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Human Kinetics
SCHOLARLY REVIEW

Fat-Free Mass Changes During Ketogenic Diets and the Potential Role of Resistance Training

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Low-carbohydrate and very-low-carbohydrate diets are often used as weight-loss strategies by exercising individuals and athletes. Very-low-carbohydrate diets can lead to a state of ketosis, in which the concentration of blood ketones (acetoacetate, 3-β-hydroxybutyrate, and acetone) increases as a result of increased fatty acid breakdown and activity of ketogenic enzymes. A potential concern of these ketogenic diets, as with other weight-loss diets, is the potential loss of fat-free mass (e.g., skeletal muscle). On examination of the literature, the majority of studies report decreases in fat-free mass in individuals following a ketogenic diet. However, some confounding factors exist, such as the use of aggressive weight-loss diets and potential concerns with fat-free mass measurement. A limited number of studies have examined combining resistance training with ketogenic diets, and further research is needed to determine whether resistance training can effectively slow or stop the loss of fat-free mass typically seen in individuals following a ketogenic diet. Mechanisms underlying the effects of a ketogenic diet on fat-free mass and the results of implementing exercise interventions in combination with this diet should also be examined.

Keywords: ketogenic diet, fat-free mass, resistance training, very-low-carbohydrate diet

Nutritional interventions designed to achieve reductions in body fat in exercising individuals and athletes continue to be a topic of interest. Low-carbohydrate and very-low-carbohydrate diets are strategies often used by individuals trying to lose weight. If the carbohydrate content of the diet is low enough, the body enters a state of ketosis, in which blood ketone concentrations rise as a result of increased fatty acid breakdown and activity of ketogenic enzymes. The exact level of carbohydrate restriction necessary to achieve ketosis varies individually, but a frequently used intake level associated with ketosis is 50 g/day or less (Mullins et al., 2011; Sumithran & Proietto, 2008). The metabolic state of ketosis has been described as clinically benign and should not be confused with the pathological state of ketoacidosis. Ketosis in individuals typically leads to maximum ketone concentrations of 2–3 mM, whereas concentrations in ketoacidosis are often more than 10 times higher (Mullins et al., 2011).

Three ketone bodies are produced through ketogenesis in the mitochondria of hepatocytes from the oxidation of fatty acids. These three compounds are acetoacetate (AcAc), 3-β-hydroxybutyrate (3HB), and acetone (Figure 1). 3HB is not technically a ketone but, along with AcAc, is one of the primary ketone bodies used for energy during fasting and low carbohydrate intake (Sumithran & Proietto, 2008). Ketones supply a minor amount of the body's energy requirements after an overnight fast (~2%–6%), but a sizable amount after 3 days of fasting (30%–40%; Laffel, 1999).

Adipocyte lipolysis under fasting and low-carbohydrate conditions leads to the liberation of fatty acids (Soeters et al., 2012). These fatty acids are transported by albumin through circulation and can enter hepatocytes where they are broken down through β-oxidation, producing acetyl coenzyme A (CoA). Ketogenesis begins with two acetyl CoA molecules that are converted to acetoacetyl CoA in a reversible reaction. Acetoacetyl CoA is then converted to 3-hydroxy-3-methyl-glutaryl-CoA (HMG CoA) and then to the ketone body, AcAc (Boron & Boulpaep, 2009). AcAc can be converted to acetone or 3HB. Figure 2 depicts the enzymes and intermediates of the ketogenic pathway.

Rationale for Ketogenic Diets

Ketogenic diets can be effective at reducing body fat, as well as improving some blood lipid components (Sumithran & Proietto, 2008). Many weight-loss diets that reduce body fat are accompanied by a concomitant decrease in fat-free mass (Stiegler & Cunliffe, 2006). Nutritional interventions that could lead to superior retention of skeletal muscle (a major component of fat-free mass) during weight loss would be beneficial for

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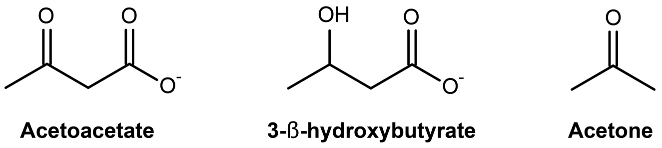

Figure 1 — Structure of ketone bodies.

