The Effect of Dietary Intervention by Low Carbohydrate Diet, and Low Fat Diet, on Weight Loss, Leptin and Adiponectin

Mervat Youssef

Clinical Nutrition Program, KSA, Holly Makkah, Faculty of Applied Medical Sciences, Umm-Alqura University
Mervatqalon@gamil.com

Abstract: Background: caloric restriction by very low carbohydrate diet (LC) and low-fat diet (LF) dietary patterns reduce body weight and fat mass and favorably modify leptin and possibly adiponectin. Aim: To compare the effects of an energy restricted very low carbohydrate (LC) and a low-fat diet (LF) on body weight loss and leptin and adiponectin after 6 weeks of diet intervention. Methods: Eighteen overweight subjects (age 20-22 years, BMI 27.68 ± 1.43 kg/m^2 were randomized to either an energy-restricted (control group), planned isocaloric LC or LF for six weeks. Body weight, fat %, waist circumference (WC), glucose, lipid profile, leptin, and adiponectin, were assessed. All data are mean ± SD. Results: The significant decline in mean difference and SD was 4.57±0.42, 3.70± 0.52 and 5.14±1.55 for body weight; and 4.7±1.44, 5.5±2.84 and 5.7±2.12 cm for WC in control, LC and LF, respectively. Waist circumference and fat% decreased significantly in all study subjects but no difference between different groups. Group results indicated that LDL cholesterol levels decreased in both LF (-28.8%) and control group (-29.6%) more than LC group (-28). No significant difference was detected for leptin and adiponectin among the studied groups. Leptin/fat percentage showed a significant decrease in subjects on LF diet by (14.8%) and on control diet by (14.3%), and increased by (4.8%) on LC diet. Adiponectin/Leptin ratio [A/L] decreased insignificantly by 9.1%, 26.3%, in control and LC groups respectively, while it increased insignificantly by 42% in LF group. Conclusion: Both LC and LF hypoenergetic diets achieved similar reductions in body weight and fat percent and lipid profile (TC, LDL, and TG) but without significant improvement of leptin/fat and adiponectin/leptin ratio.
[Mervat Youssef. **The Effect of Dietary Intervention by Low Carbohydrate Diet, and Low Fat Diet, on Weight Loss, Leptin and Adiponectin.** *Life Sci J* 2015;12(4):33-42]. (ISSN:1097-8135). http://www.lifesciencesite.com. 5

Key words; weight loss, low carbohydrate, low fat diet and adipokines

1. Introduction:

Obesity is a major health problem worldwide (NHANES, 2000) (Ng *et al.,*2014). Obesity rate increased dramatically in children by (47%) and adults by (28%) in the last four decades globally. The number of overweight and obese people increased from 857 million in 1980 to 2.1 billion in 2013 (NHANES 2000) (Ng *et al.,*2014).

Several studies suggested that the modern lifestyle of developed countries characterized by high levels of physical inactivity and high caloric intake, leads to greater adiposity (Byers *et al.,*2002). Proposed explanations for this association include involvement of obesity-related adipokines, such as adiponectin and leptin (Van de Voorde *et al.,*2013). Adipokines are suggested to have a role in insulin sensitivity (Diez and Iglesias,2003). Leptin and TNF-alpha are elevated in obesity with insulin resistance while adiponectin that enhances insulin action is reduced in abdominal obesity (Smits *et al.,*2013).

Weight loss accompanied by fat mass reduction is associated with improved adipokine levels and its action in both nondiabetic and diabetic participants (Wing *et al.,* 1996; Trakhtenbroit *et al.,*2009). Following low caloric diet in obese subjects for one year, lower leptin concentrations were observed at 6 months (Cardillo *et al.,*2006). However, this beneficial change cannot be maintained over time (Cardillo *et al.,*2006). Previous studies documented that successful weight loss is accompanied by an improvement in the blood glucose, lipid profile and cardiovascular markers (Henry*et al.,*1986)(Harder *et al.,*2004).

High carbohydrate intake provokes higher insulin concentrations and promotes lipogenesis (Bilsborough and Crowe, 2003); hence the benefits of low carbohydrate diet (e.g., Atkins diet) which are popular for weight loss reduction among the general populations.Several studies of low-carbohydrate diet (LC) in obese subjects for short-term (e.g., ≤6 months) have reported marked loss of body fat and greater maintenance of lean body mass compared with diets high in carbohydrates (Foster *et al.,* 2003).A recent study by Llanos *et al.,*(2014), suggested that caloric restriction by LC and low-fat diet (LF) dietary patterns favorably modify leptin and possibly the adiponectin-to-leptin ratio (Llanos *et al.,* 2014). A study by Phillips *et al.*, (2010) demonstrated reduction in leptin and resistin and increased adiponectin concentrations may contribute to improvement of the endothelial function during weight loss on LF but not LC diets (Westman *et al.,* 2008).Adiponectin may reverse microvascular

endothelial dysfunction induced by high fat, LCD diets (Westman *et al.,* 2008).

In addition, several studies were performed on weight loss trials, of which the durations were variable from four, six months, one year, and up to two years showed significantly more weight loss for the LCD group versus LF/low calorie diet (Aude *et al.,* 2004; Volek *et al.,* 2004; Yancy *et al.,* 2004). The same results were obtained for overweight patients with type 2 diabetes (Daly *et al.,* 2006). Compared to LFD, LCD improved a range of other disease markers including blood pressure, triglycerides, HDL cholesterol, and blood sugar levels (Summer *et al.,* 2011). A recent study by Bazzano*et al.,* (2014), showed "that low-carbohydrate diet was more effective for weight loss and cardiovascular risk factor reduction than the low-fat diet"(Lydia Bazzano2014).

