REVIEW

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Very-low-carbohydrate weight-loss diets revisited

ABSTRACT

Much scientific and anecdotal data demonstrate favorable metabolic responses to very-low-carbohydrate diets. We believe that very-low-carbohydrate diets merit further study for weight loss, and that criticisms of these diets lack scientific evidence.

KEY POINTS

Most studies have found that people lose more weight on very-low-carbohydrate diets than on standard weight-loss diets.

Mechanisms of weight loss on these diets may go beyond water loss and include suppression of appetite, increasing the metabolic rate, decreasing metabolic efficiency, and shunting of nutrients away from fat storage.

Weight loss is usually associated with small to moderate reductions in lean tissue, but low-energy, very-low-carbohydrate diets may have a protein-sparing effect compared with low-fat diets.

These diets may also have favorable effects on specific risk factors for cardiovascular disease (eg, fasting and postprandial triglyceride levels, high-density lipoprotein levels, and low-density lipoprotein particle size).

IN THE SEARCH for an effective method of losing weight, many people have adopted various diets that limit carbohydrate intake, commonly called *ketogenic diets* or *very-low-carbohydrate diets*.

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Experts have criticized this dietary approach in several articles, including one recently published in the *Cleveland Clinic Journal of Medicine*,[1] on the grounds that it jeopardizes health. Indeed, very-low-carbohydrate diets are an easy target for criticism, since they are diametrically opposed to the low-fat/high-carbohydrate dietary recommendations put forth by national organizations such as the National Cholesterol Education Program.[2]

Our hypothesis is that there is a lack of scientific evidence for the criticisms commonly laid against very-low-carbohydrate diets, especially regarding the metabolic mechanisms involved. Quite the contrary, we feel there is a significant amount of scientific and anecdotal data demonstrating favorable metabolic responses to very-low-carbohydrate diets. A recent US Department of Agriculture review has called for further research into the safety and efficacy of low-carbohydrate diets.[3]

This review provides a slightly different perspective on very-low-carbohydrate diets, based on scientific data and clinical experience. We hope this overview provides a background on which to formulate ideas and testable hypotheses, stimulating further discussion and research in this area.

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DEFINITIONS

Diets that limit carbohydrate intake have been called *low-carbohydrate*, *very-low-carbohydrate*, *high-protein*, *high-fat*, and *ketogenic*. For the purpose of this review, we use the term *very-low-carbohydrate diet*, defined as less than 50 g of carbohydrate per day.

Not all very-low-carbohydrate diets are high-protein diets, and vice versa. For example, a mixed diet with "high protein" would not be a very-low-carbohydrate diet if it contained more than 50 g of carbohydrates per day. In general, the studies presented in this review examined very-low-carbohydrate diets that contained less than 10% carbohydrate, 25% to 35% protein, and 55% to 65% fat (TABLE 1).

TABLE 1

Typical day's menu on a very-low-carbohydrate diet

Breakfast	
Ham and cheese omelet	
Whole eggs	3
Cheddar cheese	2 ounces
Ham	2 ounces
Bacon	2 slices
Coffee	1 cup
Cream	2 tablespoons
Lunch	
Chicken salad	
Tossed greens	2 cups
Chicken breast	4 ounces
Mozzarella cheese	1.5 ounces
Ranch dressing	3 tablespoons
Almonds	1 ounce
Diet soda	1 cup
Dinner	
Grilled salmon	4 ounces
Green beans	1 cup
Tossed greens	1 cup
Vinegar and oil dressing	4 tablespoons
Sugar-free gelatin	1 cup
Red wine	4 ounces
Daily nutrient content	
Kilocalories	2,000
Carbohydrate	10%
Fat	58%
Protein	28%
Alcohol	4%

IMPORTANT QUESTIONS

Important questions need to be addressed concerning the advantages and disadvantages of very-low-carbohydrate diets. Hard data are limited but suggest that these diets are not harmful in the short term and may have therapeutic value for weight loss and certain other medical conditions.

