; (3) report of post-intervention values with standard deviations; when the results of a study were published more than once, only the most recent or most complete article was included in the analysis; (4) participants age > 18 years; (5) exclusion of subjects with CHD.

A meta-analysis was carried out in order to determine the pooled effect of the intervention in terms of weighted mean differences (WMD) between the post-intervention values of the LC group and those of the LF group. All data were analysed using the Review Manager 5.1 software, provided by the Cochrane Collaboration (<http://ims.cochrane.org/revman>). Overall, six trials with a sample size of 210 subjects were included^(4–9). Study duration ranged between 3.5 weeks and 12 months. Decreases in FMD (WMD: -1.01

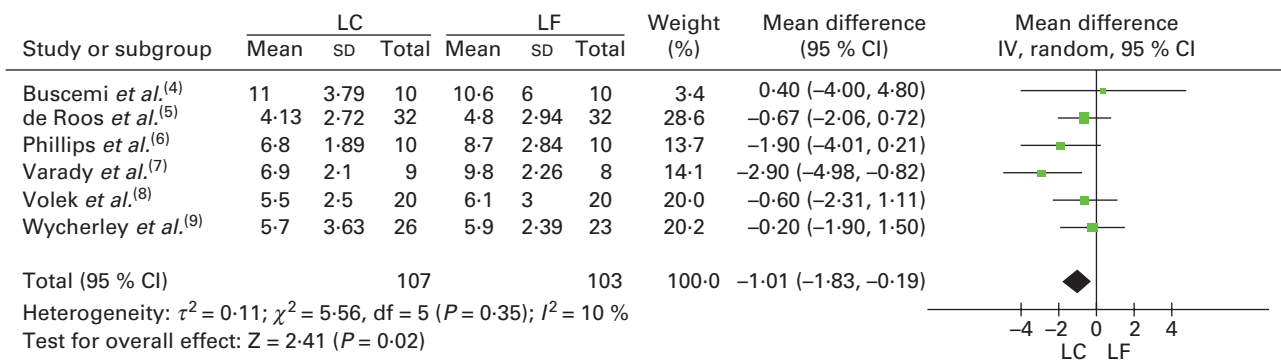


Fig. 1. Forest plot showing pooled weighted mean differences (WMD) with 95% CI for flow-mediated dilatation (%) of six randomised controlled low-carbohydrate diet studies. For each low-carbohydrate trial, ■ represents the point estimate of the intervention effects. The horizontal line joins the lower and upper limits of the 95% CI of these effects. The area of ■ reflects the relative weight of the study in the respective meta-analysis. At the bottom of the graph, ◆ represents the pooled WMD with 95% CI. (A colour version of this figure can be found online at <http://www.journals.cambridge.org/bjn>).

(95% CI -1.83 , -0.19)%, $P=0.02$) were significantly more pronounced following consumption of LC diets than following that of LF diets (Fig. 1). The I^2 test showed very low heterogeneity ($I^2 = 10\%$).

In our meta-analysis, LC dietary protocols were associated with a significant decrease in FMD when compared with their LF counterparts. A recent meta-analysis of observational studies including a sample size of 5·547 subjects has observed that a 1% decrease in FMD is associated with a 13% increase in the risk of future cardiovascular events⁽²⁾. In another recent meta-analysis of cohort studies carried out by Noto *et al.*⁽¹⁰⁾, an association between LC diets and increased risk of all-cause mortality could be observed, although not for cardiovascular (CVD) mortality as well as CVD incidence⁽¹⁰⁾. It should be noted that in direct comparison with the meta-analysis carried out by Bueno *et al.*⁽¹⁾, we had to modify the inclusion criteria, since only a few dietary intervention trials had reported FMD as an outcome parameter. However, in consideration of the fact that LC was associated with a higher all-cause mortality risk, further trials are required to confirm the mechanisms of FMD impairment following LC regimens.

Supplementary material

To view the supplementary material for this article, please visit <http://dx.doi.org/10.1017/S000711451300216X>

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