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The low-carbohydrate diet and cardiovascular risk factors: Evidence from epidemiologic studies

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Abstract

Aims—Obesity is an important public health issue because of its high prevalence and concomitant increase in risk of cardiovascular diseases. Low carbohydrate diets are popular for weight loss and weight management but are not recommended in leading guidelines due to the perception that increases in dietary fat intake may lead to an adverse cardiovascular risk profile. To clarify the effects of a low-carbohydrate diet for weight loss on cardiovascular disease risk factors as compared to a low fat diet for weight loss, we systematically reviewed data from randomized controlled clinical trials and large observational studies.

Data synthesis—We searched the MEDLINE database (Jan 1966–Nov 2013) to identify studies that examined a low-carbohydrate diet as compared to a low-fat diet for weight loss or the improvement of cardiovascular disease risk factors.

Conclusions—Recent randomized controlled trials document that low-carbohydrate diets not only decrease body weight but also improve cardiovascular risk factors. In light of this evidence from randomized controlled trials, dietary guidelines should be re-visited advocating a healthy low carbohydrate dietary pattern as an alternative dietary strategy for the prevention of obesity and cardiovascular disease risk factors.

Keywords

Low carbohydrate diet; Cardiovascular disease; Risk factors; Weight loss

Introduction

Obesity is an important public health issue. In 2005, there were roughly 937 million overweight and 396 million obese people in the world, and the high prevalence is still projected to increase [1]. Further, obesity is a well-known risk factor for cardiovascular disease, type-2 diabetes and metabolic syndrome, and recently recognized as a disease by

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the American Medical Association. Therefore, the spread of obesity requires an intensive and effective intervention.

There has been increasing interest in the low-carbohydrate diet for weight loss and weight management. Nevertheless, the low-carbohydrate diet has never been recommended in leading guidelines because there is the perception that a low-carbohydrate diet will have adverse effects on cardiovascular disease risk factors, mostly due to the idea that saturated fats will be increased on a low-carbohydrate diet as compared to other weight-loss regimens [2–4]. Several professional organizations, such as the American Dietetic Association, have even cautioned against the use of a low-carbohydrate diet [5]. However, recent randomized controlled trials document that low-carbohydrate diets not only decrease body weight but also improve cardiovascular risk factors [6–9]. Since lowering the quantity of carbohydrate intake decreases total energy intake which is related to obesity [10], it remains unknown whether the cardiovascular effects of a low-carbohydrate diet are results of the decrease in dietary carbohydrates or total energy intake. To clarify this issue, we systematically reviewed data from randomized controlled clinical trials that examined the effects of low-carbohydrate diets as compared to an isocaloric low-fat diet for weight loss. We also reviewed data from large observational cohort studies to assess long-term associations of low carbohydrate diets with cardiovascular events, including specific food choices which may be included as a part of a low-carbohydrate dietary intervention and their potential influence on cardiovascular health.

Low-carbohydrate diets and cardiovascular risk factors: evidence from randomized controlled trials

We used the MEDLINE online database (Jan 1966–Nov 2013) to identify studies that examined the low-carbohydrate diet as compared to the low-fat diet. The following key words or medical subject headings in MEDLINE were used: (“low-carbohydrate diet”, “carbohydrate restriction”, “carbohydrate”, “fiber”, “body mass index”, “waist circumference”, “fat mass”, “obesity”, “diabetes”, “insulin resistance”, “blood glucose”, “hypertension”, “HDL”, “LDL”, “triglycerides”, “cholesterol”, “lipids”, “dyslipidemias”, “blood pressure”, “adipocytokines”, “inflammatory cytokines”, “C-reactive protein”, “heart diseases”, “cardiovascular diseases”, and “seizure”).

In this systematic literature review, we included randomized controlled trials conducted in adults, which compared a low-carbohydrate diet (≤45% of energy from carbohydrates) with a low-fat diet (≤30% of energy from fat) over an intervention duration of at least 6 months and reported cardiovascular risk factors as outcomes [11–13]. Thus we include both ketogenic and non-ketogenic low-carbohydrate diets in this review.

Body weight, body composition, and waist circumference

Randomized controlled trials have consistently shown that low-carbohydrate diets reduce body weight, with mean reductions ranging from 2.1 to 14.3 kg over at least 6 months of intervention [6,8,9,14–21]. The body weight reduction may not differ by level of carbohydrate restriction. A study comparing ketogenic diets with non-ketogenic low-

carbohydrate diets demonstrated that their efficacy at reducing body weight was equivalent over a 4-week intervention period [22], but long-term comparison has not been conducted. Moreover, both fat mass and lean mass were decreased but fat mass comprises the majority of weight lost on low-carbohydrate diets [14,15,17,18,20].

