

Carbohydrate-restricted versus low-glycemic-index diets for the treatment of insulin resistance and metabolic syndrome

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Carbohydrate-restricted diets (CRD) and diets comprised of foods with a low glycemic index (low-GI) are postulated to improve insulin resistance and metabolic syndrome, potentially preventing the development of type 2 diabetes mellitus (T2DM). In this article, recent findings concerning the effects of CRD and low-GI diets on measures associated with the metabolic syndrome and T2DM are discussed. An important problem that is encountered when trying to compare the effects of these different diets is the heterogeneity of carbohydrate consumption (8–40% of total kcal) used in interventions examining the effects of CRD. In contrast, there is a consensus definition for low-GI foods. However, since both quantity and type of carbohydrate powerfully affect metabolic outcomes, this review emphasizes that control of these factors in future studies will be important for determining the efficacy of either dietary approach in preventing the development of T2DM.

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INTRODUCTION

It is well known that the metabolic syndrome is characterized by accumulation of fat in the abdominal area, dyslipidemias (including elevated triglycerides and low HDL cholesterol), elevated blood glucose, and high blood pressure.¹ All of these undesirable features are associated with insulin resistance and increased risk of development of type 2 diabetes mellitus (T2DM).¹ The growing obesity epidemic in the United States and elsewhere is causing an increase in the already high number of individuals diagnosed with T2DM.² It is therefore imperative to devise dietary strategies or exercise programs to treat the metabolic syndrome before symptoms become exacerbated and diabetes emerges.

Although dietary modification is considered a cornerstone of therapy for the prevention of T2DM, the ideal dietary therapy remains controversial. Consumption of foods with a low glycemic index (low-GI), i.e., foods that promote a lower postprandial rise in blood glucose, has been advocated for the amelioration of dysfunctional glucose metabolism for more than two decades.³ In addition,

diet therapy based on varying degrees of total carbohydrate restriction are not new and have demonstrated efficacy in improving dysfunctional glucose metabolism and associated metabolic aberrations.⁴ In this article we review and compare new evidence regarding the effects of modifying carbohydrate intake or ingesting low-GI foods on the features of the metabolic syndrome and on insulin resistance.

WHAT IS A CARBOHYDRATE-RESTRICTED DIET?

In the past several years there has been a resurgence of carbohydrate-restricted diets (CRD) for use in the management of body weight and chronic metabolic disease risk factors. However, the use of CRD for these purposes is not new; for example, as highlighted by Westman et al.,⁵ early pioneers in diabetes treatment, such as Elliott Proctor Joslin, discussed the use of CRD as early as 1893 for the treatment of diabetes, as did Frederick Madison Allen between 1915 and 1920. The diet has also been used to treat other medical conditions.⁶ Low-carbohydrate

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Table 1 End-of-study carbohydrate intake (energy contribution and g/d) in select studies in which diet was considered carbohydrate restricted.

Reference	Percentage of carbohydrate (kcal)	Carbohydrate intake (g/day)
Sondike et al. (2003) ⁷	8	37
Yancy et al. (2003) ⁷	8	30
Sharman et al. (2004) ¹⁸	8	36
Volek et al. (2006) ²⁰	9	29
Wood et al. (2007) ¹⁷	13	50
McAuley et al. (2005) ¹¹	26	107
Brehm et al. (2003) ⁹	30	98
de Luis et al. (2007) ¹³	31	122
Gardner et al. (2008) ¹⁰	35	138
Samaha et al. (2003) ¹²	37	151
Dansinger et al. (2005) ¹⁵	40	190

(low-CHO) diets have been used in a range of different populations, such as adolescents,⁷ patients with T2DM,⁸ healthy women,⁹ and overweight premenopausal women,¹⁰ as well as in conditions such as insulin resistance¹¹ or obesity.^{12,13} The ebb and flow of public and medical interest in CRD continues – with the major difference between past and present being the rapid expansion in scientific literature on the topic.

