The low-fat, low-carb debate and the theory of relativity

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The 2013 American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society (1) reviewed the available evidence-based literature with regard to the macronutrient content of diets and their health benefits and concluded that weight loss was similar with all types of diets as long as the diets achieved similar calorie restriction. There was moderate evidence to conclude that lower-fat/higher-carbohydrate diets, compared with higher-fat/lower-carbohydrate diets, resulted in a greater reduction in LDL cholesterol, lesser reductions in triglycerides, and lesser increases in HDL cholesterol. Despite the differences in lipids, one point goes to those who claim that “a calorie is a calorie.”

However, in this issue of the Journal, the low-fat/low-carbohydrate debate continues to rage on beyond the conclusion that a calorie is a calorie, especially in those with cardiovascular disease risk (2). We still consider that a calorie is a calorie, but evidence continues to accumulate since the publication of the guidelines that a calorie is metabolized differently depending on the underlying physiologic and genetic status of the human consuming that calorie (3). In fact, the weight loss seems to be similar because we are talking about the same number of calories restricted; however, depending on the metabolic status of the patient, cardiovascular disease risk markers are affected differently. Perhaps we should use the theory of relativity in physics and apply it to human physiology: i.e., a calorie’s worth is relative to the physiologic status of the person ingesting that calorie. That calorie exerts its influence relative to the host’s genetic makeup.

In this issue of the Journal, Tay et al. (4) report the results of a 52-wk randomized trial of low- vs. high-carbohydrate diets in 115 obese adults with type 2 diabetes. Completion rates were similar in the 2 groups as were weight loss, blood pressure, glycated hemoglobin (HbA1c), and reduction in fasting glucose. The low-carbohydrate-diet group showed greater reductions in diabetes medications and glycemic variability, as well as triglycerides, and greater increases in HDL cholesterol. Several aspects of the design of this study allow it to stand out and add to the knowledge obtained from previous studies. Other studies lasting for up to 1 y that compared low-fat with low-carbohydrate approaches in those with or without type 2 diabetes concluded that there were negligible differences in weight loss but reported changes in HDL cholesterol and triglycerides; this would favor a low-carbohydrate approach at least in this time period (5). Shorter studies were able to document reduced inflammatory markers in low-carbohydrate compared with low-fat interventions (6). The studies came to these similar conclusions despite variability in terms of subject characteristics and health risks, duration of intervention, primary outcomes, and the monitoring of compliance to diet, as well as definitions of low-carbohydrate and low-fat diet. In addition, a confounder for the health effects of macronutrient content is always weight loss (7).

What does the study by Tay et al. add to the literature? Several aspects of this study relating to methodology increase the confidence one has in its conclusions, as follows:

1) Subject homogeneity: The subjects examined were relatively homogenous in terms of comorbidities and all had type 2 diabetes block-matched for age, sex, BMI, HbA1c, and diabetes medications.
2) Diet homogeneity: Both of the diets reflected conventional dietary guidelines for low fat and low carbohydrate, and both diets limited saturated fat to <10% of energy, so that a high-saturated-fat diet was eliminated as a confounder. Similarly, the carbohydrate in each diet had a low glycemic index to avoid the additional detrimental effects on lipids and glycemic control that a simple carbohydrate with a high glycemic index would exert and confound the outcomes. Diets were individualized and matched for energy levels to facilitate weight loss (500–1000-kcal deficit/d).
3) Diet adherence: Adherence to each diet was maximized by one-on-one visits with the dietitian, and in addition, 30% of total energy in the form of key foods was provided to each subject for 12 wk. Thereafter, key foods or vouchers were provided on alternate months.
4) Choice of outcomes: Controlling weight-loss studies in patients with type 2 diabetes can be challenging due to antidiabetic medications and protocols for decreasing these medications as weight loss occurs. The method used for monitoring changes in these medications included a score computed on the basis of potency and dosage of medications and changes in these variables. In addition to the usual glycemic variables of fasting glucose and HbA1c, glucose variability was assessed by 48-h continuous glucose monitoring.

What is still left unanswered and why?
1) Subject heterogeneity: Although all of the subjects had type 2 diabetes, some had more advanced disease than others on

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the basis of the variability of insulin use, and years of diabetes diagnosis was not documented. This can affect the generalizability of the conclusions that in all cases type 2 diabetes is best treated with a low-carbohydrate diet.

2) Diet homogeneity and diet adherence: Although control was optimal for a nonfeeding study, one can only be sure of dietary compliance if the subject is monitored. This is hard to do in a 52-wk trial and adds to the expense of the trial.

What should be measured in the future?

1) A method to avoid the confounding that diabetes medications can generate is to study an insulin-resistant vs. an insulin-sensitive population characterized by oral-glucose-tolerance testing before intervention. In this study design you would be testing an at-risk population for type 2 diabetes vs. one not at risk and controlling the degree of comorbidity to avoid mixing advanced vs. early diabetes. This type of study is more relevant for the prevention of type 2 diabetes rather than for treatment as was the study by Tay et al.

2) A feeding study in which subjects are monitored during all meals would increase confidence in compliance to the diet and ensure additional consumption of foods that are highly processed with simple carbohydrate and saturated fat, adding confounders.

3) There is a significant involvement of certain gut bacteria in host metabolism, and therapeutic manipulation of the gut microbiota has been proposed for those with type 2 diabetes and well as for those at risk of type 2 diabetes (8, 9). A measure of gut microbiome changes before and after an intervention with additional measures of gut hormones, specifically glucagon-like peptide 1 and peptide YY, which change with macronutrient changes in the diet, would provide insight into the mechanism of metabolic changes due to diets with differing macronutrient content. Gut hormones are especially relevant in type 2 diabetes and glycemic control. In addition, studies have also linked high-fiber, complex-carbohydrate diets to improvements in carbohydrate and lipid metabolism due to the fermentation of these fibers by the gut microbiota (10). The effect of fats, carbohydrate, and protein contents of the diet on the gut microbiome and the changes in the gut microbiome in health and disease is an expanding research question that is relevant here, and studies should continue.

The American College of Cardiology/American Heart Association/The Obesity Society Practice Guidelines still stand because to ensure weight loss a calorie is still a calorie. However, with this study we have added solid data to extend the phrase “a calorie is a calorie.” Because of the controlled design of this study, there is more robust evidence that a lower carbohydrate diet could be beneficial in terms of glycemic variability, lipids, and blood pressure and prevent further complications of type 2 diabetes in those who already have type 2 diabetes. Perhaps of more importance is research that compares diets differing in macronutrient content in delaying or preventing progression to type 2 diabetes in those who are at risk. A calorie would still be a calorie but worth so much more in the prevention of the number-one disease of the 21st century. It is all relative in science and medicine.

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