Compared to a low-fat diet, an isocaloric low-carbohydrate diet is at least as effective at reducing body weight. A 2006 meta-analysis including 5 randomized controlled trials showed that low-carbohydrate diets resulted in significantly more reduction in body weight than isocaloric low-fat diets at 6 months (net changes −3.3 kg, 95%CI: −5.3 to −1.4), but non-significantly more reduction at 12 months (net changes: −1.0 kg, 95%CI: −3.5 to 1.5) [23]. Those on low-carbohydrate diets experienced a similar reduction in fat mass and non-fat mass as those on low-fat diets, so that the changes in body composition were not significantly different between the two diets [9,14,15,17,18,20].

Low-carbohydrate diets may have the added benefit of decreasing the risk of central obesity. Brinkworth and colleagues reported that a low-carbohydrate diet decreased abdominal fat mass by approximately 30% as assessed using dual-energy X-ray absorptiometry scanning over a one-year intervention period compared to an isocaloric low fat diet [15]. While dual-energy X-ray absorptiometry scanning provides highly specific information on the anatomic location of fat, waist circumference is a much more commonly used measure of central obesity. Decreases in waist circumference on low-carbohydrate diets have ranged from 2.2 to 9.5 cm across studies and are comparable or greater than those seen on low fat diets [8,16,18].

Glucose, insulin, and HOMA

Most published randomized controlled trials also show that low-carbohydrate diets decrease fasting levels of blood glucose [9,14–16,18,21], HbA1c [18,19,24,25], serum insulin and/or HOMA [9,14–16,21] to a similar extent as seen on isocaloric low-fat diets. Moreover, reductions in insulin resistance do not appear to be different between ketogenic and non-ketogenic low-carbohydrate diets [22].

Lipids

Despite widely held beliefs, with the exception of a few studies, most randomized controlled trials have shown that low-carbohydrate diets increase HDL cholesterol and decrease total and LDL cholesterol [6,8,9,14–21]. Results from a 2006 meta-analysis did, however, show a greater increase in HDL (net change 3.1 mg/dL, 95%CI: −0.8 to 7.0) and a lesser reduction in total cholesterol (net change 10.1 mg/dL, 95%CI: 3.5 to 10.2) and LDL cholesterol (net changes 7.7 mg/dL, 95%CI: 1.9 to 13.9) on low-carbohydrate diets as compared to low-fat diets [23]. In addition, the ratio of total to HDL cholesterol decreased among those on low-carbohydrate diets, and this decrease was not significantly different from those seen on isocaloric low-fat diets in most trials [16,17,20,21] except for one study showing a greater decrease on the low-carbohydrate diet [8]. Moreover, studies consistently reported that the low-carbohydrate diet reduced triglycerides, and to a greater extent than the isocaloric low-fat diet (net change −31.0 mg/dL, 95%CI: −59.3 to −2.7) [6,8,9,14–21].

Despite fears of more atherogenic lipid profiles on low carbohydrate diets as compared to low-fat diets for weight loss, in general, the low-carbohydrate diet itself improved lipids profiles including total cholesterol, LDL cholesterol, HDL cholesterol, total/HDL ratio, and triglycerides. In fact, both low carbohydrate and low fat diets appeared to improve the lipids profiles, without strong evidence that either one was better.

Blood pressure

Current randomized controlled trials demonstrated that low-carbohydrate diets decrease systolic and diastolic blood pressure to a similar extent as isocaloric low fat diets [6,8,9,14–21]. This is logical as presumably, weight loss would be the driving factor in decreasing levels of blood pressure, and overall weight loss on both diets appears to be similar [23].

Emerging risk factors

The low-carbohydrate diets may also improve carotid endothelial function [26–29], inflammatory cytokines [30], C-reactive protein [27,30], homocysteine [27], and adipocytokines [28]. To date, however, most of the existing information comes from small clinical trials, and few studies have explored these relationships in larger samples.