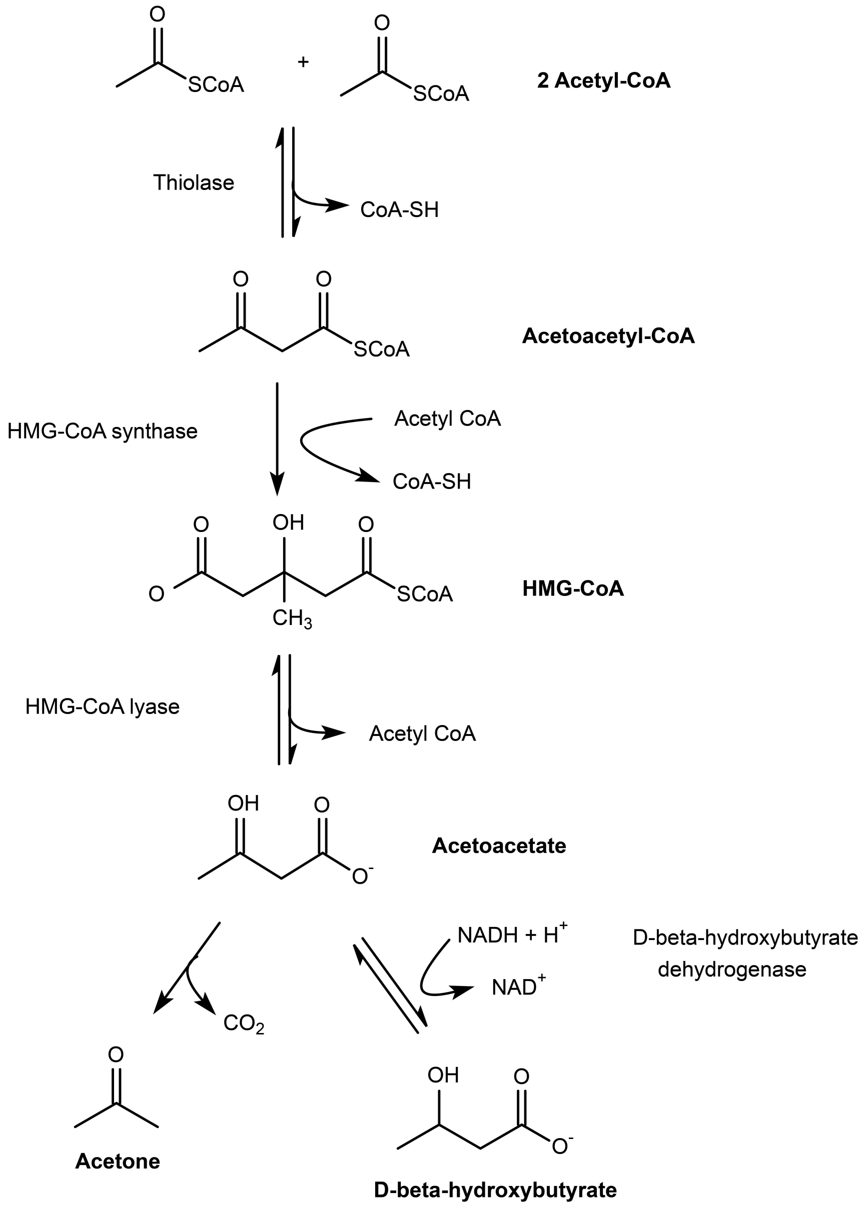

Figure 2 — Ketogenesis. CoA = coenzyme A; HMG CoA = hydroxymethyl-glutaryl-Coenzyme A; NAD = nicotinamide adenine dinucleotide; CO2 = carbon dioxide.

a number of reasons, including maintenance of resting metabolic rate (Stiegler & Cunliffe, 2006) and functional abilities, particularly in older adults. Some authors have reported that very-low-carbohydrate diets lead to sizable losses of lean body mass (Noakes et al., 2006), but others disagree (Manninen, 2006; Volek et al., 2002). Carbohydrate restriction leads to decreases in blood glucose, and it is possible that increased gluconeogenic activity could promote the breakdown of muscle tissue to provide amino acid substrate. Although this is known to occur during complete fasting, ketogenic diets promote a pseudofasted state in which oxidation of fatty acids primarily meets energy needs because of the lack of dietary carbohydrate, but catabolism is not as pronounced as during a complete fast (Benoit et al., 1965; Freeman et al., 2006; Soeters et al., 2012). Benoit et al. (1965) reported that obese young men lost only 3% of weight as fat-free mass during a 10-day hypocaloric ketogenic diet compared with 65% of weight as fat-free mass during a 10-day fast. It is possible that fatty acid oxidation and ketone body metabolism are able to provide enough energy to compensate for the decreased availability of glucose, thus sparing muscle protein and maintaining lean mass. Moreover, tissues that can derive energy from ketone bodies (e.g., the brain) allow glucose to be used by glycolytic tissues (e.g., erythrocytes) in a state of decreased glucose availability.

The purpose of this narrative review article is to examine the relationship between ketogenic diets and fat-free mass changes through a summary of research studies conducted in the past 15 years. This comparison includes a discussion of some difficulties in measuring the changes in fat-free mass and the potential to improve retention of fat-free mass via resistance training while following a ketogenic diet.

Literature Search

Although this is a narrative review, a literature search was conducted for studies using ketogenic diet programs that measured changes in fat-free mass (or lean body mass) to ensure a balanced view of the topic. Electronic databases (PubMed, ScienceDirect, and Wiley Online Library) were searched for studies published in the past 15 years using combinations of the terms *ketogenic diet, very low carbohydrate diet, fat-free mass,* and *lean body mass.* Additional studies published in the past 15 years were located using the review of literature conducted by the Nutrition Science Initiative (2012). Inclusion criteria for all studies included (a) use of a ketogenic (very low carbohydrate) diet that contained 50 g or less carbohydrate per day (or ≤10% of energy from carbohydrates); (b) measurement of fat-free mass at beginning and end of intervention; (c) duration of 4 or more weeks; (d) eight or more participants per group; (e) adult subjects of any ethnicity, age, and body weight; and (f) publication in the past 15 years. A total of 13 studies meeting these criteria were located (Table 1).

Effects of Ketogenic Diets on Fat-Free Mass

Table 1 summarizes the objectives, methods, subjects, and major results of the studies included in this review article. The vast majority of the research reported a decrease in fat-free mass after following a ketogenic diet (Brehm et al., 2003, 2005; Brinkworth et al., 2009a, 2009b; Johnstone et al., 2008; Landers et al., 2002; Noakes et al., 2006; Ruth et al., 2013; Wood et al., 2007; Yancy et al., 2004), two studies reported no change (Johnston et al., 2006; Paoli et al., 2012), and one study reported an increase (Volek et al., 2002). The quantity of fat-free mass lost was approximately 1–3.5 kg, and the majority of the studies reported weight loss of approximately 5–13 kg and fat mass loss of approximately 3.5–11 kg.

The Volek et al. (2002) study is the only one that described an increase in fat-free mass. Several potential explanations could contribute to the different result. First, the research subjects were normal-weight men. All other located studies, except Paoli et al. (2012), used overweight and obese individuals. The subjects used were of a similar age to those in a number of other studies, but were on the younger end of the spectrum. Second, inducing weight loss was not the goal of Volek et al. Subjects were encouraged to maintain body weight and were even instructed to consume more food to do so. Almost all other located studies reported greater weight loss than Volek et al., and a number of studies intentionally imposed a caloric deficit. Energy restriction of approximately 25%–30% was implemented in several studies (Brinkworth et al., 2009a, 2009b; Johnston et al., 2006; Ruth et al., 2013), but others did not specifically assign a level of energy intake (Brehm et al., 2005, 2003; Johnstone et al., 2008; Landers et al., 2002; Wood et al., 2007; Yancy et al., 2004).

Several studies used ad libitum diets in regard to fat and protein (Brehm et al., 2005, 2003; Landers et al., 2002; Yancy et al., 2004), and others prescribed specific intake guidelines for all macronutrients (Johnston et al., 2006; Johnstone et al., 2008; Noakes et al., 2006; Volek et al., 2002; Wood et al., 2007). The studies assigning macronutrient intake implemented diets with approximately 30%–35% of energy intake from protein, 60%–65% from fat, and 5%–10% from carbohydrate. These low-carbohydrate diets were compared with low-fat diets in several instances. With the exception of Noakes et al. (2006), all the studies using a low-fat group assigned a fat intake of approximately 25%–30% of energy. Of these studies, two reported a greater decrease in fat-free mass in the low-carbohydrate groups (Brehm et al., 2003; Brinkworth et al., 2009b), and Yancy et al. (2004) reported a strong trend toward greater lean mass loss in the low carbohydrate group. Three studies reported no difference in fat-free mass lost (Brehm et al., 2005; Brinkworth et al., 2009a; Ruth et al., 2013). Noakes et al. (2006) used a very-low-fat group (10% of energy from fat) and a low-saturated-fat–high-unsaturated-fat group (30% of energy from fat) in addition to the ketogenic diet group. Superior lean mass retention was observed in the low-saturated-fat–high-unsaturated-fat group compared with the ketogenic diet and very-low-fat groups, and the percentage of energy from fat in this group was equal to that of most of the low-fat groups in other studies. Although the VLF group in Noakes et al. (2006) falls below the acceptable macronutrient distribution range for