Further studies are necessary to elucidate the association between changes in leptin and adiponectin levels during weight loss protocol by different dietary manipulations. We hypothesized that an association exists between leptin, adiponectin, and weight loss response in overweight subjects. We aimed to investigate the effect of different diet protocols for weight loss on body weight changes, leptin and adiponectin levels in overweight female subjects (pilot study) on an energy-restricted low-fat (LF) diet, compared with energy-restricted low-carbohydrate (LC) diet over 6 weeks.

2.Materials and methods

Study area and setting:

A total of 18 overweight females were assigned to the two dietary groups and the control. All the subjects were recruited from Qatar University, female students.

Subjects and selection:

The overweight females, with body mass index (BMI) between 25 and 30 kg/m^{2}were recruited from Qatar University(QU) students. The age range was 20-22 years. Subjects were randomly assigned to the different dietary groups and the control. The present study was approved by QU and followed the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. All the study subjects signed an informed consent to participate in the study after details of the study were explained to all candidates.

The study groups were:

1-Energy-restricted low-fat (LF) diet: with 15% of the total energy expenditure from fat, 30%from protein, and 55% from carbohydrates.

2-Energy-restricted low-carbohydrate (LC) diet: with 30% of the total energy expenditure from carbohydrates, 30% from protein, and 40% from fat.

3-Energy-restricted low balanced diet (Control): with 15% of the total energy expenditure from protein, 25% from fat, and 60% from carbohydrates.

The energy intake was based on the participant's resting energy expenditure. The study continued for six weeks. Assigned participants to each group took their breakfast and lunch in an observed setting at the nutrition program at the Health Sciences Department in College of Arts and Sciences at Qatar University. Dinner, which was taken at home and snacks were recorded in the food diary. All food intakes were submitted weekly for six weeks.

Study design:

Study design: Case-control association study.

Sample Size: As a pilot study, 18 subjects were recruited.

Sampling Technique: The candidates were randomly assigned to each studied group.

Data Collection:

Baseline data were collected and repeated weekly. Data included weight, BMI, waist and hip measurements, blood pressure. Body composition measurements were also taken including body fat mass (BFM), resting metabolic rate (RMR), and total body water (TBW). Plasma lipids including total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides were measured weekly. Insulin levels, plasma glucose, and ketone bodies in urine were evaluated.

Measurements and assays

1. Anthropometric andblood pressure measurements:

a. BMI, waist, hip and arterial blood pressure measurements:

Body weight was measured weekly using a calibrated scale while the subjects are wearing lightweight clothing and no shoes. Standing height was measured to the nearest 0.1 cm with the use of a stadiometer in bare foot, with the shoulders in relaxed position and arms hanging freely. Body mass index "BMI" was calculated by dividing weight into [Kg] by height squared meter [m^2]. BMI of 18.5 to 24.9 Kg/m^2 was considered healthy, 25 to 29.9 Kg/m^2 overweight, and 30 Kg/m^2 or more as obese (Health 1998). Waist (WC) and hip (HC) circumferences were measured in duplicate with the subjects standing dressed in light clothes. WC was measured at the minimum circumference at the umbilical level. HC was measured at the maximum circumference over the buttocks. Both measurements were recorded to the nearest 0.1 cm. Correct posture of the subject was ensured by maintaining the Frank Front plane. Abdominal obesity was defined by waist circumference of > 102 cm (> 40 inches) in male, and

> 88 cm (> 35 inches) in female (National Cholesterol Education Program Expert Panel on Detection and Treatment of High Blood Cholesterol in 2002). WHO criteria defined obesity as waist/hip ratio > 0.90 in males and > 0.85 in females (Alberti and Zimmet 1998). Blood Pressure was measured twice weekly according to the standards in the supine position by a well calibrated manual sphygmomanometer by an experienced nurse. Blood pressure values of <130/85 mmHg were considered normal (National Cholesterol Education Program Expert Panel on Detection and Treatment of High Blood Cholesterol in 2002).

b. Body composition analysis:

Body fat mass (BFM), resting metabolic rate (RMR), and total body water (TBW) were measured using the Bioelectric impendence analysis (BIA) (bioscan-916 model, Maltron, UK). The measurements were performed after an overnight fasting and after voiding of the urine at least one hour before testing. Electrodes were placed on the dorsal surface of the right foot and ankle, and right wrist and hand. A current was applied at a frequency of 50 kHz. Body fat percent (BF %) for females with physical fitness is 20-25%, with 10-13% essential fat, corresponding to 12-15% and 2-5% in males respectively (AC,2009).

2. Food intake:

Data recording diary was used to get information regarding food intake, by type, amount, time of intake and any variation from the planned diet. All food intakes were recorded daily and submitted weekly by all participants in the study. Evaluation of food intake was evaluated by an experienced dietitian.

3. Biochemical assays:

A venous blood sample after fasting (10 to 12 hours) was drawn for each participant at the beginning of the study and weekly afterward. Serum was separated and aliquoted for routine chemistry, and another part was stored at -80^{o}C for further hormone analysis. All chemical biomarkers were determined weekly. Blood glucose and lipid profile including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG) were measured as previously published (Rizk *et al.,* 2011). The cut-off values for glucose and lipid profiles were adopted as previously published (National Cholesterol Education Program Expert Panel on Detection and Treatment of High Blood Cholesterol in 2002) (4). TC/HDL was used to assess the Atherogenic index [AI]. Ketone bodies were tested in urine biweekly by Combur 10 Test Miditron (Roche).

Hormonal assay: Insulin/Leptin/Adiponectin:

Serum was aliquoted and stored at 0-80^{o}C and later was used for Elisa assays. Insulin was assessed in venous blood biweekly. Serum insulin was measured by DRG Insulin Enzyme Immunoassay Kit (DRG Instruments GmbH, Germany). Leptin and adiponectin were measured by Elisa according to the manufacturer's instructions (Ray-biotech).

