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Which cheese to choose?

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It is well established that SFAs increase LDL cholesterol when they replace all other macronutrients except for *trans* fatty acids, and there are now emerging data that suggest differential effects of SFAs from various food sources, such as dairy foods and red meat, on lipid profiles and other cardiovascular disease (CVD) risk factors (as reviewed in reference 1). Small metabolic studies, including some with biomarkers of dairy intake, have shown neutral or beneficial effects of dairy consumption, particularly fermented foods such as cheese and yogurt, on lipid profiles (2, 3). Moreover, epidemiologic studies have pointed to neutral or inverse associations of dairy intake with CVD, although there are also reports of adverse associations (1).

The study by Raziani et al. (4) in this issue of Journal adds to the growing literature supporting a foods-based rather than macronutrient-focused approach toward optimal diets for cardiovascular health. Cheese, in its regular-fat or reduced-fat version, replaced habitually consumed foods in a 12-wk clinical trial in 139 Danish subjects who were randomly assigned to 1 of the 2 cheese arms (80 g each) or to a control arm in which bread and jam were substituted for habitual foods instead of cheese. Changes in metabolic risk factors for CVD—lipids, glucose, insulin, blood pressure, and anthropomorphic measures, including fat distribution measured by dual-energy X-ray absorptiometry—were assessed. This was a real-world study, a departure from the meticulously controlled and much more expensive interventions that have traditionally been undertaken. Participants lived as they normally would, with the exception of incorporating the provided test foods. It is a credit to the study team that body weight, a significant confounder of many diet studies, did not change significantly. Quite notably, neither did any of the other evaluated variables.

The findings were suggested to support the contention that SFAs in the context of cheese as a food source do not adversely affect CVD risk profiles. This may very well be, but there are some caveats to consider. For one, study compliance, although estimated at 95%, was based on participant self-report, which can overestimate the level of true compliance. Also, it is unclear what food items were being replaced by the supplementary foods, and consideration for the effect of this food substitution in the context of the overall dietary pattern could not be rigorously assessed. Furthermore, the reduction in SFAs and increased carbohydrate content of the control arm relative to the regular-fat arm would have been expected to yield lower LDL-cholesterol concentrations (5), but this was not the case, although the failure to detect this difference may have been due to limited statistical power. Hence, it is uncertain whether the overall null results of Raziani et al. can be attributed to the specified dietary interventions or to weaknesses in study design, implementation, or both. Moreover, it would have been more relevant in light of current dietary recommendations if the control diet had included increased polyunsaturated fat rather than exclusively carbohydrate.

It is important to point out that the biomarkers measured in this study may not have been sufficiently sensitive or specific for identifying metabolic effects that could have consequences for CVD risk. For example, it was shown that HOMA-IR failed to detect marked diet-induced changes in insulin sensitivity in animals as determined by the minimal model method (6). In the case of LDL, LDL-cholesterol concentration may not accurately reflect numbers of LDL particles, particularly small, dense LDL, which may more reliably predict CVD risk (7, 8). In this regard, it has been shown that a higher intake of carbohydrate, particularly simple sugars, increases numbers of small, dense LDL particles independently of LDL cholesterol (9), and that dietary saturated fat in the context of moderate carbohydrate intake (26% of total energy) primarily affects larger and more buoyant LDL particles (10). Because these were the main dietary components varied by Raziani et al., it may have been more informative had these measurements been performed in addition to the standard lipid profile.

Despite these concerns, it can be argued that studies such as that of Raziani et al. may be of more practical significance than those performed under more rigorous metabolically controlled settings. Moreover, there are some intriguing questions that the study raises. For example, given the great diversity of cheeses and heterogeneity of nutrients including the content of SFAs and salt (both of which are targeted nutrients whose reduction is recommended by current dietary guidelines), can one extrapolate the findings of this study from one type of cheese to another? What are the effects of regular-fat compared with reduced-fat cheese, or of various cheeses, on the intestinal microbiome, for which accumulating data support a critical and dynamic role in modulating cardiometabolic risk factors? Is there interindividual

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variability in response to cheese, and how can we best combine science (e.g., genetic markers for responsiveness and improved biomarkers of CVD risk) with common sense to optimize food choices for individuals in the context of their families, lives, and culture?

Given the increased appreciation for the role of the food matrix in modulating health effects of macronutrients, including those of SFAs (1), the Dutch have appropriately issued dietary guidelines that are food- rather than macronutrient-based (11). Ultimately, such population-level advice should be considered in the context of individual responsiveness to diet, metabolic status, and food preferences. Finally, we have yet to fully understand the potential metabolic and health effects of macronutrients in the context of processed foods.

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