Physicians should be open to this possibility and stay abreast of the research in this area. The challenge will be to link the metabolic advantages commonly associated with short-term consumption of very-low-carbohydrate diets to long-term outcomes.

Are all calories equivalent?

The basic principle behind all weight-loss diets is to reduce dietary energy intake below the energy needs of the body. Whether the relative distribution of protein, carbohydrate, and fat can influence the magnitude of weight loss achieved remains unclear, however.

According to the first law of thermodynamics, changes in energy store equal energy intake minus energy expenditure.

But are all calories equivalent? With one exception,[4] most studies[5–9] have reported that people lost more weight on very-low-carbohydrate diets than on diets that contained the same number of calories but more carbohydrates. The experimental diets in these studies contained from 600 to 1,900 calories and 46 to 115 g of protein per day. Subjects included obese men and women, and the diets were consumed for 10 to 63 days.

In the only study that did not demonstrate greater weight loss with the very-low-carbohydrate diet,[4] the energy content of the diet was low (600 kcal/day) and the subjects were morbidly obese (> 45 kg of excess body weight).

Is the weight loss from water?

The greater weight loss is presumed to be from water.[1] However, several other possibilities exist:

- Very-low-carbohydrate diets may alter the metabolic rate by preserving more lean body mass[9]
- They may decrease metabolic efficiency, resulting in greater loss of heat[10]

TABLE 2

Very-low-carbohydrate diets decrease fat mass, spare lean body mass

STUDY	YEAR	DIET	SUBJECTS	DURATION (DAYS)	ENERGY (KCAL)	CHO (G)	BODY MASS CHANGE (KG)	FAT MASS CHANGE (KG)	LEAN BODY MASS CHANGE (KG)	METHOD
Benoit et al[11]	1965	Fasting	7 M, obese	10	0	0	–9.6	–3.4	–6.2	UWW
		VLCD		10	1,000	10	–6.6	–6.4	–0.2	
Young et al[9]	1971	VLCD	2 M, obese	63	1,800	104	–11.2	–8.4	–2.8	K40
		VLCD	3 M, obese	63	1,800	60	–12.3	–10.2	–2.1	
		VLCD	3 M, obese	63	1,800	30	–15.6	–14.9	–0.7	
Phinney et al[22]	1980	VLCD	5 F, 1 M, obese	42	500–750	0	–10.6	–7.1	–3.5	UWW
Willi et al[12]	1998	VLCD	6, obese	56	650–725	25	–15.4	–16.8	1.4	DXA
Volek et al[13]	2002	VLCD	12 M, lean	42	2,335	46	–2.2	–3.3	1.1	DXA
		Control	8 M, lean	42	2,190	330	0.4	0.0	0.4	DXA

CHO = carbohydrate, M = male, F = female, UWW = underwater weighing, VLCD = very-low-carbohydrate diet, K40 = potassium-40, DXA = dual-energy x-ray absorptiometry

Very-low-carb diets:
- **< 10% carbs**
- **25%–35% protein**
- **55%–65% fat**

- They may promote loss of energy in the form of ketones in urine, feces, and sweat
- They may also result in partitioning of nutrients away from fat storage and toward accumulation of lean tissue. The few studies that have assessed body composition on a very-low-carbohydrate diet suggest a preferential loss of fat mass and preservation of lean body mass (TABLE 2).[9,11,12]

We recently used dual-energy x-ray absorptiometry to examine the change in body composition in subjects who switched from their habitual diet (48% carbohydrate, 32% fat) to a very-low-carbohydrate diet (8% carbohydrate, 61% fat) for 6 weeks.[13] Surprisingly, fat mass decreased significantly (–3.3 kg) and lean body mass increased significantly (+1.1 kg), despite no change in physical activity. There were no significant changes in the control group.