Statistical Analysis:

Continuous data were expressed as mean ± SD for normally distributed variables unless mentioned otherwise and the number and (percentage) for categorical data. Normal distribution of data was checked using the Kolmogorov-Smirnov normality test. Two student's t-tests and nonparametric Mann-Whitney evaluated differences between continuous variables, and 2-independent samples t-tests were used accordingly for the analysis. Descriptive statistics (means and standard deviations) were computed for each body variable in Group 1 (Control), Group 2 (Low Carbohydrate), and Group 3 (Low Fat) with respect to time. Linear regression models of the form $Y = \beta o + \beta 1\ X$ where Y = body variable, βo = intercept (value of Y when X = 0); β1 = slope (rate of change of Y per unit change in X), and X = time (weeks) were computed separately for Group 1, Group 2, and Group 3. Significant linear relationships were visualized by fitted line plots. The significance of each regression was determined using R2 (coefficients of determination), F (variance ratios) from the analysis of variance, and t-statistics to determine if the intercepts and slopes were significantly different from zero.Analysis of covariance (ANCOVA) using a general linear model with time as a covariate was performed to compare the intercept and slope of each linear regression model in Group 1 with the corresponding intercept and slope of each model in Group 2. The models in Group 1 were similarly compared with those in Group 3, and the models in Group 2 and Group 3 were also compared. The design of the experiment was unbalanced (i.e., unequal number of samples in each variable, and inclusion of missing values). In addition, the samples were dependent (i.e., repeated successively on the same subjects at intervals over time). Consequently, it was necessary to perform multi-factorial analysis of variance (ANOVA) assuming a general linear model with repeated measures and an unbalanced design to compare the changes in the body variables between the 18 subjects and the 3 groups over the 6 week period. Subjects were assumed to be random effects. Groups were assumed to be fixed effects. Body weight was incorporated in the model as a covariate (controlling or confounding variable). The assumption that body weight was a confounding variable was based on the results of correlation analysis (Spearman's

correlation coefficients) between body weights and other body variables. Spearman's correlation coefficients between changes in Body Mass Index (BMI) and changes in other body variables were also computed separately for Group 1, Group 2, and Group 3. All statistical analysis was performed using SPSS program for Windows [Version 20 statistical software; Texas Instruments, IL, USA] and GraphPad Prism version 6.00 for Windows, GraphPad Software, La Jolla California USA, www.graphpad.com]. Two-tailed *P* value < 0.05 is statistically significant.

3.Results

1. Baseline and 6- week's diet intervention on anthropometric and biochemical parameters in overweight subjects.

As shown in tables (1 and 2), no significant difference were observed between the study groups in any of the baseline measurements. None of the study subjects in control and LF groups had ketonuria during the study. Linear regression models with significant negative slopes indicated that certain body variables declined during the six week period. An analysis of the different variables in different groups on caloric restriction and LC and LF diet intervention shows significant decrease of the following measures: body weight, BMI, waist, hip, fat weight mass, fat %, and lipid parameters including TC, TG, LDL-C and TC/HDL ratio as shown in Table 1, 2. Figures 1 -3, shows the mean difference and % change between initial and final measures for body weight, waist circumference, and TC/HDL ratio in three studied groups with their *p*- values. The data showed that overweight subjects on the control diet, LC and LF diets for 6 weeks showed significant reductions in BW, waist and TC/HDL ratio in all groups. The significant decline in mean difference and SD was 4.57±0.42, 3.70± 0.52 and 5.14±1.55 for body weight; and 4. 7±1.44, 5.5±2.84 and 5.7±2.12 for WC in control, LC and LF, respectively. The significant decline in BMI (kg/m^2) in control group was 1.74±0.28 (p=0.007) [-6.2%], in LC group was 1.44±0.34 (p=0.028) [-5.1%] and in LF group was 1.84±0.29 (p=0.0003) [-6.8%] as shown in figure 4. Losses in fat weight were observed in all groups (LF, -1.46 kg (-6.5%); LC, -1.77 kg (-5.5%); Contol,-3.7 Kg (-7.1%). Waist was significantly decreased among groups (*P*=0.005) and by the end of the study with (*p*=0.004). Both LC group and LF group decreased approximately 5.5 (-7.8%) -5.7 (-7.4%) cm of their waists, respectively, while the control group decreased by 4.7 cm (-6.0 %) of their waist. The significant improvements in total cholesterol values were more observed in the LF group (-28.2%); in LC (-27.6%) and in control was (-26.9%). Group results indicated that LDL cholesterol levels decreased in both LF (-28.8%) and Control groups (-29.6%) more than LC group (-28). The blood pressures in the three groups were within the normal range at the outset of the study and remained so throughout the study (Table 2). No Significant differences in blood pressure were found between the groups during the study.

No significant difference was detected for the glucose, leptin, insulin and adiponectin observed between baseline and after 6 weeks of intervention among the study groups as shown in (Table 2). Leptin decreases after 6 weeks of diet intervention by 22.6%, 9.0% and 18.2% in control, LC, and LF groups, respectively as shown in Table 2. Leptin/fat percentage showed a significant decrease in subjects on LF diet by (14.8%) and on control diet by (14.3%), and increased by (4.8%) on LC diet. Adiponectin insignificantly decreased in the control group by 23.6 and 4.8% in LF group but increased insignificantly in LC group by 5.2% after 6 weeks of diet intervention. Adiponectin/Leptin ratio [A/L] decreased insignificantly by 9.1%, 26.3%, in control and LC groups respectively, while it increased insignificantly by 42% in LF group, respectively as shown in Table 2. Insulin increased insignificantly in control by 113% and in LC group by 22.7% while it decreased insignificantly in LF group by 25.0%.

Repeated measures ANOVA (Table 3), indicated many significant effects between subjects and groups. The majority of body variables varied significantly between subjects when body weight was held statistically constant in the model. Although the observed changes in body variables with respect to time were dominated by intrinsic random physical, biochemical, and physiological differences between the subjects, the repeated measures ANOVA was nevertheless able to identify certain variables which varied significantly between the three fixed groups, i.e., total cholesterol, LDL cholesterol, fat%, total body water%, and leptin/fat.

