**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 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: \(-1.01\)) reflect the relative weight of the study in the respective meta-analysis. At the bottom of the graph, \(\blacklozenge\) 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 (2). 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

Lukas Schwingshackl
Georg Hoffmann

Department of Nutritional Sciences,
Faculty of Life Sciences, University of Vienna,
Althanstreet 14 UZA II, A-1090 Vienna,
Austria
email lukas.schwingshackl@univie.ac.at
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