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

Grant M. Tinsley[1] and Darryn S. Willoughby[1]

Baylor University

[1]Department of Health, Human Performance, and Recreation, Baylor University. One Bear Place #97313, Baylor University, Waco, TX, 76798.

Running head: Ketogenic Diets and Fat-Free Mass Changes

Abstract

Low-carbohydrate and very-low-carbohydrate diets are often employed as weight loss strategies in 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 due to 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). Upon 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

Introduction

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 employed 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 due to 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 (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 (Mullins et al., 2011). Ketosis in individuals typically leads to maximum ketone concentrations of 2-3 mM, whereas concentrations in ketoacidosis are often over ten 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 CoA. Ketogenesis begins with two acetyl CoA molecules which 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, acetoacetate (Boron & Boulpaep, 2009). Acetoacetate 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 a number of reasons, including maintenance of resting metabolic rate (Stiegler & Cunliffe, 2006) and functional abilities, particularly in the elderly. 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 in order to provide amino acid substrate. While this is known to occur during complete fasting, ketogenic diets promote a pseudo-fasted state in which oxidation of fatty acids primarily meets energy needs due to 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 as compared to 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 last 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 employing ketogenic diet programs that measured changes in fat-free mass (or lean body mass) in order 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 Nutritional Science Initiative ("Nutritional Science Initiative Review of the Literature," 2012). Inclusion criteria for all studies included the following: 1) employed ketogenic (very low carbohydrate) diet that contained ≤ 50 g carbohydrate per day (or ≤ 10% of energy from carbohydrates), 2) measured fat-free mass at beginning and end of intervention, 3) duration of ≥ 4 weeks, 4) ≥ 8 participants per group, 5) adults subjects of any ethnicity, age, and body weight, 6) publication in the last 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., 2005; Brehm et al. 2003; Brinkworth et al. 2009 (a); Brinkworth et al., 2009 (b); Johnstone et al. 2008; Landers et al. 2002; Noakes et al., 2006; Ruth et al., 2013; Wood et al., 2007; Yancy et al. 2004), while 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 ~1 – 3.5 kg, while the majority of the studies reported weight loss of ~5 – 13 kg and fat mass loss of ~3.5 – 11 kg.

The study of Volek et al. (2002) is the only one that described an increase in fat-free mass. There are several potential explanations that could contribute to the different result. First, the research subjects were normal-weight men. All other located studies, except Paoli et al. (2012), utilized overweight and obese individuals. The subjects used were of a similar age as 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. (2002). Subjects were encouraged to maintain body weight, and were even instructed to consume more food in order 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 ~25 – 30% was implemented in several studies (Brinkworth 2009 (a); Brinkworth et al. 2009 (b); 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 utilized ad libitum diets in regards to fat and protein (Brehm et al., 2005, 2003; Landers et al., 2002; Yancy et al., 2004), while 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 ~30 – 35% of energy intake from protein, ~60 – 65% from fat, and ~5 – 10% from carbohydrate. These low-carbohydrate diets were compared to low-fat diets in several instances. With the exception of Noakes et al. (2006), all the studies utilizing low fat groups assigned a fat intake of ~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. 2009 (a)), and Yancy et al. (2004) reported a strong trend towards 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., 2009; Ruth et al., 2013). Noakes et al. (2006) employed a very low fat group (VLF: 10% of energy from fat) and a low saturated fat high unsaturated fat group (HUF: 30% of energy from fat) in addition to the ketogenic diet group. Superior lean mass retention was observed in the HUF group as compared to the ketogenic diet and VLF groups, and the percentage of energy from fat in this group is equal to most of the low-fat groups in other studies. While the VLF group in Noakes et al. (2006) falls below the Acceptable Macronutrient Distribution Range (AMDR) for fat (20 – 35%), the ketogenic diet groups in all studies typically exceed this range considerably (Institute of Medicine of The National Academies, 2005). Based on the examinations of low-fat versus ketogenic diets, lean mass seems to be equally or superiorly retained in subjects following a low-fat diet as compared to 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., 2006; Weinheimer et al., 2010). Based on the studies included in this review that reported a ketogenic diet group and non-ketogenic diet group that both lost weight (i.e. all studies included in Table 1 except Volek et al. and Paoli et al.), the average percent of weight loss as fat-free mass was ~27% in ketogenic diet groups and ~23% in non-ketogenic diet groups. Therefore, it appears that the percent of weight loss that is lean mass is similar, if not higher, when individuals follow a ketogenic diet based on the available information.