These results suggest that a very-low-carbohydrate diet favors loss of fat. Water may account for some of the initial rapid weight loss, but it appears that fat loss accelerates and lean tissue is preserved over longer periods. There is no evidence that prolonged very-low-carbohydrate diets cause chronic dehydration.

Do these diets increase the risk of cardiovascular disease?

The possibility that very-low-carbohydrate diets increase the risk of cardiovascular disease has received widespread attention. Although no single diet is appropriate or ideal for everyone, our experience is that very-low-carbohydrate diets may improve the cardiovascular risk profile in selected individuals, even without significant weight loss.

Triglycerides. The most dramatic and consistent lipid response to a very-low-carbohydrate diet is a moderate to large decrease in fasting triglyceride levels and postprandial triglyceride responses to a fat-rich meal,[14] both independent risk factors for cardiovascular disease.[15,16]

Total cholesterol. Studies that examined blood lipid responses indicate that very-low-carbohydrate diets generally result in small increases in total cholesterol,[14,17–21] which can be prevented or even reversed if significant weight loss occurs.[7,12,22]

LDL and HDL. Although the data are limited, very-low-carbohydrate diets tend to result in moderate increases in low-density lipoprotein (LDL) and high-density lipopro-

tein (HDL), but the ratio of total cholesterol to HDL is not altered significantly.[14,18,23]

Further work is warranted to examine the effects of a very-low-carbohydrate diet in different populations over longer periods.

Atherogenic lipoprotein phenotype. An impaired ability to clear circulating triglyceride-rich lipoproteins during the postprandial period is the driving force underlying the lipid abnormalities of the *atherogenic lipoprotein phenotype*: increased hepatic production of very-low-density lipoprotein (VLDL), reduced HDL, and a predominance of small LDL particles.[24] Approximately 25% of adult men have this constellation of lipid abnormalities, which confers increased risk of cardiovascular disease upon otherwise-healthy people.[25]

Paradoxically, a low-fat/high-carbohydrate diet exacerbates atherogenic dyslipidemia if the patient does not lose a significant amount of weight or increase his or her level of physical activity.[26,27] However, a very-low-carbohydrate diet improves all aspects of atherogenic dyslipidemia, decreasing fasting and postprandial triglyceride levels, increasing HDL, increasing LDL size, and decreasing insulin, independent of weight loss.[14,23]

We have studied the response to a very-low-carbohydrate diet in a group of healthy subjects with the atherogenic lipoprotein phenotype (fasting triglyceride level > 150 mg/dL and peak postprandial triglyceride level > 400 mg/dL).[14] These subjects consistently demonstrated significant improvements in fasting and postprandial triglyceride levels (FIGURE 1), HDL levels, and LDL particle size.

We also recently examined the effects of a 6-week very-low-carbohydrate diet on fasting and postprandial serum lipid levels in healthy, normal-weight, normolipemic men who switched from their habitual diet (17% protein, 47% carbohydrate, 32% fat) to a very-low-carbohydrate diet (30% protein, 8% carbohydrate, 61% fat).[28] There were significant decreases in fasting serum triglycerides (–33%), postprandial lipemia after a fat-rich meal (–29%), and fasting serum insulin concentrations (–34%). Fasting serum total and LDL cholesterol and oxidized LDL were unaffected, and HDL cholesterol tended to be increased (+11.5%). In subjects with a predominance of small LDL particles ("pattern B"), there were significant increases in mean and peak LDL particle diameter and in the percentage of large LDL particles after the very-low-carbohydrate diet.

These findings suggest that a very-low-carbohydrate diet does not have a deleterious effect on the cardiovascular risk profile in the short term and may improve the lipid disorders characteristic of atherogenic dyslipidemia.