In summary, low carbohydrate diets had beneficial effects on weight loss and cardiovascular risk factors, and these effects were comparable to those seen on low-fat diets in general. In addition, ketogenic low carbohydrate diets did not show a greater reduction in body weight or more improvement in cardiovascular risk factors than non-ketogenic low carbohydrate diets. Given that ketogenic low carbohydrate diets are more difficult to adhere to long-term, non ketogenic low carbohydrate diets may be more practical for inducing weight loss and improving cardiovascular risk factors. Due to the limited number of available trials, additional studies are needed to investigate the potential influence of age, gender, and race/ethnicity on the association.

Special populations

Diabetic populations

A literature review published in 2003 indicated that there was insufficient evidence to evaluate the use of low-carbohydrate diets among diabetic patients in part due to lack of data on long-term intervention [31]. Since then, several long-term trials of low-carbohydrate interventions have been conducted among diabetic patients [24,25,32]. All of these trials demonstrated that low-carbohydrate diets were as effective as isocaloric low-fat diets at reducing body weight and inducing favorable changes in lipids, blood pressure, blood glucose and plasma insulin among diabetic patients over at least 1 year of follow-up [24,32]. During the study intervention periods, no severe hypoglycemic episodes were reported. Based on this emerging evidence, low-carbohydrate diets could also be recommended among diabetic patients for the purpose of weight loss.

Children with seizure disorder

The ketogenic low-carbohydrate diet has been broadly used for seizure control in children with epilepsy [33–35]. At least one study indicated that children with seizure disorders may

prefer foods with a high fat content, compatible with a ketogenic low-carbohydrate diet [36]. However, the ketogenic low-carbohydrate diet may have adverse cardiovascular effects in epileptic children. Studies have shown that a ketogenic diet may be associated with excess risk of cardiac arrhythmias [37] and potentially unfavorable changes in total, LDL and HDL cholesterol over a two-year intervention [38]. Given these potential adverse effects, a ketogenic may not be advisable in children with seizure disorders.

Should we restrict all carbohydrates?

The source and quality of carbohydrates are additional factors in the decision of which and to what extent carbohydrates should be restricted. Carbohydrates derived from the intake of nutrient-rich fruits, vegetables, legumes and some whole grains are often accompanied by significant amounts of dietary fiber and tend to have a lower glycemic index than carbohydrates derived from the intake of refined grain products. Dietary fiber, which is abundant in many fruits, vegetables, whole grains, and legumes, cannot be broken down and absorbed by the body as are most carbohydrate fractions, and has been shown to delay the absorption of carbohydrates after a meal and thereby decrease the insulinemic response to dietary carbohydrates [39].

Many epidemiologic studies have documented that intake of dietary fiber, especially soluble fiber in cereal grains and some fruits, is inversely associated with risk of type 2 diabetes, coronary heart disease, myocardial infarction, congestive heart failure, and cardiovascular mortality [40–50]. For example, Schulze and colleagues conducted a meta-analysis of observational studies including 9 large cohorts and reported a reduced diabetes risk with higher dietary fiber intake from cereal grains (RR for the highest quartile [weighted median intakes: 11.6 g/ day] vs. the lowest quartile [weighted median intakes: 3.7 g/day]: 0.67; 95%CI: 0.62 to 0.72) [51]. Intake of whole grains in general has been shown to be beneficial for the prevention of type 2 diabetes, ischemic stroke, cardiovascular disease, and all-cause mortality [52–67]. A meta-analysis of observational studies including 7 large cohorts suggested that, after adjustment for cardiovascular risk factors, greater whole grain intake (pooled average 2.5 servings versus 0.2 servings per day) was associated with 21% (OR: 0.79, 95%CI: 0.73 to 0.85), 24% (OR: 0.76, 95%CI: 0.69 to 0.83), and 17% (OR: 0.83, 95%CI: 0.68 to 1.02) lower risks of cardiovascular events, incident coronary heart disease, and incident stroke, respectively [68]. The exact underlying mechanisms that may account for the protective effects of whole grain intake are not clear but evidence suggests that whole grain intake may assist in regulation of in body weight, waist circumference, blood pressure and blood glucose, and improvement in lipid profile [69,70].

Unlike whole grain, refined grain products do not appear to have protective effects for cardiovascular and metabolic diseases. Investigators have examined the association of refined grain intake with cardiovascular and all-cause mortality using data from the Iowa Women’s Health Study, Health Professional Follow-Up Study, and Nurses’ Health Study. These studies did not detect a protective effect of refined grain intake [61,66,71]. A meta-analysis of observational studies including 3 large cohort studies showed no evidence for a protective effect on cardiovascular events when comparing high with low intakes of refined grain products (RR: 1.07; 95%CI: 0.94 to 1.22) [68]. In contrast observational studies have

shown that limiting white rice, as a main source of refined grain, by substituting brown rice or beans may lower the risk of metabolic syndrome or type 2 diabetes mellitus [72,73].