Resistance Training and Ketogenic Diets

It is well established that 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 have 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 utilized 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 regards to the efficacy of a ketogenic diet and resistance training because fat-free mass was not lost, while a relatively large amount of fat mass was lost (- 5.6 ± 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 regards to whether or not an energy restriction as imposed. The relatively large calorie restriction used in several of these studies (Brinkworth et al. 2009 (a); Brinkworth et al. 2009 (b); 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 diets designed to increase weight (i.e. promote muscle accretion). Several studies 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). Some diets were ad libitum diets in regards to fat and protein (Brehm et al., 2005, 2003; Landers et al., 2002; Yancy et al., 2004), while 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 utilize exercise interventions, which can spare lean body mass during weight loss (Stiegler & Cunliffe, 2006).

Additionally, 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 utilized dual-energy x-ray absorptiometry (DXA) to measure body composition, except for two (Johnston et al., 2006; Yancy et al., 2004), which utilized 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). Since glycogen and water are both components of DXA's lean soft tissue measurement, it is worth considering whether estimations of body composition in glycogen-depleted individuals can be accurately compared to non-depleted individuals (e.g. comparisons of body composition changes in low-carbohydrate versus low-fat groups).

Ferrari et al. (2014) published a report demonstrating how changes in hydration can impact DXA measurements. Twenty-two patients underwent a DXA immediately before and two hours 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 non-bone lean mass was observed at the second two 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 indicate a greater amount of weight loss during ketogenic diets when compared to 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) contends that the metabolic adaptations to a ketogenic diet leads to the sparing of 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 following 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 utilized aggressive caloric deficits and did not implement an exercise intervention (which could have potentially helped retain muscle mass during weight loss). Additionally, there are some important questions regarding the measurement of fat-free mass changes given that individuals following ketogenic diets will be chronically glycogen-depleted.

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. Lastly, due to the mixed results and extremely limited number of studies, future research should be conducted in males and females of different ages, training statuses, and body characteristics.

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Table 1. Summary of Studies

Study	Subjects/ Groups	Duration	Methods	Hypo-caloric Diet (Y/N) (a)	Daily Energy & Macronutrient Intake (%C/P/F)	BCA	FFM or LBM (b)	Body Weight (b)	Body fat (b)	Retention
Volek et al. 2002 (c)	20 normal weight M. 12 (age 36.7 ± 11.6 y, body fat % 20.5 ± 6.2%) volunteered to switch to VLCD. The remaining 8 were the controls (age 35.0 ± 13.0 y, body fat % 22.2 ± 9.0%)	6 weeks	The goal was to reduce CHO intake 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 (C) continued regular dietary patterns.	N	VLCD: 2334 kcal 8/30/61 C: 1949 kcal 58/16/26	DXA	↑ in VLCD group VLCD: + 1.1; + 1.8% C: +0.4; +0.6%	↓ in VLCD group VLCD: - 2.2 C: +0.4	↓ in VLCD group VLCD: -3.4; - 24.6% (fat mass) C: -0.5% (fat mass)	All participants completed study.
Landers et al. 2002 (c)	49 obese subjects (ages 18 to 55) in generally good health were randomly assigned to LCHP, Zone diet, or conventional diet (CD) group.	12 weeks	LCHP group consumed less than 30 g/d 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% protein, and 30% fat. CD group was given diet plan with goal of 0.45 kg per week weight loss and a macronutrient composition of 50% CHO, 20% protein, and 30% fat.	LCHP: N Zone: NR CD: Y	NR	DXA	↓ in all groups LCHP: - 1.73 ± 1.71 Zone: - 0.82 ± 2.02 CD: - 1.90 ± 1.52	↓ in all groups LCHP: - 5.24 ± 2.85 Zone: - 4.44 ± 3.21 CD: - 5.40 ± 2.75	↓ 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% the LCHP, 60% of the Zone, and 36% of the CD diet withdrew
Brehm et al. 2003 (c)	53 obese F were randomized into either the VLCD (age 44.2 ± 6.8) or LF (age 43.1 ± 8.6) group.	24 weeks	VLCD consumed ad libitum diet with maximum intake of 20 g/d CHO for the first 2 weeks (and up to 40 to 60 g/d CHO after that as long as ketosis was maintained). LF group followed calorie-restricted diet with a macronutrient composition of 55% CHO, 15% protein, and 30% fat.	VLCD: N LF: Y	VLCD: 1156 kcal 14/27/56 LF: 1245 kcal 54/18/29	DXA	↓ in both groups, but greater decrease in VLCD VLCD: -1.97 LF: -0.73	↓ in both groups, but greater decrease in VLCD VLCD: -8.5 ± 1.0 LF: 3.9 ± 1.0	↓ in both groups, but greater decrease in VLCD VLCD: -4.8 ± 0.67 LF: -2.0 ± 0.75	42/53 (79% completed t study. 7 dropped fro LF and 4 fr VLCD.
Yancy et al. 2004 (c)	120 obese generally healthy adults with elevated cholesterol or triglyceride concentrations were randomized into a low fat (LF, age 45.6 ± 9.0) or low-CHO ketogenic (LC, age 44.2 ± 10.1) group.	24 weeks	The LC group was given a popular diet book and handouts. LC group had a goal CHO consumption of ≤ 20 g/d until participants were halfway to goal body weight. 5 g/d 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 fat, < 10% from saturated fat, and < 300 mg of cholesterol per day. LF group was advised to consume 500-1000 kcal fewer than weight maintenance energy needs.	LC: N LF: Y	LC: 1461 kcal 8/26/68 LF: 1502 kcal 52/19/29	BIA	↓ in both groups (p = 0.054 for greater loss in LC group) LC: - 3.3 LF: - 2.4	↓ in both groups, but greater decrease in LC LC: -12.0 (-13.8 to - 10.2) (d); - 12.9 % LF: -6.5 (-8.4 to - 4.6) (d); - 6.7%	↓ in both groups, but greater decrease in LC LC: -9.4 (-10.9 to -7.9) (d) LF: -4.8 (-6.3 to - 3.2) (d)	34/60 (57% participants completed l interventior and 45/59 (76%) participants completed l interventior (p=0.02)