Table 1 Summary of Studies

Study	Subjects and groups	Duration	Methods	Hypocaloric diet (yes–no)[a]	Daily energy and macronutrient intake (%CHO/P/F)	BCA	FFM or LBM[b]	Body weight[b]	Body fat[b]	Retention
Volek et al. (2002)[c]	20 normal-weight men; 12 volunteered to switch to VLCD (age 36.7 ± 11.6 years, body fat % 20.5 ± 6.2%). The remaining 8 were the controls (age 35.0 ± 13.0 years, body fat % 22.2 ± 9.0%).	6 weeks	The goal was to reduce CHO intake in the VLCD group to 5%–10% of energy intake (with fat making up ~60% of energy intake). ~30%–40% of kcal were provided to subjects in weekly meetings with RD. Control group continued regular dietary patterns.	No	VLCD: 2,334 kcal (8/30/61) Control: 1,949 kcal (58/16/26)	DXA	Decreased in VLCD group. VLCD: +1.1 FFM; +1.8% LBM Control: +0.4 FFM; +0.6% LBM	Decreased in VLCD group. VLCD: −2.2 Control: +0.4	Decreased in VLCD group. VLCD: −3.4; −24.6% (fat mass) Control: −0.5% (fat mass)	All participants completed the study.
Landers et al. (2002)[c]	49 obese subjects (ages 18–55) in generally good health were randomly assigned to LCHP, Zone diet, or CD group.	12 weeks	LCHP group consumed <30 g/day CHO and were given a booklet to track CHO. No other component of the diet was restricted. Zone diet group consumed food 5 times per day with a macronutrient composition of 40% CHO, 30% P, and 30% F. CD group was given diet plan with goal of 0.45 kg per week weight loss and a macronutrient composition of 50% CHO, 20% P, and 30% F.	LCHP: No Zone: NR CD: Yes	NR	DXA	Decreased in all groups. LCHP: −1.73 ± 1.71 Zone: −0.82 ± 2.02 CD: −1.90 ± 1.52	Decreased in all groups. LCHP: −5.24 ± 2.85 Zone: −4.44 ± 3.21 CD: −5.40 ± 2.75	Decreased in all groups. LCHP: −3.50 ± 1.85 kg Zone: −3.62 ± 2.28 CD: −3.52 ± 2.62	49/91 (54%) completed study. 43% of the LCHP, 60% of the Zone, and 36% of the CD groups withdrew.

(continued)

Table 1 *(continued)*

Study	Subjects and groups	Duration	Methods	Hypocaloric diet (yes–no)[a]	Daily energy and macronutrient intake (%CHO/P/F)	BCA	FFM or LBM[b]	Body weight[b]	Body fat[b]	Retention
Brehm et al. (2003)[c]	53 obese women were randomized into either the VLCD (age 44.2 ± 6.8 years) or the LF (age 43.1 ± 8.6 years) group.	24 weeks	VLCD group consumed ad libitum diet with maximum intake of 20 g/day CHO for the first 2 weeks (and ≤40–60 g/day CHO after that as long as ketosis was maintained). LF group followed calorie-restricted diet with a macronutrient composition of 55% CHO, 15% P, and 30% F.	VLCD: No LF: Yes	VLCD: 1,156 kcal (14/27/56) LF: 1,245 kcal (54/18/29)	DXA	Decreased in both groups, but greater decrease in VLCD group. VLCD: –1.97 LF: –0.73	Decreased in both groups, but greater decrease in VLCD group. VLCD: –8.5 ± 1.0 LF: 3.9 ± 1.0	Decreased in both groups, but greater decrease in VLCD group. VLCD: –4.8 ± 0.67 LF: –2.0 ± 0.75	42/53 (79%) completed the study. 7 dropped from LF group and 4 from VLCD group.
Yancy et al. (2004)[c]	120 obese, generally healthy adults with elevated cholesterol or triglyceride concentrations were randomized into an LF (age 45.6 ± 9.0 years) or LC (age 44.2 ± 10.1 years) group.	24 weeks	The LC group was given a popular diet book and handouts. LC group had a CHO consumption goal of ≤20 g/day until subjects were halfway to goal body weight. 5 g/day CHO was added weekly after that point. LC group also consumed dietary supplements provided by researchers. LF group was advised to consume <30% of daily kcal from F, <10% from saturated F, and <300 mg of cholesterol per day. LF group was advised to consume 500–1,000 kcal fewer than weight maintenance energy needs.	LC: No LF: Yes	LC: 1,461 kcal (8/26/68) LF: 1,502 kcal (52/19/29)	BIA	Decreased in both groups (*p* = .054 for greater loss in LC group). LC: –3.3 LF: –2.4	Decreased in both groups, but greater decrease in LC group. LC: –12.0 (–13.8 to –10.2);[d] –12.9% LF: –6.5 (–8.4 to –4.6);[d] –6.7%	Decreased in both groups, but greater decrease in LC group. LC: –9.4 (–10.9 to –7.9) [d] LF: –4.8 (–6.3 to –3.2)[d]	34/60 (57%) participants completed LF intervention, and 45/59 (76%) participants completed LC intervention (*p* = .02).