2. Correlations between BMI and anthropometric and biochemical parameters in overweight subjects.

Spearman's correlation coefficient between BMI and the studied variables are shown in table 3. Of interest, subjects on caloric restriction diet as a control diet, the BMI is significantly correlated with waist (r=0.84), W/H (r=0.47), TC (r=0.85), LDL-C (0.63), leptin (r=0.81), leptin/fat (r=0.71) and inversely with adiponectin (r=-.69) and Adiponectin/leptin ratio (r=-0.67). In groups on LC diet, BMI is significantly correlated with the following parameters; waist (r=0.82), hip (r=0.956), leptin (r=0.69) and leptin /fat ratio (r=0.58). In subjects on LF diet, BMI is significantly correlated

with hip (r=0.85), HDL-C (r=0.35) and inversely with W/H ratio (r=-0.48), and adiponectin/leptin ratio (r=-0.67).

Table (1): Baseline and wk-6 characteristics of study population/Table 1Changes in anthropometric variables and blood pressure

	Control(N=6)		LC (N=6)		LF(N=6)	
	Baseline	Wk6	Baseline	Wk6	Baseline	Wk6
BMI (kg/m2)	28.14±1.53	26.40±1.87	27.72±1.90	26.32±2.39	27.38±1.38	25.54±1.38
Body weight (kg)	74.77±6.39	70.20±7.46	71 .30±9.17	67.6±9.75	76.36±1.79	71.22±1.73
Waist (cm)	79.53±3.16	74.83±4.64	71.16±1.52	65.66±4.19	77.1±5.38	71.4±3.36
Hip (cm)	108.00±3.60	103.66±3.21	110.06±3.17	105±5.56	106.8±4.60	101.3±2.88
W/H ratio	0.73±0.04	0.72±0.04	0.65±0.04	0.62±0.2	0.726±0.04	0.70±0.04
Fat weight (kg)	28.60±4.23	24.54±3.78	26.58±7.30	24..81±3.65	26.72±2.19	25.26±5.21
Fat weight (%)	38.29±3.08	35.59±4.23	37.03±5.37	35.02±4.78	35.31±5.23	35.05±5.72
FFM (%)	61.71±3.08	64.98±4.63	62.96±5.59	64.345.94	64.69±3,26	64.94±3.26
TBW (%)	44.42±2.81	46.53±2.94	45.62±4.23	47.82±1.24	46.35±2.26	46.91±3.34
SBP (mmHg)	104.66±9.29	104.33±5.68	102.66±8.50	89.33±6.03	102.60±10.59	107.80±7.79
DBP (mmHg)	54.00±1.00	62.00±9.54	65.33±16.65	55.00±4.00	64.60±7.53	66.40±8.17

Table 2: Blood Biochemistry at baseline and after 6 weeks intervention with LC, LF, ControlHypocaloric diet in the subjects.

Variables	Control		LC		LF	
	Baseline	Intervention	Baseline	Intervention	Baseline	Intervention
TC (mg/dl)	241.66±47.72	176.33±35.23	199.66±41.63	144.33±35.80	202.20±23.12	145.20±21.39
LDL-C (mg/dl)	151.00±9.16	106.33±12.66	126.00±25.35	90.66±21.73	126.20±15.03	89.80±21.94
HDL C (mg/dl)	50.33±9.86	48.00±11.13	57.66±17.47	54.66±13.65	52.6±15.01	51.20±8.04
TG (mg/dl)	143.33±77.86	109.33±75.50	82.00±15.09	47.33±13.79	136.00±104.40	69.60±39.36
TC/HDL ratio	4.06±1.05	3.70±0.47	3.53±0.50	2.6±0.34	4.20±0.82	2.84±1.02
Glucose (mg/dl)	78.66±7.02	75.66±5.77	76.66±8.62	76.66±8.14	89.20±8.75	87.80±6.90
Leptin (ng/ml)	11.50±6.25	8.9±4.4	11.27±6.47	14.26±6.95	9.73±5.28	7.95±5.64
Leptin/ fat	0.28±0.14	0.24±0.10	0.27±0.13	0.40±0.16	0.27±0.14	0.23±0.17
Adiponectin (µg/ml)	15.7±6.7	12.0±6.9	15.4±2.6	16.2±3.0	12.5±6.4	11.9±4.8
Adiponectin/Leptin	2.2±2.1	2.0±2.1	1.9±1.5	1.4±0.7	1.9±1.8	2.7±2.2
Insulin (µIU/ml)	10.0±4.1	21.3±8.3	18.8±5.6	23.1±26.7	32.7±36.9	24.55±4.70

Data are presented as mean and SD.

Table 3: Comparison of body variables between subjects (random effects) and groups (fixed effects) using repeated measures Analysis of Variance incorporating body weight as a controlled variable

VARIABLES	REPEATED MEASURES ANOVA Control variable = body weight			
	Between Subjects (Random Effects)		Between Groups (Fixed Effects)	
	F	*P*	F	*P*
BMI (kg/m2)	1086.78	0.000 ***	0.14	0.989 ns
Waist (cm)	9.11	0.004 ***	1.10	0.371 ns
Hip (cm)	23.01	0.000 ***	1.24	0.297 ns
Waist/Hip	0.738	0.110 ns	1.14	0.352 ns
Systolic Blood Pressure	2.21	0.029 *	0.58	0.747 ns
Diastolic Blood Pressure	1.69	0.104 ns	0.67	0.672 ns
Glucose	1.02	0.058	1.50	0.078 ns
Total Cholesterol	9.68	0.000 ***	6.61	0.000 ***
HDL Cholesterol	3.02	0.004 **	6.37	0.000 ***
LDL Cholesterol	6.23	0.000 ***	5.69	0.000 ***
Total/HDL Cholesterol	5.74	0.000 ***	6.47	0.000 ***
Total Lipids	4.42	0.001 ***	0.46	0.713 ns
Non-esterified free fatty acids	3.43	0.004 **	1.22	0.320 ns
Fat %	21.05	0.000 ***	3.11	0.016 *
Leptin	10.49	0.000 ***	0.63	0.601 ns
Adiponectin	9.63	0.000 ***	0.21	0.889 ns
Adiponectin/Leptin	4.74	0.000 ***	0.62	0.605 ns
Leptin/Fat	6.90	0.000 ***	7.43	0.001 ***
Insulin	1.13	0.372 ns	1.07	0.377 ns