Despite the recent rapid expansion of the literature, there is still no clear definition of what level of carbohydrate restriction constitutes a CRD. For example, some reports consider CRDs those diets in which carbohydrates constitute 40% of total energy intake,^{14,15} while other investigators consider 26% of energy from carbohydrates, a carbohydrate-restricted diet.¹⁶ In our laboratory, we consider carbohydrate-restricted diets to be those ketogenic diets in which carbohydrates contribute 10–15% of total energy intake, amounting to approximately 50 g/day or less.^{17–22} While the pragmatism of a single clear definition of CRD is debatable, it is important to recognize that not all interventions employing carbohydrate restriction are testing the same degree of dietary carbohydrate reduction. For illustration, Table 1 lists some studies in which carbohydrate restriction was used (i.e., “low-CHO diet” or “ketogenic diet” or “very-low-CHO ketogenic diet”). Of note is the considerable heterogeneity in the level of carbohydrate consumption used in various studies. Although the actual reduction in consumption of carbohydrate does not always match the prescription, metabolic improvements appear to result from any degree of carbohydrate restriction (in respect to habitual intake). As such, this heterogeneity brings to the fore the fact that there are differences between the diet, as prescribed, and the diet, as followed.

We have conducted numerous weight-loss intervention trials in which carbohydrate has been restricted to 10–15% of energy, and dramatic responses have been

observed in all the measures used to classify individuals with the metabolic syndrome.^{17–22} One of the most striking effects observed following consumption of a CRD at this level is a 40–70% reduction in plasma triglycerides^{17,18} and a significant increase in HDL cholesterol (HDL-C).^{19,20} Improvements in HDL-C during weight loss on a CRD are notable given that this effect was previously believed to occur only after weight loss ceased and body weight stabilized.²¹ Reductions in blood pressure,²² plasma glucose,²³ and waist circumference are consistent findings after following a CRD.^{17–21,23} In addition, other beneficial effects have been reported, including reductions in inflammatory markers^{18,23} and lipoprotein (a)²⁴ and increases in adiponectin.²³ It has been hypothesized that the degree of carbohydrate restriction is a primary determinant of the metabolic response: the greater the restriction of carbohydrate, the greater the improvement in the aforementioned parameters.⁴ Furthermore, the response to carbohydrate restriction does not appear to be a function of weight loss, as demonstrated by Krauss et al.¹⁶ and others.²⁵

Is the glycemic index useful for the consumer?

Glycemic index is a term used to explain the different postprandial glucose responses associated with intake of carbohydrates.³ While the concept has been adopted by certain individuals and organizations,²⁶ there is currently some reluctance to universally recommend glycemic index as a basis for dietary guidelines.²⁷ For example, in a recent study by Vega Lopez et al.,²⁸ within-individual variability in postprandial glucose response to foods (i.e., glycemic index) was reported to contribute more to glycemic index calculations than inter-individual variability; therefore, a question remains about the reliability of data and interpretation. In this study,²⁷ 14 subjects were analyzed for their glycemic index response to white bread; although the mean for the 14 subjects was 71, in agree-

ment with reported values,²⁹ the variability was between 44 and 132, indicating that similar to all dietary interventions, individuals also have different postprandial glucose responses to foods. Nevertheless, a reduction in the glycemic index value of foods in the diet has multiple beneficial effects on the features of metabolic syndrome and on inflammation.³ Brand-Miller et al.³⁰ concluded from their meta-analysis on the effects of low glycemic foods in the management of diabetes that a small, but useful, clinical effect was observed in glycemic control in patients with diabetes, although there is some controversy regarding the findings of this meta analysis.³¹ In addition to plasma glucose responses, other studies have reported different postprandial insulin responses to foods, and these are associated with specific modulations of inflammatory markers.³²

Some of the foods classified as having a low GI value, such as beans, fruits, and vegetables, seem appropriate for producing a low postprandial glucose response. However, there are other food items, such as pizza and certain cookies, that are also classified as having a low GI value; thus, controversy exists about the validity of these values. Furthermore, conveying information to the public about the glycemic index can be confusing because both glucose and white bread can be used as a reference standard in calculating a food's GI value, leading to the appearance of two totally different GI values for the same food. Some recently reported GI values for select foods are presented in Table 2 to illustrate the apparent discrepancies in existing GI values.³³ For example, Coke soda has a value of 53 if produced in Australia versus a value of 63 if produced in the United States (Table 2). Using glucose as a standard GI reference value, pizza can have a GI value as low as 36, while oatmeal has a value of 69; this confuses the public regarding the correlation between foods regarded as

healthy and low-GI foods. In addition, as seen in Table 2, there is a wide range of values for food items such as bread, breakfast cereals, or rice, which can further confuse the message to consumers.