Table 1 *(continued)*

Study	Subjects and groups	Duration	Methods	Hypocaloric diet (yes–no)[a]	Daily energy and macronutrient intake (%CHO/P/F)	BCA	FFM or LBM[b]	Body weight[b]	Body fat[b]	Retention
Brehm et al. (2005)[e]	50 obese women were randomized into either the VLCD (age 44.8 ± 2.4 years) or the LF (age 41.4 ± 3.2 years) group.	16 weeks	VLCD group consumed ad libitum diet with maximum intake of 20 g/day CHO for the first 2 weeks (and ≤40–60 g/day CHO after that as long as ketosis was maintained). LF group followed calorie-restricted diet with a macronutrient composition of 55% CHO, 15% P, and 30% F.	VLCD: No LF: Yes	VLCD: 1,288 kcal (15/28/57) LF: 1,339 kcal (53/18/29)	DXA	Decreased in both groups over time, but no difference between groups. LC: –3.4 LF: –2.0	Decreased in both groups, but larger decrease in LC group. LC: –9.8 ± 0.7 LF: –6.14 ± 0.9	Decreased in both groups, but larger decrease in LC group. LC: –6.9 LF: –3.24	80% completed study, with equal dropout from each group.
Noakes et al. (2006)[e]	83 overweight and obese men and women (age 48 ± 8 years) were randomized into the VLCD, VLF, and HUF groups.	12 weeks	Each diet was designed with a 30% energy restriction and the following macronutrient compositions (CHO:F:P): VLCD, 4:61:35; VLF, 70:10:20; HUF, 50:30:20.	Yes	VLCD: 1,480 kcal (9/33/55) VLF: 1,448 kcal (68/20/12) HUF: 1,433 kcal (48/21/27)	DXA	Decreased more in VLCD and VLF groups than in HUF group. VLCD: –2.6 VLF: –2.0 HUF: –1.4	Decreased more in VLCD and VLF groups than in HUF group (% change). VLCD: –8.0 ± 0.6; –9.2% VLF: –6.7 ± 0.7; –7.3% HUF: –6.4 ± 0.6; –7.0%	Decreased in all groups. VLCD: –4.5 ± 0.5 VLF: –4.0 ± 0.5 HUF: –4.4 ± 0.6	67/83 (81%) completed study. 4 withdrew from VLCD group, 6 from VLF group, and 6 from HUF group.

(continued)

Table 1 ***(continued)***

Study	Subjects and groups	Duration	Methods	Hypocaloric diet (yes–no)[a]	Daily energy and macronutrient intake (%CHO/P/F)	BCA	FFM or LBM[b]	Body weight[b]	Body fat[b]	Retention
Johnston et al. (2006)[e]	19 overweight and obese men (*n* = 4) and women (*n* = 15) were randomly assigned to KLC diet (age 38.4 ± 3.9 years) or NLC diet (age 37.2 ± 3.9 years).	6 weeks	Both groups consumed ~30% of energy from P. KLC group consumed 60% of energy from F and began with ~5% from CHO. NLC group consumed 30% of energy from F and ~40% from CHO. All food and beverages were provided. A ~30% energy deficit was imposed.	Yes	KLC: 1,500 kcal (9/33/60) NLC: 1,500 kcal (42/31/30)	BIA	No change (time or Group × Time) KLC: −1.7 NLC: −2.2	Decreased in both groups. KLC: −6.3 ± 0.6 NLC: −7.2 ± 0.8	Decreased in both groups. KLC: −3.4 NLC: −5.5	1 subject dropped out in first week due to heart arrhythmia.
Wood et al. (2007)[c]	30 overweight and obese men (age 38.8 ± 14.4 years) were randomly assigned to either a CRD-F or a CRD-P diet.	12 weeks	All subjects were assigned to a diet with 60% of energy from F, 30% from P, and 10% from CHO. No guidelines about total caloric intake or type of fat consumption were given. No food was provided. The CRD-F group consumed 3 g/day of soluble fiber (via capsules), and CRD-P group consumed placebo capsules.	No	CRD-F: 1,641 kcal (13/28/61) CRD-P: 1,677 kcal (13/27/60)	DXA	Decreased in both groups. CRD-F: −1.4 ± 1.7 CRD-P: −1.4 ± 2.0	Decreased in both groups. CRD-F: −7.4 ± 3.1 CRD-P: −7.5 ± 1.8	Decreased in both groups. CRD-F: −5.6 ± 2.8 CRD-P: −5.8 ± 2.6	1 subject withdrew because of military commitment.

Table 1 *(continued)*

Study	Subjects and groups	Duration	Methods	Hypocaloric diet (yes–no)[a]	Daily energy and macronutrient intake (%CHO/P/F)	BCA	FFM or LBM[b]	Body weight[b]	Body fat[b]	Retention
Johnstone et al. (2008)[e]	17 obese men (age 38 ± 10 years) completed a randomized crossover design with two conditions: KLC diet and MC nonketogenic diet.	4 weeks/ condition	Subjects were residents at research facility, and food was provided daily. Both groups were allowed ad libitum feeding. The LC group consumed 4% of energy from CHO, 30% from P, and 66% from F. The MC group consumed 35% of energy from CHO, 30% from P, and 35% from F.	No	KLC: 1,732 kcal (5/30/66) MC: 1,899 kcal (36/30/3)	DXA	No difference between groups ($p = .054$ for greater loss in KLC group). KLC: –1.20 MC: –0.26	Decreased more in KLC group. KLC: –6.34 MC: –4.35	Decreased in both groups. KLC: –5.13 MC: –4.09	3 subjects withdrew for personal reasons.
Brinkworth et al. (2009b)[e]	66 sedentary, overweight, and obese men and women were divided into an LC group (age 48.8 ± 1.6 years) and an HC group (age 49.3 ± 1.7 years).	8 weeks	LC group goal consumption was 35% of kcal as P, 61% as F, and 4% as CHO. HC group goal consumption was 24% of kcal as P, 30% as F, and 46% as CHO. Both diets represented ~30% energy restriction. Some foods were provided at Weeks 0, 2, 4, and 6 to aid compliance.	Yes	LC: 1,557 kcal (5/35/59) HC: 1,547 kcal (47/24/27)	DXA	Decreased in both groups. LC: men, –2.0; women, –2.4 HC: men, –2.2; women, –1.1	Decreased in both groups. LC: –8.1; –8.4 ± 0.4% HC: –6.7; –6.7 ± 0.5% LC weight loss was only greater than HC in men.[f]	Decreased in both groups. LC: men, –8.2; women, –5.2 HC: men, –4.5; women, –5.6 LC weight loss was only greater than HC in men.[f]	60/66 (91%) of participants completed study. 4 withdrew from LC group and 2 withdrew from HC group.