Table 4: Correlations (r = Spearman's correlation coefficient) between BMI and body variables

VARIABLES	GROUP 1 (Control)		GROUP 2 (Low Carbohydrate)		GROUP 3 (Low Fat)	
	Spearman's r	*P*	Spearman's r	*P*	Spearman's r	*P*
Waist (cm)	0.839	0.000 ***	0.818	0.000 ***	0.065	0.710 ns
Hip (cm)	0.340	0.131 ns	0.957	0.000 ***	0.858	0.000 ***
Waist/Hip	0.470	0.032 *	0.068	0.768 ns	-0.482	0.003 **
Systolic Blood Pressure	0.337	0.135 ns	0.330	0.144 ns	-0.326	0.056
Diastolic Blood Pressure	0.266	0.244 ns	0.398	0.074	-0.090	0.606 ns
Glucose	-0.011	0.962 ns	0.321	0.156 ns	0.047	0.789 ns
Total Cholesterol	0.848	0.000 ***	-0.245	0.285 ns	0.241	0.164 ns
HDL Cholesterol	0.399	0.073 ns	-0.367	0.102 ns	0.348	0.040 *
LDL Cholesterol	0.630	0.002 **	-0.290	0.203 ns	0.114	0.515 ns
Total/HDL Cholesterol	0.314	0.165 ns	0.165	0.475 ns	-0.257	0.136 ns
Leptin	0.810	0.001 ***	0.685	0.010 **	0.431	0.058
Adiponectin	-0.696	0.012 *	-0.115	0.722 ns	-0.282	0.229 ns
Adiponectin/Leptin	-0.668	0.017 *	-0.495	0.100	-0.666	0.001 ***
Leptin/Fat	0.709	0.010**	0.582	0.047 *	0.324	0.163 ns
Insulin	0.218	0.496 ns	0.573	0.052	0.107	0.652 ns

ns not significant (P > 0.1); * significant (P ≤ 0.05); ** very significant (P ≤ 0.01); *** very highly significant (P < 0.001).

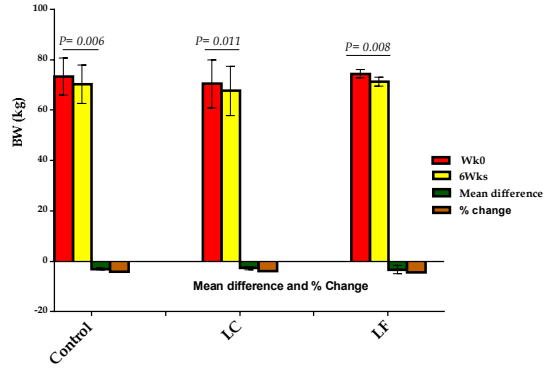

Fig 1. Body weight changes in different group after 6 weeks of dietary intervention with control diet, low carbohydrate diet (LC) and low fat diet (LF)
Data are presented as mean and SD, with mean difference and % change.
Two-tailed P value < 0.05 is statistically significant

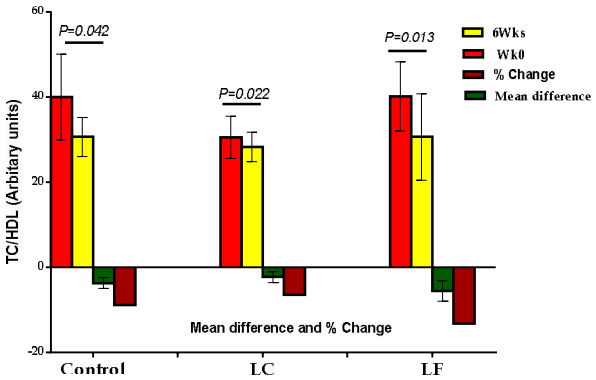

Fig 3. TC/HDL ratio changes in different group after 6 weeks of dietary intervention with control diet, low carbohydrate diet (LC) and low fat diet (LF)
Data are presented as mean and SD, with mean difference and % change.
Two-tailed P value < 0.05 is statistically significant

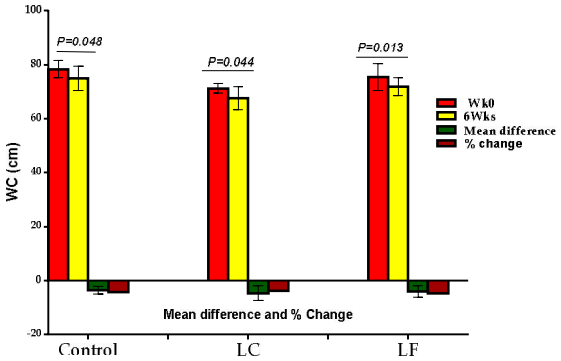

Fig 2. Waist circumference changes in different group after 6 weeks of dietary intervention with control diet, low carbohydrate diet (LC) and low fat diet (LF)
Data are presented as mean and SD, with mean difference and % change.
Two-tailed P value < 0.05 is statistically significant

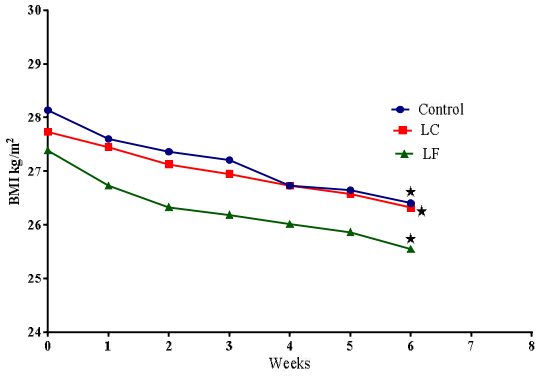

Fig 4. Weekly changes in BMI in different group of dietary intervention with control diet, low carbohydrate diet (LC) and low fat diet (LF).
Data are presented as mean and SD. Two-tailed P value < 0.05 is statistically significant.