A very-low-carbohydrate diet lowers triglyceride levels

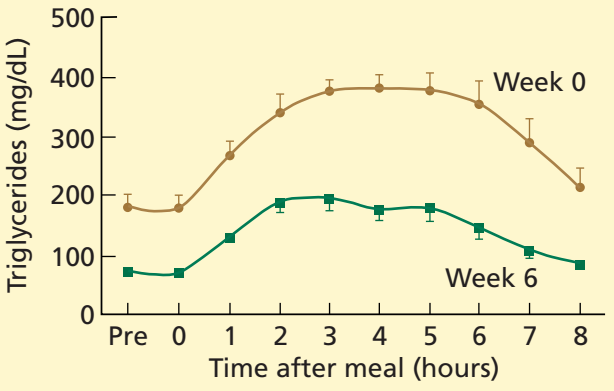

FIGURE 1. Data from nine subjects in two previous studies of very-low-carbohydrate diets performed in our laboratory[14,28] who had elevated fasting triglyceride levels greater than 150 mg/dL and exaggerated postprandial lipemia. Serum triglyceride responses to the same fat-rich meal were determined after their habitual high-carbohydrate diet and after 6 weeks of a very-low-carbohydrate diet.

Americans have lowered their fat intake but keep getting fatter

Do dietary carbohydrates or fat lead to obesity?

Obesity is multifactorial; its causes include both excess energy intake and inadequate energy expenditure. A great deal of controversy exists about the role of dietary carbohydrate and fat in contributing to obesity. Current dietary guidelines focus on lowering dietary fat and increasing carbohydrate intake.[29]

Americans have steadily reduced their reported intake of dietary fat, yet we are in the midst of a national epidemic of obesity. The prevalence of obesity has risen progressively from the mid-1970s to the mid-1990s, and

over 50% of Americans are overweight, defined as a body mass index greater than 25 kg/m^2.[30] These statistics suggest that the cause of obesity is probably not related to consumption of dietary fat.

Several long-term intervention studies have examined whether high-fat diets promote weight gain and whether low-fat diets can lead to weight loss.[31] Generally, the weight loss was small (< 1 kg) in studies of up to 1 year, leading us to conclude that the effects of diets differing in macronutrients on energy intake and body fatness remain unclear.

How might a low-fat/high-carbohydrate diet promote weight gain? Consumption of carbohydrates with a high glycemic index (a measure of how quickly and how high specific foods raise the blood sugar level) promotes a short-term increase in energy intake,[32] although no studies have linked this to long-term changes in body weight.

In theory, the stimulatory effect of increased carbohydrate intake (especially sugar or processed carbohydrates) on insulin concentrations provides a sound biological mechanism linking high-glycemic carbohydrate diets to weight gain, given the potent antilipolytic effects of insulin at physiologic concentrations.[33] In contrast, very-low-carbohydrate diets result in lower insulin concentrations,[13,34] in addition to suppressing appetite, both of which could enhance long-term weight loss and weight maintenance.

Ketone bodies may be the perfect fuel for dieters

Are ketones bad?

During prolonged fasting or adherence to a very-low-carbohydrate diet, whole-body metabolism gradually shifts toward obtaining a greater percentage of energy from lipid sources, which can result in the production of ketone bodies in the liver. Clinically, ketone body production indicates that lipid metabolism has been accelerated and that all the enzymes involved in metabolic pathways of lipid metabolism (eg, lipolysis, fatty acid transport, beta-oxidation, and ketogenesis) are operational.

During starvation or periods when carbohydrate intake is very low, ketone bodies serve as an alternative oxidative fuel for peripheral tissues to spare carbohydrate and protein. In this sense, ketone bodies could be considered the perfect fuel for dieters.

Catabolism of protein is reduced by ketones,[35] which probably explains the preservation of lean tissue observed during very-low-carbohydrate diets.[9,11,12] The small amount of glucose required by the brain and red blood cells can easily be met via gluconeogenesis from protein and fat. There are no direct data from which we can ascertain whether the low level of ketosis accompanying this diet is harmful or harmless.

Do very-low-carbohydrate diets cause insulin resistance?