(continued)

Table 1 *(continued)*

Study	Subjects and groups	Duration	Methods	Hypocaloric diet (yes–no)[a]	Daily energy and macronutrient intake (%CHO/P/F)	BCA	FFM or LBM[b]	Body weight[b]	Body fat[b]	Retention
Brinkworth et al. (2009a)[c]	After randomization into the LC and LF groups, 107 overweight and obese individuals began the study. 69 subjects completed the study (LC group: age 51.5 ± 7.7 years; LF group: age 51.4 ± 6.5 years).	12 months	LC and LF diets were designed to be isocaloric with moderate energy restriction (~6,000 kJ/d for women and ~7,000 kJ/d for men). The planned macronutrient content of the LC diet was 4% CHO, 35% P, and 61% F; for the LF diet, it was 46% CHO, 24% P, and 30% F.	Yes	LC: 1,644 kcal (9/32/55) LF: 1,625 kcal (47/22/27)	DXA	Decreased in LC group relative to LF group (Time × Diet). LC: −3.2 LF: −2.3	Decreased in both groups. LC: −13.1 ± 1.6 LF: −11.6 ± 1.6	Decreased in both groups. LC: −11.3 ± 1.5 LF: −9.4 ± 1.2	69/107 (64%) completed study. 22 withdrew from LC group, and 16 withdrew from LF group.
Paoli et al. (2012)	8 high-level male gymnasts (age 21 ± 5.5 years) underwent 30 days of VLCD, with pre- and postintervention assessments. 3 months later, subjects underwent 30 days of an ND, with the same assessments.	4 weeks/ condition	Both dietary conditions were ad libitum. Herbal supplements and a multivitamin–mineral supplement were consumed during the VLCD.	No	VLCD: 1,972 kcal (5/41/55) ND: 2,276 kcal (47/15/39)	Skinfolds	No change from baseline. VLCD: +0.3 ND: +0.2	Decreased in VLCD group. VLCD: −1.6 ND: −0.1	Decreased in VLCD group. VLCD: −1.9 ND: −0.2	NR

Table 1 *(continued)*

Study	Subjects and groups	Duration	Methods	Hypocaloric diet (yes–no)[a]	Daily energy and macronutrient intake (%CHO/P/F)	BCA	FFM or LBM[b]	Body weight[b]	Body fat[b]	Retention
Ruth et al. (2013)[c]	Obese men and women were randomized into LFHC (age 41.5 ± 12.8 years) or HFLC (age 43.5 ± 11.5 years) groups. 55 subjects were randomized, and 33 completed the study.	12 weeks	Both groups were instructed to consume a daily 500-kcal deficit diet targeted at reducing body weight by 0.5–1 lb per week. The LFHC group was counseled to consume ~60% of calories from complex CHO, 25% from F, and 15% from P. The HFLC group was counseled to consume <40 g/day CHO, 60% of calories from F, and ~35% from P. The study lasted 12 weeks.	Yes	LFHC: 1,439 kcal (56/22/25) HFLC: 1,532 kcal (10/34/56)	DXA	No difference between groups. LFHC: –0.3 ± 2.3 HFLC: –1.6 ± 1.3	Decreased in both groups. LFHC: –5.3; –5.3 ± 4.7% HFLC: –7.1; –7.1 ± 4.6%	Decreased in both groups. LFHC: –4.8 ± 3.1 HFLC: –5.2 ± 4.0	33/55 (60%) completed the study, with equal dropout between groups. Dropout likely due to adipose tissue biopsies.

Note. BCA = body content assessment; BIA = bioelectrical impedance analysis; CD = conventional diet; CHO = carbohydrate; CHO/P/F = carbohydrate/protein/fat; CRD-F = CHO-restricted diet with supplemental soluble fiber consumption; CRD-P = CHO-restricted diet with placebo capsules; DXA = dual-energy X-ray absorptiometry; FFM = fat-free mass; HC = high carbohydrate; HFLC = high fat, low carbohydrate; HUF = high unsaturated fat ; KLC = ketogenic low-carbohydrate; LBM = lean body mass; LC = low carbohydrate; LCHP = low carbohydrate, high protein ; LF = low fat; LFHC = low fat, high carbohydrate; MC = medium carbohydrate ; ND = normal diet; NLC = nonketogenic low-CHO diet; NR = not reported ; RD = registered dietician; VLCD = very-low-carbohydrate diet.

[a] Based on whether diet was intentionally designed to by hypocaloric. [b] Reported in kilograms unless otherwise noted. [c] Variation reported as standard deviation. [d] 95% confidence interval. [e] Variation reported as standard error. [f] Diet × gender × time effect with a greater reduction in LC than HC in M, but no difference between LC and HC in F.

fat (20%–35%), the ketogenic diet groups in all studies typically exceeded this range considerably (Panel on Macronutrients et al., 2005). On the basis of the examinations of low-fat versus ketogenic diets, lean mass seems to be equally or superiorly retained in subjects following a low-fat diet compared with those following a ketogenic diet.

It is well established that energy restriction typically leads to loss of lean mass in the absence of resistance training (Chaston et al., 2007; Weinheimer et al., 2010). On the basis of the studies included in this review that reported a ketogenic diet group and nonketogenic diet group that both lost weight (i.e., all studies included in Table 1 except Volek et al., 2002, and Paoli et al., 2012), the average percentage of weight loss as fat-free mass was approximately 27% in ketogenic diet groups and 23% in nonketogenic diet groups. Therefore, based on the available information, it appears that the percentage of weight loss that is lean mass is similar, if not higher, when individuals follow a ketogenic diet.

Resistance Training and Ketogenic Diets

Resistance training can increase muscle mass and help mitigate loss of fat-free mass during weight loss (Ballor et al., 1988; Delmonico & Lofgren, 2010; Stiegler & Cunliffe, 2006). Only two studies were located that investigated whether combining resistance training with a ketogenic diet provides superior changes in body composition relative to other diets in combination with resistance training (Jabekk et al., 2010; Wood et al., 2012). These studies are summarized in Table 2.

Both interventions lasted 10–12 weeks and used two or three sessions of progressive resistance training each week. As detailed in Table 2, these studies were markedly different on a number of factors, including subject age and gender, frequency of strength training, exercise selection, sets and repetitions performed, and method of body composition assessment.

Jabekk et al. (2010) reported no change in fat-free mass in subjects following a resistance training program in combination with a ketogenic diet, and Wood et al. (2012) reported a decrease. However, the results from Wood et al. (2012) indicated that, without exercise, a ketogenic diet led to less fat-free mass loss than a low-fat diet and similar losses as compared to a low-fat diet plus resistance training. The results of Jabekk et al. (2010) could also be viewed as positive in regard to the efficacy of a ketogenic diet and resistance training because fat-free mass was not lost, whereas a relatively large amount of fat mass was lost ($M \pm SD = -5.6 \pm 2.6$ kg).

Possible Limitations of Current Research

There are several important issues to discuss relative to the results of the studies presented in Table 1. The studies varied in regard to whether an energy restriction was imposed. The relatively large calorie restriction used in several of these studies (Brinkworth et al., 2009a, 2009b; Johnston et al., 2006; Ruth et al., 2013) could have provided different effects on fat-free mass than a weight maintenance diet, a less aggressive weight loss diet, or a diet designed to increase weight (i.e., promote muscle accretion). Several studies did not specifically assign a level of energy intake (Brehm et al., 2003, 2005; Johnstone et al., 2008; Landers et al., 2002; Wood et al., 2007; Yancy et al., 2004). Some diets were ad libitum diets in regard to fat and protein (Brehm et al., 2005, 2003; Landers et al., 2002; Yancy et al., 2004), and others prescribed specific intake guidelines for all macronutrients (Johnston et al., 2006; Johnstone et al., 2008; Noakes et al., 2006; Volek et al., 2002; Wood et al., 2007). The studies also did not use exercise interventions, which can spare lean body mass during weight loss (Stiegler & Cunliffe, 2006).