4.Discussion

In the current study, there was a significant weight loss at 6 weeks for the study subjects on the three (LF) diet, (LC) diet and hypocaloric control (HC) diet. Changes in leptin and adiponectin were not significantly different over time of diet intervention among the three studied groups. The waist circumference is a measure of abdominal obesity significantly decreased by (HC), LF, and LC diets. Moreover, the lipid profile; total cholesterol, triglycerides, LDL and TC/HDL decreased significantly with each group but no significant difference was observed between different groups. The implications of these findings will be highlighted in the next paragraphs.

Central adiposity can predict cardiometabolic risks such as hyperlipidemia, metabolic syndrome and diabetes mellitus (Poyrazoglu *et al.,*2014). Central adiposity assessed by WC and W/H ratio is significantly reduced in all groups; such finding is consistent with previous studies (Meckling *et al.,* 2004) (Nordmann *et al.,*2006). There is a considerable body of evidence indicating that low-carbohydrate diets are effective for weight loss as comparable to low-fat diet and energy restriction balanced diet (McAuley *et al.,* 2006). A key finding in this study is that LC, LF and HC diets reduce body fat% and improve lipid profile as cardiovascular risk factors. Previous studies demonstrated that both diets improved lipid profiles with reductions in total cholesterol, triglycerides and LDL-C (Luscombe-Marsh *et al.,* 2005)(Samaha *et al.,* 2007; Bazzano*et al.,*2014).

In addition, the current data showed that leptin is involved in body weight regulation and BMI response to three (LF) diet, (LC) diet and hypocaloric control diets. Although most of the measured variables are significant with other anthropometric and biochemical variables, but only lipid profile and fat % and leptin /fat ratio is significantly different between the different groups.

Several dietary trials have evaluated the effects of LFD and/or LCD interventions on adipokine concentrations (Havel, 2000); (Heinonen *et al.,* 2009); (Kalupahana *et al.,* 2011); (Rolland *et al.,* 2011) (Bluher *et al.,* 2012) (Oberhauser *et al.,* 2012). Leptin is a hormone secreted by adipose tissue and has a positive correlation with fat % and BMI (Filozof *et al.,* 2000). Body weight loss in this study is accompanied by the parallel decrease in fat % in all study groups. Both HC and LF groups showed progressively decreased levels of leptin and the parallel decrease in leptin/fat ratio but not in LC group. Previous studies showed that leptin decreased in response to weight loss in hypocaloric diet (Miyawaki *et al.,* 2002) and LF and LC diets (Okazaki *et al.,* 1999; Xenachis *et al.,*2001; de Luis *et al.,* 2007). The decreased fat oxidation with fat % in diet restriction by macronutrients could explain the decreased leptin concentrations after 6 weeks of intervention with decreased weight loss in the current study (Filozof *et al.,*2000). The current study showed non-significant change in adiponectin during the 6 weeks of intervention on different macronutrients. These findings are consistent with studies (de Luis et al. 2007; Heinonen et al. 2009) where no significant change could be observed, while in other studies significant improvement of adiponectin and decrease of leptin could be observed in several studies (Vetter *et al.,* 2010) (Rolland *et al.,* 2011);(Oberhauser *et al.,* 2012); (Kelly *et al.,*2014) with an improvement of insulin resistant marker adiponectin/leptin ratio.This contrast with our findings could be due to the short duration of our study (6 week intervention) while in most of these studies it extended up to 3-6 months or longer, the second reason is the limited sample size in our study and the third cause may be due to fewer weight changes observed in our study (less than 5%). Varady *et al.,*(2008) suggested that a minimum of weight loss of 5% is required to detect significant changes in adipokines (Varady *et al.,* 2009) while in other studies it suggested at least 10% weight loss could explain why we cannot detect significant changes in adipokines as discussed in earlier study by Madsen *et al.*(2008) (Madsen *et al.,*2008)

These current data have important clinical and public health consequences. Over the preceding several years, low-fat diets have been acclaimed for weight loss primarily because of their appreciated effects on cardiometabolic risk factors (Frisch *et al.,* 2009) . Our study suggests that low-carbohydrate diets might afford a different attitude for weight reduction without worsening metabolic risk factors and could benefit overweight and obese subjects. We found that both diets were similarly effective in reducing body weight and waist circumference. Both diets reduced total cholesterol, LDL cholesterol, triglycerides, TC/HDL ratio and fat % with improvement in leptin/fat in both dietary intervention and adiponectin/leptin ratio only observed on LF diets.

This study has limitations that should be reflected. The small sample which included only overweight women, and the short duration of the study (6weeks) that restricted our power to detect significant changes in adipokine concentrations between diets as well as limited the generalizability of our findings.

In summary, conclusions from this small pilot randomized trial support that LC and LF and LCD dietary interventions are potentially attractive methods for obesity-related management, particularly through favorable modification of fat %, WC and lipid profile as they represent cardiovascular risk factors. Further

studies are neededwith larger sample size including both gender and monitoring such changes over one year at least is required to detect changes in adipokine levels and its impact on weight loss management.