Also of note when comparing CRD and low-GI diets is that the foods prescribed for consumption during a CRD (e.g., unlimited amounts of meat, poultry, fish, and eggs, and moderate amounts of low-CHO vegetables, salad dressings, nuts, and seeds)²⁴ are foods with a very low GI, which perhaps introduces an easier way to implement the key principles of a low-GI diet

COMPARISONS BETWEEN CRD AND LOW-GI: WHICH IS BETTER FOR THE TREATMENT OF INSULIN RESISTANCE AND THE METABOLIC SYNDROME?

In a recent report by Wolever et al.,³⁴ the authors concluded that consumption of a low-GI diet for 1 year by subjects with type 2 diabetes increases the disposition index, which is an index of pancreatic beta cell function based on the product of insulin sensitivity and insulin secretion, compared with a low-CHO diet. This analysis was a follow-up of their previous report in which comparisons were made among three groups: high-carbohydrate (high-CHO), high-GI diet; high-CHO, low-GI diet; and low-CHO (39.3% of total energy)¹⁴ diet. It is important to note that a diet with 39% of total energy coming from carbohydrates is not the usual definition of a low-CHO diet, although it is lower than the 46.5% of the high-GI group and the 51.9% of the low-GI group.¹⁴ The key finding of this paper is that the subjects with dyslipidemia associated with type 2 diabetes who consumed the lower concentration of carbohydrates (39%) had greater levels of improvement than the subjects consuming the other diets; the improvements were mainly seen as lower plasma triglyceride (TG) levels and higher high-density lipoprotein-cholesterol (HDL-C) levels. Plasma C-reactive protein (CRP), an inflammatory biomarker, was lower in both the low-GI and the low-CHO diet groups compared to the high-GI diet group. CRP concentrations in the low-GI and low-CHO groups were not different. In a follow-up article,³³ the researchers point out that after one year on the low-GI diet, subjects had better pancreatic beta cell function, based on the disposition index, compared to subjects on the high-GI and the low-CHO diets.

In our opinion, it is not possible to conclude from these findings that subjects with type 2 diabetes have a better outcome with a low-GI diet than with a low-CHO diet. First, what these authors call a low-CHO diet (39% of energy) is what we, and other authors, consider baseline carbohydrate intake in certain populations.²¹ Second, the low-CHO diet had more favorable effects on dyslipidemias than the low-GI diet and the same effect as the

Table 2 Glycemic index values for select food items.

Food	Glucose as a reference*	White bread as a reference*
Apple	28–50	41–73
Apple juice	37–44	53–63
Banana	35–72	67–103
Beans	20–56	28–80
Bread	20–85	37–122
Breakfast cereals	30–113	43–161
Cake	36–87	52–124
Coke	53–63	76–90
Cookies	47–73	67–104
Oatmeal	69	98
Rice	43–109	69–156
Pizza	36–54	51–78

* A range of values is used because of variability that exists depending on the type of food and the country in which the food is produced.

Adapted from Atkinson et al.³²

low-GI diet with respect to decreases in plasma CRP.¹⁴ The only measure for which a better outcome was observed with the low-GI diet was the disposition index after 1 year on the diet, but no effect was observed with this measure at 6 months on the diet.³³ Additional studies using a more restricted CHO intake need to be done before this question can be put to rest. Since 10–15% of energy from CHO is considered to be highly restrictive for some individuals; a diet with 25% CHO should be used. Therefore, until further information is collected, it is not possible to conclude that a low-GI diet is better than a low-CHO diet for the treatment of patients with type 2 diabetes.

CONCLUSION

It is intuitive that diets composed of foods that are aimed at reducing the postprandial glucose response are the best diets for individuals with metabolic syndrome or for those who present with insulin resistance or T2DM. The current debate is about whether or not carbohydrate restriction or foods with low GI values will have more favorable outcomes on the biomarkers underlying these conditions. In order to gain a clear picture of what these dietary treatments are doing and to provide meaningful information to the general public, several lines of action are recommended for future studies. 1) Provide a clear definition of carbohydrate restriction or low-CHO, since the amount of carbohydrate in the diet has a distinctive effect on the metabolic response. 2) Be aware that the existing data reporting glycemic index presents great variability among high-CHO food items, which may impact the food items chosen as low-GI foods for a given intervention. 3) Design future studies comparing a diet with low-GI foods with a CRD in which the contribution of carbohydrate to total energy is at least 25% in order to have a more accurate estimate of the effects of carbohydrate restriction and low-GI foods on the features of metabolic syndrome, insulin resistance, and T2DM.

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