In addition, it is important to consider whether the nature of ketogenic diets and the method of body composition assessment could affect the changes in fat-free mass observed. All studies used dual-energy X-ray absorptiometry (DXA) to measure body composition, except for two (Johnston et al., 2006; Yancy et al., 2004) that used bioelectrical impedance analysis. DXA provides a measure of lean soft tissue, which can be affected by water distribution within the body between intracellular and extracellular compartments (St-Onge et al., 2004). Glycogen is stored with three to four parts water, and very-low-carbohydrate diets can lead to the loss of glycogen stores and the associated water (Kreitzman et al., 1992). Because glycogen and water are both components of DXA's lean soft tissue measurement, it is worth considering whether estimations of body composition in individuals who may have altered glycogen concentrations can be accurately compared with those in nondepleted individuals (e.g., comparisons of body composition changes in low-carbohydrate vs. low-fat groups).

Ferrari et al. (2014) published a report demonstrating how changes in hydration can affect DXA measurements. Twenty-two patients underwent a DXA immediately before and 2 hr after undergoing hemodialysis. The amount of fluid removed during hemodialysis was 2.1 L (2.8% of body mass). A significant decrease in the amount of nonbone lean mass was observed at the second DXA scan (–4.9%), and the change was not uniform throughout the body. No significant difference in total fat mass was observed, meaning that the body fat percentage did change as a result of fluid removal.

Several of the studies included in this review indicated a greater amount of weight loss with ketogenic diets than other diets, which is potentially a confounding factor when comparing changes in lean mass. It is plausible that a greater loss of carbohydrate stores and associated water could account for some amount of the difference in weight loss, but it is not clear to what extent this may occur.

Manninen (2006) contended that the metabolic adaptations to a ketogenic diet lead to the sparing of

Table 2 Summary of Resistance Training Studies

Study	Subjects/ Groups	Duration	Methods	Exercise program	Daily energy and macronutrient intake (%CHO/ P/F)	BCA	FFM or LBM change[a]	BW change[a]	BF change[a]	Retention
Jabekk et al. (2010)[b]	18 untrained women (age 20–40 years, body mass index ≥ 25) were randomly assigned to RT with regular diet (Ex) group or RT with ketogenic diet (LC+Ex) group.	10 weeks	Both groups were counseled in diet and exercise and were given a daily multivitamin and mineral supplement. LC+Ex group was given commercial book on low-CHO ketogenic diet. Total energy intake was not limited.	Both groups performed 60–100 min of supervised varied resistance exercise twice per week. The exercises consisted of supine leg press, seated leg extension, seated leg curl, seated chest press, seated rowing, seated shoulder press, seated pulldown, and standing biceps curl. For the first 5 weeks, 3 sets at 12 RM were performed for lower body exercises and 1 set at 12 RM was performed for upper body exercises. After 5 weeks, an additional set was added to upper body exercises, and weight was increased to 8 RM. Rest time was ~90 s between sets.	Ex: 1,974 kcal (41/17/34) LC+Ex: 1,756 kcal (6/22/66)	DXA	Increased in Ex group only. Ex: 1.6 ± 1.8 kg LC+Ex: 0.1 ± 1.7 kg	Decreased in LC+Ex group only. Ex: 0.8 ± 1.5 kg LC+Ex: −5.6 ± 2.6 kg	Decreased in LC+Ex group only. Ex: −0.6 ± 0.8 kg LC+Ex: −5.6 ± 2.9 kg	1 subject from each group was excluded from analysis.
Wood et al. (2012)[b]	42 men (age 59 ± 7 years) were randomized to LFD, LFD + RT, CRD, or CRD + RT groups. 32 men completed the intervention.	12 weeks	LFD group was instructed to consume 1,800 kcal per day, with <30% of energy from F (<10% from saturated F) and were instructed to consume <300 mg/day of dietary cholesterol. CRD group was instructed to consume <50 g CHO per day with no energy restriction requirements.	RT groups performed supervised strength exercise 3 times per week. For the first 6 weeks, each session consisted of a warm-up, followed by 1 set of 10–15 repetitions of the following exercises: bent-knee sit up, hyperextensions, leg press, chest press, hamstring curl, lat pulldown, calf raises, shoulder press, seated row, triceps press, and biceps curl. During Weeks 7–12, 2 sets of 8–12 repetitions of the same exercises were performed. Non-RT groups continued baseline level of physical activity.	LFD: 1,780 kcal (55/18/25) LFD+RT: 1,590 kcal (59/20/23) CRD: 1,707 kcal (15/27/55) CRD+RT: 1,573 kcal (13/31/56)	BIA	Decreased in all groups.[c] LFD: −2.8 ± 1.3; % of weight loss as FFM: 27.5 LFD+RT: −2.5 ± 2.4; % as FFM: 15.9 CRD: −2.1 ± 2.5; % as FFM: 15.7 CRD+RT: −2.3 ± 2.0; % as FFM: 17.3	Decreased in all groups. LFD: −8.2 ± 3.4 LFD+RT: −9.0 ± 5.82 CRD: −9.2 ± 3.6 CRD+RT: −10.3 ± 2.7	Decreased in all groups. LFD: −5.4 LFD+RT: −6.4 CRD: −7.1 CRD+RT: −8.0	Attrition was similar between groups (24%).

Note. BCA = body composition analysis; BF = body fat; BIA = bioelectrical impedance analysis; BW = body weight; CHO = carbohydrate; CRD = carbohydrate-restricted diet; Ex = resistance training; FFM = fat-free mass; kcal = kilocalories; LBM = lean body mass; LC+Ex = low carbohydrate plus resistance training; LFD = low-fat diet; RM = repetition maximum; RT = resistance training.