Acknowledgement

This work was supported by grant #CAS05002 from Qatar University, Qatar. We would like to thank the students who volunteered and participated in such study. We would like to thank biomedical program where biochemical assays were performed and Dr. Nasser Rizk at biomedical program-Qatar University for his generous help and technical support.

References

1. AC, E. 2009. ACE lifestyle and Weight Management Consultant Manual, The Ultimate Resource for Fitness Professionals. *American Council on Exercise (ACE)*.
2. Alberti, K. G., and P. Z. Zimmet. 1998. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med* 15 (7):539-553.
3. Aude, Y. W., A. S. Agatston, F. Lopez-Jimenez, E. H. Lieberman, A. Marie, M. Hansen, G. Rojas, G. A. Lamas, and C. H. Hennekens. 2004. The national cholesterol education program diet vs a diet lower in carbohydrates and higher in protein and monounsaturated fat: a randomized trial. *Arch Intern Med* 164 (19):2141-2146.
4. Bazzano, L. A., T. Hu, K. Reynolds, L. Yao, C. Bunol, Y. Liu, C. S. Chen, M. J. Klag, P. K. Whelton, and J. He. 2014. Effects of low-carbohydrate and low-fat diets: a randomized trial. *Ann Intern Med* 161 (5):309-318.
5. Bilsborough, S. A., and T. C. Crowe. 2003. Low-carbohydrate diets: what are the potential short- and long-term health implications? *Asia Pac J Clin Nutr* 12 (4):396-404.
6. Bluher, M., A. Rudich, N. Kloting, R. Golan, Y. Henkin, E. Rubin, D. Schwarzfuchs, Y. Gepner, M. J. Stampfer, M. Fiedler, J. Thiery, M. Stumvoll, and I. Shai. 2012. Two patterns of adipokine and other biomarker dynamics in a long-term weight loss intervention. *Diabetes Care* 35 (2):342-349.
7. Byers, T., M. Nestle, A. McTiernan, C. Doyle, A. Currie-Williams, T. Gansler, M. Thun, N. American Cancer Society, and C. Physical Activity Guidelines Advisory. 2002. American Cancer Society guidelines on nutrition and physical activity for cancer prevention: Reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin* 52 (2):92-119.
8. Cardillo, S., P. Seshadri, and N. Iqbal. 2006. The effects of a low-carbohydrate versus low-fat diet on adipocytokines in severely obese adults: three-year follow-up of a randomized trial. *Eur Rev Med Pharmacol Sci* 10 (3):99-106.
9. Daly, M. E., R. Paisey, R. Paisey, B. A. Millward, C. Eccles, K. Williams, S. Hammersley, K. M. MacLeod, and T. J. Gale. 2006. Short-term effects of severe dietary carbohydrate-restriction advice in Type 2 diabetes--a randomized controlled trial. *Diabet Med* 23 (1):15-20.
10. de Luis, D. A., R. Aller, O. Izaola, M. Gonzalez Sagrado, D. Bellioo, and R. Conde. 2007. Effects of a low-fat versus a low-carbohydrate diet on adipocytokines in obese adults. *Horm Res* 67 (6):296-300.
11. Diez, J. J., and P. Iglesias. 2003. The role of the novel adipocyte-derived hormone adiponectin in human disease. *Eur J Endocrinol* 148 (3):293-300.
12. Filozof, C. M., C. Murua, M. P. Sanchez, C. Brailovsky, M. Perman, C. D. Gonzalez, and E. Ravussin. 2000. Low plasma leptin concentration and low rates of fat oxidation in weight-stable post-obese subjects. *Obes Res* 8 (3):205-210.
13. Foster, G. D., H. R. Wyatt, J. O. Hill, B. G. McGuckin, C. Brill, B. S. Mohammed, P. O. Szapary, D. J. Rader, J. S. Edman, and S. Klein. 2003. A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med* 348 (21):2082-2090.
14. Frisch, S., A. Zittermann, H. K. Berthold, C. Gotting, J. Kuhn, K. Kleesiek, P. Stehle, and H. Kortke. 2009. A randomized controlled trial on the efficacy of carbohydrate-reduced or fat-reduced diets in patients attending a telemedically guided weight loss program. *Cardiovasc Diabetol* 8:36.
15. Harder, H., B. Dinesen, and A. Astrup. 2004. The effect of a rapid weight loss on lipid profile and glycemic control in obese type 2 diabetic patients. *Int J Obes Relat Metab Disord* 28 (1):180-182.
16. Havel, P. J. 2000. Role of adipose tissue in body-weight regulation: mechanisms regulating leptin production and energy balance. *Proc Nutr Soc* 59 (3):359-371.
17. Health, N. I. o. 1998. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults-the evidence report. *Obesity Res* 6 ((Suppl 2)):51S-209S.
18. Heinonen, M. V., D. E. Laaksonen, T. Karhu, L. Karhunen, T. Laitinen, S. Kainulainen, A. Rissanen, L. Niskanen, and K. H. Herzig. 2009. Effect of diet-induced weight loss on plasma apelin and cytokine levels in individuals with the metabolic syndrome. *Nutr Metab Cardiovasc Dis* 19 (9):626-633.
19. Henry, R. R., T. A. Wiest-Kent, L. Scheaffer, O. G. Kolterman, and J. M. Olefsky. 1986. Metabolic consequences of very-low-calorie diet therapy in obese non-insulin-dependent diabetic and nondiabetic subjects. *Diabetes* 35 (2):155-164.
20. Kalupahana, N. S., B. H. Voy, A. M. Saxton, and N. Moustaid-Moussa. 2011. Energy-restricted high-fat diets only partially improve markers of systemic