Despite concern that very-low-carbohydrate diets, especially if high in saturated fat, might lead to insulin resistance, the link between saturated fat and insulin resistance is tenuous. Further, data from three recent studies that used the insulin clamp technique indicate that very-low-carbohydrate diets do not have an adverse effect on glucose metabolism or insulin resistance.[36–38]

Collectively, these studies indicate that very-low-carbohydrate diets alter the effects of insulin on oxidative and nonoxidative glucose disposal, favoring storage of glucose as glycogen in muscle. They also appear to prevent insulin-stimulated inhibition of lipid oxidation.

Data from these studies do not support the notion that very-low-carbohydrate diets exacerbate the risk of type 2 diabetes and insulin resistance; rather, they actually show a potential favorable effect as evidenced by decreased basal endogenous glucose production and improved insulin-stimulated nonoxidative glucose disposal.

Do very-low-carbohydrate diets suppress appetite?

Scientific and anecdotal evidence clearly indicate that very-low-carbohydrate diets reduce appetite and caloric intake.[14,39] This may be partially due to the fewer food choices available on the diet, but a more likely explanation is the higher satiety value of fat and protein or the anorectic effect of ketosis.[40]

Increased circulating levels of beta-hydroxybutyrate (the primary ketone in the blood) act as a satiety signal.[41] Given that most people who lose weight find it difficult to

keep the weight off, the high level of appetite satiation associated with very-low-carbohydrate diets could enhance successful adherence to a long-term low-energy diet.

Do these diets decrease athletic performance?

Several studies have shown that chronic consumption of very-low-carbohydrate diets leads to several metabolic and hormonal adaptations that facilitate increased fat oxidation and promote a glycogen-sparing effect within muscle.[42]

The effects of a very-low-carbohydrate diet on prolonged exercise performance are unclear; studies have produced inconclusive results. Although high-carbohydrate diets have historically been considered superior to high-fat diets for this type of exercise, studies have shown that very-low-carbohydrate diets may result in improved[43] or maintained[42] endurance exercise performance.

Are there other possible adverse effects?

Although research on very-low-carbohydrate diets is limited, information about potential adverse effects may come from two different but related dietary approaches: the ketogenic diet and the protein-sparing modified fast.

The ketogenic diet, a treatment for epilepsy, consists of high fat intake, low carbohydrate intake, and low protein intake.[44] Side effects of the ketogenic diet in children have included calcium oxylate and urate kidney stones (from 0.5% to 5.0% incidence over 1 year), vomiting, amenorrhea (21%), hypercholesterolemia, and water-soluble vitamin deficiencies.[45,46]

The protein-sparing modified fast is a specific type of very-low-calorie diet, with extreme limitation of carbohydrate and calories (< 800 kcal daily).[47,48] Because the currently popular very-low-carbohydrate diets typically provide more than 800 kcal daily, they may not cause the side effects seen with the much more stringent protein-sparing modified fast.

Another criticism relates to the potential adverse health effects of reducing intake of foods generally recognized as healthy, including fruits, vegetables, and whole grains. This is a legitimate concern; however, a very-low-carbohydrate diet can include a wide range of vegetables (eg, tomatoes, cucumbers, peppers) and even small amounts of fruit. It would also be prudent to take a multivitamin/mineral supplement to ensure adequate intakes of all essential micronutrients.

MORE RESEARCH NEEDED

Substantial evidence from short-term controlled studies indicates that very-low-carbohydrate diets are effective for weight loss. Because research methods and techniques have advanced since many of these studies were done, several research teams are revisiting very-low-carbohydrate diets in view of the urgent need for effective therapies for obesity and other metabolic disorders.

Ketosis suppresses appetite, helping keep weight off

Because there are very few ad libitum ("free-living") outpatient studies and no controlled studies longer than 8 weeks, no conclusion can be made yet regarding the long-term safety and efficacy of this approach.

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