Brehm et al. 2005 (e)	50 obese F were randomized into either the VLCD (age 44.8 ± 2.4) or LF (age 41.4 ± 3.2) group.	16 weeks	VLCD consumed ad libitum diet with maximum intake of 20 g/d CHO for the first 2 weeks (and up to 40 to 60 g/d CHO after that as long as ketosis was maintained). LF group followed calorie-restricted diet with a macronutrient composition of 55% CHO, 15% protein, and 30% fat.	VLCD: N LF: Y	VLCD: 1288 kcal 15/28/57 LF: 1339 kcal 53/18/29	DXA	↓ in both groups over time, but no difference between groups LC: -3.4 LF: -2.0	↓ in both groups, but larger decrease in LC LC: - 9.8 ± 0.7 LF: -6.14 ± 0.9	↓ in both groups, but larger decrease in LC LC: -6.9 LF: -3.24	80% completed study, with equal dropc from each group
Noakes et al. 2006 (e)	83 overweight and obese M and F (age 48 ± 8) 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:fat:protein): VLCD (4:61:35), VLF (70:10:20), HUF (50:30:20).	Y	VLCD: 1480 kcal 9/33/55 VLF: 1448 kcal 68/20/12 HUF: 1433 kcal 48/21/27	DXA	↓ more in VLCD and VLF than HUF VLCD: -2.6 VLF: -2.0 HUF: -1.4	↓ more in VLCD than VLF than HUF (% change) VLCD: -8.0 ± 0.6; -9.2% VLF: -6.7 ± 0.7; -7.3% HUF: -6.4 ± 0.6; -7.0%	↓ 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 fr VLCD, 6 fr VLF, and 6 from HUF
Johnston et al. 2006 (e)	19 overweight and obese M (n=4) and F (n=15) randomly assigned to ketogenic low-CHO diet (KLC, age 38.4 ± 3.9) or nonketogenic low-CHO diet (NLC, age 37.2 ± 3.9).	6 weeks	Both groups consumed ~30% of energy from protein. KLC consumed 60% of energy from fat and began with ~5% from CHO. NLC consumed 30% of energy from fat and ~40% from CHO. All food and beverages were provided. A ~30% energy deficit was imposed.	Y	KLC: 1500 kcal 9/33/60 NLC: 1500 kcal 42/31/30	BIA	No change (time or group x time) KLC: -1.7 NLC: -2.2	↓ in both groups KLC: - 6.3 ± 0.6 NLC: - 7.2 ± 0.8	↓ in both groups KLC: - 3.4 NLC: - 5.5	1 subject dropped ou first week d to heart arrhythmia.
Wood et al. 2007 (c)	30 overweight and obese M (age 38.8 ± 14.4) were randomly assigned to either a CHO-resticted diet with supplemental soluble fiber consumption (CRD-F) or a CHO-restricted diet with placebo capsules (CRD-P).	12 weeks	All subjects were assigned to a diet with 60% of energy from fat, 30% protein, and 10% CHO. No guidelines about total caloric intake or type of fat consumption were given. No food was provided. The fiber group consumed 3 g/d of soluble fiber (via capsules), while the placebo group consumed placebo capsules.	N	CRD-F: 1641 kcal 13/28/61 CRD-P: 1677 kcal 13/27/60	DXA	↓ in both groups CRD-F: -1.4 ± 1.7 CRD-P: -1.4 ± 2.0	↓ in both groups CRD-F: - 7.4 ± 3.1 CRD-P: - 7.5 ± 1.8	↓ in both groups CRD-F: - 5.6 ± 2.8 CRD-P: - 5.8 ± 2.6	1 subject withdrew d to military commitmer
Johnstone et al. 2008 (e)	17 obese M (age 38 ± 10) completed a randomized crossover design with two conditions: LC ketogenic diet and MC nonketogenic diet.	4 weeks per condition	Subjects were resident 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 protein, and 66% from fat. The MC group consumed 35% of energy from CHO, 30% from protein, and 35% from fat.	N	LC: 1732 kcal 5/30/66 MC: 1899 kcal 36/30/34	DXA	LC: -1.20 MC: -0.26 no difference between groups (p = 0.054 for greater loss in LC group)	↓ more in LC group LC: - 6.34 MC: - 4.35	↓ in both groups LC: -5.13 MC: -4.09	3 subjects withdrew fc personal reasons.