[a] Reported in kilograms unless otherwise noted. [b] Variation reported as standard deviation. [c] Trend was found between the LFD (27.5%) and the LFD&PRE (15.9%) groups ($p = .068$) as well as between the LFD (27.5%) and CRD (15.7%) groups ($p = .072$) for percentage of weight loss from appendicular FFM.

muscle protein for several reasons. 3HB has been shown to decrease the oxidation of leucine and promote protein synthesis in humans (Nair et al., 1988). Ketogenic diets are often high in protein, which increases amino acid availability for muscle protein synthesis. High protein intake during weight loss can reduce the loss of muscle mass (Bopp et al., 2008; Wycherley et al., 2012), and this may be one way ketogenic diets could theoretically help preserve muscle. Ketone body metabolism may able to provide enough energy to spare muscle mass (Manninen, 2004). Specifically, 3HB and AcAc may make large enough contributions to energy needs to spare the breakdown of muscle to provide amino acid substrate for gluconeogenesis. The recycling of glucose through the Cori cycle also helps meet the glucose needs of the glycolytic tissues (e.g., erythrocytes).

Conclusions

The majority of located publications reported a decrease in fat-free mass after adherence to a very-low-carbohydrate diet. These changes appear to be as great, if not greater, than decreases seen in individuals following a low-fat diet. However, many of these studies used aggressive caloric deficits and did not implement an exercise intervention (which could potentially have helped retain muscle mass during weight loss). In addition, there are some important questions regarding the measurement of fat-free mass changes given that individuals following ketogenic diets could have altered glycogen and body water stores.

The addition of a structured resistance training program to a ketogenic diet may enhance changes in body composition. Further research is needed to determine whether resistance training can effectively slow or stop the loss of fat-free mass typically seen in individuals following a ketogenic diet.

Further research should investigate the potential interactions between hormone and ketone body concentrations, caloric intake, macronutrient composition of the diet, and fat-free mass changes during ketogenic diets. A nutrition and exercise strategy that can lead to maximal fat-free mass retention during weight loss may provide metabolic and functional benefits. The current need for effective and feasible weight-loss strategies and the prevalence of low- and very-low-carbohydrate diets should compel researchers to continue to investigate these issues. Last, because of the mixed results and extremely limited number of studies, future research should be conducted in male and female subjects of different ages, training statuses, and body characteristics.

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References

Ballor, D.L., Katch, V.L., Becque, M.D., & Marks, C.R. (1988). Resistance weight training during caloric restriction enhances lean body weight maintenance. *American Journal of Clinical Nutrition, 47,* 19–25. PubMed

Benoit, F.L., Martin, R.L., & Watten, R.H. (1965). Changes in body composition during weight reduction in obesity: Balance studies comparing effects of fasting and a ketogenic diet. *Annals of Internal Medicine, 63,* 604–612. PubMed doi:10.7326/0003-4819-63-4-604

Bopp, M.J., Houston, D.K., Lenchik, L., Easter, L., Kritchevsky, S.B., & Nicklas, B.J. (2008). Lean mass loss is associated with low protein intake during dietary-induced weight loss in postmenopausal women. *Journal of the American Dietetic Association, 108,* 1216–1220. PubMed doi:10.1016/j.jada.2008.04.017

Boron, W.F., & Boulpaep, E.L. (2009). *Medical physiology: A cellular and molecular approach* (2nd ed.). Philadelphia, PA: W.B. Saunders. Retrieved from http://catalog.hathitrust.org/Record/004298630

Brehm, B.J., Seeley, R.J., Daniels, S.R., & D'Alessio, D.A. (2003). A randomized trial comparing a very low carbohydrate diet and a calorie-restricted low fat diet on body weight and cardiovascular risk factors in healthy women. *Journal of Clinical Endocrinology and Metabolism, 88,* 1617–1623. PubMed doi:10.1210/jc.2002-021480

Brehm, B.J., Spang, S.E., Lattin, B.L., Seeley, R.J., Daniels, S.R., & D'Alessio, D.A. (2005). The role of energy expenditure in the differential weight loss in obese women on low-fat and low-carbohydrate diets. *Journal of Clinical Endocrinology and Metabolism, 90,* 1475–1482. PubMed doi:10.1210/jc.2004-1540

Brinkworth, G.D., Noakes, M., Clifton, P.M., & Buckley, J.D. (2009a). Effects of a low carbohydrate weight loss diet on exercise capacity and tolerance in obese subjects. *Obesity, 17,* 1916–1923. PubMed doi:10.1038/oby.2009.134

Brinkworth, G.D., Noakes, M., Buckley, J.D., Keogh, J.B., & Clifton, P.M. (2009b). Long-term effects of a very-low-carbohydrate weight loss diet compared with an isocaloric low-fat diet after 12 mo. *American Journal of Clinical Nutrition, 90,* 23–32. PubMed doi:10.3945/ajcn.2008.27326

Chaston, T.B., Dixon, J.B., & O'Brien, P.E. (2007). Changes in fat-free mass during significant weight loss: A systematic review. *International Journal of Obesity, 31,* 743–750. PubMed

Delmonico, M.J., & Lofgren, I.E. (2010). Resistance training during weight loss in overweight and obese older adults: What are the benefits? *American Journal of Lifestyle Medicine, 4,* 309–313. doi:10.1177/1559827610368245

Ferrari, F., Diano, D., Federico, P., Battista, G., & Bazzocchi, A. (2014, March). *Impact of hydration status on body composition in patients before and after haemodialysis as measured by dual energy X-ray absorptiometry.* Poster presented at the annual meeting of the European Society of Radiology, Vienna, Austria. http://dx.doi.org/10.1594/ecr2014/C-2146

Freeman, J., Veggiotti, P., Lanzi, G., Tagliabue, A., & Perucca, E. (2006). The ketogenic diet: From molecular mechanisms to clinical effects. *Epilepsy Research, 68,* 145–180. PubMed doi:10.1016/j.eplepsyres.2005.10.003

Jabekk, P.T., Meen, H.D., Moe, I.A., Tomten, S.E., & Hostmark, A.T. (2010). Resistance training in overweight women on a ketogenic diet conserved lean body mass while reducing body fat. *Nutrition & Metabolism, 7,* 17. PubMed doi:10.1186/1743-7075-7-17

Johnston, C.S., Tjonn, S.L., Swan, P.D., White, A., Hutchins, H., & Sears, B. (2006). Ketogenic low-carbohydrate diets have no metabolic advantage over nonketogenic low-carbohydrate diets. *American Journal of Clinical Nutrition, 83,* 1055–1061. PubMed

Johnstone, A.M., Horgan, G.W., Murison, S.D., Bremner, D.M., & Lobley, G.E. (2008). Effects of a high-protein ketogenic diet on hunger, appetite, and weight loss in obese men feeding ad libitum. *American Journal of Clinical Nutrition, 87,* 44–55. PubMed

Kreitzman, S.N., Coxon, A.Y., & Szaz, K.F. (1992). Glycogen storage: Illusions of easy weight loss, excessive weight regain, and distortions in estimates of body composition. *American Journal of Clinical Nutrition, 56*(1 Suppl.), 292S–293S. PubMed