Thus, a healthy low-carbohydrate diet should include substantial amounts of dietary fiber; while refined grain products should not be recommended and should be restricted. In available clinical trials, a wide variety of low-carbohydrate diets have been tested, with different levels of dietary fiber and sources of carbohydrate within the same overall level of carbohydrate content. Future studies are needed to determine the effects of quality and source of carbohydrates within a carbohydrate restricted diet.

What food choices are best in a low-carbohydrate diet?

The choices of fat and protein sources in a low-carbohydrate diet may affect the risk of subsequent cardiovascular disease. Indeed, a prospective cohort study of 82,802 U.S. nurses reported that a low-carbohydrate dietary pattern which incorporated a high intake of vegetable protein and unsaturated fat was associated with a lower risk of coronary heart disease over 19 years of follow-up [74]. In contrast, a low-carbohydrate dietary pattern accompanied by a high intake of animal-based protein and fat was not associated with a lower risk of cardiovascular disease, but associated with higher all-cause mortality in both men and women [75].

Further, among sources of animal fat and protein red meat (especially meat from ruminants), a common source of both saturated fat and animal protein, and other sources such as fish and poultry may have different cardiovascular effects. Red meat, whether processed or unprocessed, has consistently been associated with elevated risks of cardiovascular events [54,76–85]. Rather than red meat, fish and poultry could be chosen because they are not related to excess risk of cardiovascular diseases and disorders, such as coronary heart disease, myocardial infarction, congestive heart failure, stroke, type 2 diabetes, atrial fibrillation, or hypertension [76,78,80,86–91].

Low-carbohydrate, fiber-rich and non-starchy vegetables are ideal substitutions for red meat products. In particular, several studies have reported that green leafy vegetables contributed to the apparent protective effect of total vegetables on ischemic stroke (RR comparing highest to lowest quintiles: 0.79; 95%CI: 0.62 to 0.99) [92]. Other researchers also reported that an increase of 1 serving/day in green leafy vegetable consumption was associated with significantly lower risk of type 2 diabetes (HR: 0.91; 95%CI: 0.84 to 0.98) and coronary heart disease (RR: 0.77; 95%CI: 0.64 to 0.93) [93,94]. Cruciferous vegetables have also been associated with a protective effect on ischemic stroke [92]. Olive, other vegetable oils, nuts and avocado are excellent sources of dietary unsaturated fats in a low-carbohydrate dietary pattern and may improve cardiovascular risk factors. For example a six-week crossover trial showed that consuming walnuts and flax oil decreased blood pressure and improved endothelial function [95]. Other studies have demonstrated that long-term, a high intake of vegetable oil is associated with a lower risk of stroke and type 2 diabetes mellitus [96,97]. In addition, intake of soy and soy products should also be encouraged because soy protein supplement can decrease blood pressure and lower lipids [98,99]. Moreover, high soy intake is associated with a lower risk of type 2 diabetes and cardiovascular diseases

[100]. For instance, Kokubo and colleagues reported that soy intake at least 5 times per week versus 0–2 times per week was associated with 45% and 69% lower risk of myocardial infarction and cardiovascular mortality among Japanese women [101]. In contrast, there is no evidence of favorable cardiovascular effects of starchy vegetables.

In summary, a healthy low-carbohydrate dietary pattern should emphasize dietary fiber intake derived from whole grains, fiber-rich fruit, low-carbohydrate vegetables (such as green leafy vegetables, legumes, and cruciferous vegetables), avocado, olive and vegetable oils, soy, fish and chicken, and restrict or eliminate consumption of processed and unprocessed red meat as well as starchy vegetables and refined grains.

Conclusion

A low-carbohydrate diet decreases body weight and improves cardiovascular risk factors. Reducing the quantity and improving the quality of carbohydrate intake by choosing healthy carbohydrate substitutes, such as olive oil, chicken, fish, avocado, green leafy vegetables, and soy products, may decrease the risk of cardiovascular disease in addition to producing weight loss. In light of recent evidence from randomized controlled trials, dietary guidelines should be re-visited advocating a healthy low-carbohydrate dietary pattern as an alternative dietary strategy for the prevention of obesity and cardiovascular disease.

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