Brinkworth et al. 2009b (e)	66 sedentary, overweight, and obese M and F divided into a LC group (age 48.8 ± 1.6 y) and a HC group (age 49.3 ± 1.7 y).	8 weeks	LC group goal consumption was 35% of kcal as protein, 61% as fat, and 4% as CHO. HC group goal consumption was 24% of kcal as protein, 30% as fat, and 46% as CHO. Both diets represented a ~30% energy restriction. Some foods were provided at weeks 0, 2, 4, and 6 to aid compliance.	Y	LC: 1557 kcal 5/35/59 HC: 1547 kcal 47/24/27	DXA	↓ in both groups LC M: -2.0 F: -2.4 HC M: -2.2 F: -1.1	↓ 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 M (f)	↓ in both groups LC M: -8.2 W: -5.2 HC M: -4.5 W: -5.6 LC weight loss was only greater than HC in M (f)	60/66 (91% of participa completed study. 4 withdrew fr LC group a 2 from HC group.
Brinkworth et al. 2009a (c)	After randomization into the LC and LF groups, 107 overweight and obese individuals began the study. 69 participants completed the study (age 51.5 ± 7.7 (LC), 51.4 ± 6.5 (LF)).	12 months	LC and LF diets were designed to be isocaloric with moderate energy restriction (~6,000 kJ/d for F and ~7,000 kJ/d for M). The planned macronutrient content of the LC diet was 4% CHO, 35% protein, and 61% fat, while LF diet was 46% CHO, 24% protein, and 30% fat.	Y	LC: 1644 kcal 9/32/55 LF: 1625 kcal 47/22/27	DXA	↓ in LC relative to LF (time x diet) LC: -3.2 LF: -2.3	↓ in both groups LC: -13.1 ± 1.6 LF: - 11.6 ± 1.6	↓ in both groups LC: -11.3 ± 1.5 LF: -9.4 ± 1.2	69/107 (64 completed study. 22 withdrew fr LC group a 16 from LF group.
Paoli et al., 2012	8 high-level M gymnasts (age 21 ± 5.5) underwent 30 days of VLCD, with pre- and post-intervention assessments. 3 months later, subjects underwent 30 days of a normal diet (ND), with the same assessments.	4 weeks per condition	Both dietary conditions were *ad libitum*. Herbal supplements and a multivitamin/mineral supplement were consumed during the VLCD.	N	VLCD: 1972 kcal 5/41/55 ND: 2276 kcal 47/15/39	Skinfolds	No change from baseline VLCD: +0.3 ND: +0.2	↓ in VLCD VLCD: -1.6 ND: -0.1	↓ in VLCD VLCD:-1.9 ND: -0.2	NR
Ruth et al. 2013 (c)	Obese M and F were randomized into LFHC (age 41.5 ± 12.8) or HFLC (age 43.5 ± 11.5) groups. 55 participants were randomized, and 33 completed the study.		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 fat, and 15% from protein. The HFLC group was counseled to consume less than 40 g/d CHO, 60% of calories from fat, and ~35% from protein. The study lasted 12 weeks.	Y	LFHC: 1439 kcal 56/22/25 HFLC: 1532 kcal 10/34/56	DXA	No difference between groups LFHC: - 0.3 ± 2.3 HFLC: - 1.6 ± 1.3	↓ in both groups LFHC: -5.3; - 5.3 ± 4.7% HFLC: -7.1; -7.1 ± 4.6%	↓ in both groups LFHC: - 4.8 ± 3.1 HFLC :- 5.2 ± 4.0	33/55 (60% completed t study, with equal dropo between groups. Dropout lik due to adipo tissue biopsies.