Laffel, L. (1999). Ketone bodies: A review of physiology, pathophysiology and application of monitoring to diabetes. *Diabetes/Metabolism Research and Reviews, 15,* 412–426. PubMed doi:10.1002/(SICI)1520-7560(199911/12)15:6<412::AID-DMRR72>3.0.CO;2-8

Landers, P., Wolfe, M.M., Glore, S., Guild, R., & Phillips, L. (2002). Effect of weight loss plans on body composition and diet duration. *Journal of the Oklahoma State Medical Association, 95,* 329–331. PubMed

Manninen, A.H. (2004). Metabolic effects of the very-low-carbohydrate diets: Misunderstood "villains" of human metabolism. *Journal of the International Society of Sports Nutrition, 1,* 7–11. PubMed doi:10.1186/1550-2783-1-2-7

Manninen, A.H. (2006). Very-low-carbohydrate diets and lean body mass. *Obesity Reviews, 7,* 297. PubMed doi:10.1111/j.1467-789X.2006.00271.x

Mullins, G., Hallam, C.L., & Broom, I. (2011). Ketosis, ketoacidosis and very-low-calorie diets: Putting the record straight. *Nutrition Bulletin, 36,* 397–402. doi:10.1111/j.1467-3010.2011.01916.x

Nair, K.S., Welle, S.L., Halliday, D., & Campbell, R.G. (1988). Effect of beta-hydroxybutyrate on whole-body leucine kinetics and fractional mixed skeletal muscle protein synthesis in humans. *Journal of Clinical Investigation, 82,* 198–205. PubMed doi:10.1172/JCI113570

Noakes, M., Foster, P.R., Keogh, J.B., James, A.P., Mamo, J.C., & Clifton, P.M. (2006). Comparison of isocaloric very low carbohydrate/high saturated fat and high carbohydrate/low saturated fat diets on body composition and cardiovascular risk. *Nutrition & Metabolism, 3,* 7. PubMed doi:10.1186/1743-7075-3-7

Nutrition Science Initiative. (2012). Nutrition Science Initiative review of the literature.

Panel on Macronutrients, Subcommittees on Upper Reference Levels of Nutrients and Interpretation and Uses of Dietary Reference Intakes, and the Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. (2005). *Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids (macronutrients).* Retrieved from http://www.nap.edu/catalog.php?record_id=10490

Paoli, A., Grimaldi, K., D'Agostino, D., Cenci, L., Moro, T., Bianco, A., & Palma, A. (2012). Ketogenic diet does not affect strength performance in elite artistic gymnasts. *Journal of the International Society of Sports Nutrition, 9,* 34. PubMed doi:10.1186/1550-2783-9-34

Ruth, M.R., Port, A.M., Shah, M., Bourland, A.C., Istfan, N.W., Nelson, K.P., . . . Apovian, C.M. (2013). Consuming a hypocaloric high fat low carbohydrate diet for 12 weeks lowers C-reactive protein, and raises serum adiponectin and high density lipoprotein-cholesterol in obese subjects. *Metabolism: Clinical and Experimental, 62,* 1779–1787. PubMed doi:10.1016/j.metabol.2013.07.006

Soeters, M.R., Soeters, P.B., Schooneman, M.G., Houten, S.M., & Romijn, J.A. (2012). Adaptive reciprocity of lipid and glucose metabolism in human short-term starvation. *American Journal of Physiology: Endocrinology and Metabolism, 303,* E1397–E1407. PubMed doi:10.1152/ajpendo.00397.2012

Stiegler, P., & Cunliffe, A. (2006). The role of diet and exercise for the maintenance of fat-free mass and resting metabolic rate during weight loss. *Sports Medicine, 36,* 239–262. PubMed doi:10.2165/00007256-200636030-00005

St-Onge, M.-P., Wang, Z., Horlick, M., Wang, J., & Heymsfield, S.B. (2004). Dual-energy X-ray absorptiometry lean soft tissue hydration: Independent contributions of intra- and extracellular water. *American Journal of Physiology: Endocrinology and Metabolism, 287,* E842–E847. PubMed doi:10.1152/ajpendo.00361.2003

Sumithran, P., & Proietto, J. (2008). Ketogenic diets for weight loss: A review of their principles, safety and efficacy. *Obesity Research & Clinical Practice, 2*(1), I–II. PubMed doi:10.1016/j.orcp.2007.11.003

Volek, J.S., Sharman, M.J., Love, D.M., Avery, N.G., Gómez, A.L., Scheett, T.P., & Kraemer, W.J. (2002). Body composition and hormonal responses to a carbohydrate-restricted diet. *Metabolism: Clinical and Experimental, 51,* 864–870. PubMed doi:10.1053/meta.2002.32037

Weinheimer, E.M., Sands, L.P., & Campbell, W.W. (2010). A systematic review of the separate and combined effects of energy restriction and exercise on fat-free mass in middle-aged and older adults: Implications for sarcopenic obesity. *Nutrition Reviews, 68,* 375–388. PubMed doi:10.1111/j.1753-4887.2010.00298.x

Wood, R.J., Fernandez, M.L., Sharman, M.J., Silvestre, R., Greene, C.M., Zern, T.L., . . . Volek, J.S. (2007). Effects of a carbohydrate-restricted diet with and without supplemental soluble fiber on plasma low-density lipoprotein cholesterol and other clinical markers of cardiovascular risk. *Metabolism: Clinical and Experimental, 56,* 58–67. PubMed doi:10.1016/j.metabol.2006.08.021

Wood, R.J., Gregory, S.M., Sawyer, J., Milch, C.M., Matthews, T.D., & Headley, S.A.E. (2012). Preservation of fat-free mass after two distinct weight loss diets with and without progressive resistance exercise. *Metabolic Syndrome and Related Disorders, 10,* 167–174. PubMed doi:10.1089/met.2011.0104

Wycherley, T.P., Moran, L.J., Clifton, P.M., Noakes, M., & Brinkworth, G.D. (2012). Effects of energy-restricted high-protein, low-fat compared with standard-protein, low-fat diets: A meta-analysis of randomized controlled trials. *American Journal of Clinical Nutrition, 96,* 1281–1298. PubMed doi:10.3945/ajcn.112.044321

Yancy, W.S., Olsen, M.K., Guyton, J.R., Bakst, R.P., & Westman, E.C. (2004). A low-carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia: A randomized, controlled trial. *Annals of Internal Medicine, 140,* 769–777. PubMed doi:10.7326/0003-4819-140-10-200405180-00006