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Letter to the Editor

Comment on Sergeant *et al.*: Impact of methods used to express levels of circulating fatty acids on the degree and direction of associations with blood lipids in humans

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In their paper in the January issue of this journal, Sergeant *et al.*[1], reported on the impact of different methods to express circulating fatty acids on the association with blood lipids. Using two human cohorts, the authors showed that the direction of the correlation between a number of individual circulating fatty acids and TAG reversed when expressing the circulating fatty acids as an absolute concentration *v.* a proportion of total fatty acids. On the basis of their findings, the authors suggest that expressing circulating fatty acids as concentrations is superior to expressing them as proportions, and they concluded that earlier relationships between (dietary) fatty acids and other biomarkers and indices of CHD should be re-visited with this in mind.

With their paper, Sergeant *et al.* point at an unresolved question on how to express and interpret levels of circulating fatty acids[2,3]. Both methods to express levels of circulating fatty acids have their merits and disadvantages. However, and contrary to the authors' suggestion, the reversal of the association with blood lipids when using different methods to express levels of circulating fatty acids does in itself not provide sufficient arguments for favouring one way of expression above the other. In fact, several key arguments in favour of expressing circulating fatty acids as a proportion of total fatty acids were not addressed.

First, circulating fatty acids expressed as proportions better reflect dietary intake than when expressed as concentrations, particularly for PUFA[2]. This is supported by data from our Hoorn[4] and Cohort Study on Diabetes and Atherosclerosis Maastricht (CODAM)[5] cohorts. In 1171 subjects, intakes of dietary fatty acids were measured by a FFQ and circulating fatty acids by GLC. The correlation between dietary linoleic acid (LA) and proportions of circulating LA was r 0·306, whereas the correlation between dietary LA and concentrations of LA (μg/ml) was r 0·175. Higher correlations when expressed in proportions were observed across PUFA.

Second, the pool of total circulating fatty acids comprises all individual circulating fatty acids, mainly present as TAG, cholesterl esters and phospholipids. Therefore, the concentration of individual circulating fatty acids is positively related to the concentration of TAG and LDL-cholesterol, HDL-cholesterol and total cholesterol (TC), as shown by Sergeant *et al.* and others[1,2]. Consequently, using circulating fatty acids as concentrations to study the relationship between intakes of dietary fatty acids and blood lipids can be confounded by effects of the individual dietary fatty acid on concentrations of the blood lipids itself, and may lead to spurious conclusions. In fact, strictly controlled dietary intervention studies on blood lipids provide strong evidence that increasing the intakes of dietary PUFA (mostly LA) at the expense of carbohydrates and SFA lowers TAG, LDL-cholesterol and TC concentrations[6].

We observe similar discrepancy in the associations of the concentration of TAG with circulating LA expressed in proportions (r −0·448) or concentrations (r 0·395), as shown by Sergeant *et al.*[1]. It is, however, important to note that this discrepancy may be specific to the association of circulating fatty acids with blood lipids, as circulating fatty acids are part of the pool of these blood lipids. The question whether such a discrepancy exists in the associations of circulating fatty acids with other CVD risk markers such as circulating cytokines or with the incidence of CVD or other outcomes is unresolved and deserves to be explored separately. For example, a strong association of DHA and EPA with brain atrophy rates has recently been reported, which was similarly inverse when circulating fatty acids were expressed as absolute concentrations or as proportions[7].

It can be argued that, when circulating fatty acids are used as a marker of dietary intake, the most important criterion for evaluating different methods of expressing circulating fatty acids is the strength of the relationship with their levels of dietary intake. This favours the expression of circulating fatty acids as a proportion of total fatty acids rather than as absolute concentrations, particularly for PUFA. However, our observations, combined with the findings of Sergeant *et al.*[1] and others[2,7], indicate that the optimal method of expressing fatty acid status depends on the biological assumptions and the biological question at hand.

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