(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 x gender x time effect with a greater reduction in LC than HC in M, but no difference between LC and HC in F

Abbreviations: BCA – body composition assessment, BIA – bioelectrical impedance analysis, CD – conventional diet, CHO – carbohydrate, DXA – dual-energy x-ray absorptiometry, F – females, FFM – fat-free mass, HFLC – high fat low carbohydrate, HUF – high unsaturated fat, LBM – lean body mass, LC – low carbohydrate, LCHP – low carbohydrate/high protein, LF – low fat, LFHC – low fat high carbohydrate, M – males, MC – medium-carbohydrate, ND – normal diet, NR – not reported, VLCD – very low carbohydrate diet, VLF – very low fat

Table 2. Summary of Resistance Training Studies

Study	**Subjects/Groups**	**Duration**	**Methods**	**Exercise Program**	**Daily Energy & Macronutrient Intake (%C/P/F)**	**BCA**	**FFM or LBM change** (a)	**BW Change** (a)	**BF Change** (a)	**Retentio**
Jabekk et al. 2010 (b)	18 untrained F (age 20 - 40 y, BMI ≥ 25) were randomly assigned to RT with regular diet (Ex) 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 pull down and standing biceps curl. For the first 5 weeks, 3 sets at 12 RM were performed for lower body exercises, and one set at 12 RM on 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 seconds between sets.	Ex: 1974 kcal 41/17/34 LC+Ex: 1756 kcal 6/22/66	DXA	↑ in Ex only Ex: 1.6 ± 1.8 kg LC+Ex: 0.1 ± 1.7 kg	↓ in LC+Ex only Ex: 0.8 ± 1.5 kg LC+Ex: - 5.6 ± 2.6 kg	↓ in LC+Ex only Ex: : - 0.6 ± 0.8 kg LC+Ex: - 5.6 ± 2.9 kg	1 subject each gro was excl from ana
Wood et al. 2012 (b)	42 M (age 59 ± 7 y) were randomized to LFD, LFD + RT, CRD, or CRD + RT. 32 M completed the intervention.	12 weeks	LFD was instructed to consume 1800 kcal per day, with < 30% of energy from fat, with < 10% from saturated fat, and were instructed to consume < 300 mg/day of dietary cholesterol. CRD was instructed to consume <50 g CHO per day with no energy restriction requirements.	RT groups performed supervised strength 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 pull down, calf raises, shoulder press, seated row, tricep press, and bicep curl. During weeks 7–12, two sets of 8–12 repetitions of the same exercises were performed. Non-RT groups continued baseline level of physical activity.	LFD: 1780 kcal 55/18/25 LFD+RT: 1590 kcal 59/20/23 CRD: 1707 kcal 15/27/55 CRD+RT: 1573 kcal 13/31/56	BIA	↓ 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	↓ 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	↓ in all groups LFD: -5.4 LFD + RT: -6.4 CRD: -7.1 CRD + RT: -8.0	Attrition similar between groups (2

(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=0.068) as well as between the LFD (27.5%) and CRD (15.7%) groups (p=0.072) for percentage of weight loss from appendicular FFM

Abbreviations: BCA – body composition assessment, BIA – bioelectrical impedance analysis, CHO – carbohydrate, DXA – dual-energy x-ray absorptiometry, F – females, FFM – fat-free mass, LBM – lean body mass, LFD – low fat diet, M – males, NC – no change