and adipose tissue inflammation. *Obesity (Silver Spring)* 19 (2):245-254.
21. Kelly, K. R., S. D. Navaneethan, T. P. Solomon, J. M. Haus, M. Cook, H. Barkoukis, and J. P. Kirwan. 2014. Lifestyle-induced decrease in fat mass improves adiponectin secretion in obese adults. *Med Sci Sports Exerc* 46 (5):920-926.
22. Llanos, A. A., J. L. Krok, J. Peng, M. L. Pennell, S. Olivo-Marston, M. Z. Vitolins, C. R. Degraffinreid, and E. D. Paskett. 2014. Favorable effects of low-fat and low-carbohydrate dietary patterns on serum leptin, but not adiponectin, among overweight and obese premenopausal women: a randomized trial. *Springerplus* 3:175.
23. Luscombe-Marsh, N. D., M. Noakes, G. A. Wittert, J. B. Keogh, P. Foster, and P. M. Clifton. 2005. Carbohydrate-restricted diets high in either monounsaturated fat or protein are equally effective at promoting fat loss and improving blood lipids. *Am J Clin Nutr* 81 (4):762-772.
24. Lydia A. Bazzano, M., PhD, MPH*; Tian Hu, MD, MS*; Kristi Reynolds, PhD; Lu Yao, MD, MS; Calynn Bunol, MS, RD, LDN; Yanxi Liu, MS; Chung-Shiuan Chen, MS; Michael J. Klag, MD, MPH; Paul K. Whelton, MD, MSc, MB; and Jiang He, MD, PhD. 2014. Effects of Low-Carbohydrate and Low-Fat Diets: A Randomized TrialEffects of Low-Carbohydrate and Low-Fat Diets. *Ann Intern Med* 161 ((5)):309-318.
25. Madsen, E. L., A. Rissanen, J. M. Bruun, K. Skogstrand, S. Tonstad, D. M. Hougaard, and B. Richelsen. 2008. Weight loss larger than 10% is needed for general improvement of levels of circulating adiponectin and markers of inflammation in obese subjects: a 3-year weight loss study. *Eur J Endocrinol* 158 (2):179-187.
26. McAuley, K. A., K. J. Smith, R. W. Taylor, R. T. McLay, S. M. Williams, and J. I. Mann. 2006. Long-term effects of popular dietary approaches on weight loss and features of insulin resistance. *Int J Obes (Lond)* 30 (2):342-349.
27. Meckling, K. A., C. O'Sullivan, and D. Saari. 2004. Comparison of a low-fat diet to a low-carbohydrate diet on weight loss, body composition, and risk factors for diabetes and cardiovascular disease in free-living, overweight men and women. *J Clin Endocrinol Metab* 89 (6):2717-2723.
28. Miyawaki, T., H. Masuzaki, Y. Ogawa, K. Hosoda, H. Nishimura, N. Azuma, A. Sugawara, I. Masuda, M. Murata, T. Matsuo, T. Hayashi, G. Inoue, Y. Yoshimasa, and K. Nakao. 2002. Clinical implications of leptin and its potential humoral regulators in long-term low-calorie diet therapy for obese humans. *Eur J Clin Nutr* 56 (7):593-600.
29. National Cholesterol Education Program Expert Panel on Detection, E., and A. Treatment of High Blood Cholesterol in. 2002. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 106 (25):3143-3421.
30. Ng, M., T. Fleming, M. Robinson, B. Thomson, N. Graetz, C. Margono, E. C. Mullany, S. Biryukov, C. Abbafati, S. F. Abera, J. P. Abraham, N. M. Abu-Rmeileh, T. Achoki, F. S. AlBuhairan, Z. A. Alemu, R. Alfonso, M. K. Ali, R. Ali, N. A. Guzman, W. Ammar, P. Anwari, A. Banerjee, S. Barquera, S. Basu, D. A. Bennett, Z. Bhutta, J. Blore, N. Cabral, I. C. Nonato, J. C. Chang, R. Chowdhury, K. J. Courville, M. H. Criqui, D. K. Cundiff, K. C. Dabhadkar, L. Dandona, A. Davis, A. Dayama, S. D. Dharmaratne, E. L. Ding, A. M. Durrani, A. Esteghamati, F. Farzadfar, D. F. Fay, V. L. Feigin, A. Flaxman, M. H. Forouzanfar, A. Goto, M. A. Green, R. Gupta, N. Hafezi-Nejad, G. J. Hankey, H. C. Harewood, R. Havmoeller, S. Hay, L. Hernandez, A. Husseini, B. T. Idrisov, N. Ikeda, F. Islami, E. Jahangir, S. K. Jassal, S. H. Jee, M. Jeffreys, J. B. Jonas, E. K. Kabagambe, S. E. Khalifa, A. P. Kengne, Y. S. Khader, Y. H. Khang, D. Kim, R. W. Kimokoti, J. M. Kinge, Y. Kokubo, S. Kosen, G. Kwan, T. Lai, M. Leinsalu, Y. Li, X. Liang, S. Liu, G. Logroscino, P. A. Lotufo, Y. Lu, J. Ma, N. K. Mainoo, G. A. Mensah, T. R. Merriman, A. H. Mokdad, J. Moschandreas, M. Naghavi, A. Naheed, D. Nand, K. M. Narayan, E. L. Nelson, M. L. Neuhouser, M. I. Nisar, T. Ohkubo, S. O. Oti, A. Pedroza, D. Prabhakaran, N. Roy, U. Sampson, H. Seo, S. G. Sepanlou, K. Shibuya, R. Shiri, I. Shiue, G. M. Singh, J. A. Singh, V. Skirbekk, N. J. Stapelberg, L. Sturua, B. L. Sykes, M. Tobias, B. X. Tran, L. Trasande, H. Toyoshima, S. van de Vijver, T. J. Vasankari, J. L. Veerman, G. Velasquez-Melendez, V. V. Vlassov, S. E. Vollset, T. Vos, C. Wang, X. Wang, E. Weiderpass, A. Werdecker, J. L. Wright, Y. C. Yang, H. Yatsuya, J. Yoon, S. J. Yoon, Y. Zhao, M. Zhou, S. Zhu, A. D. Lopez, C. J. Murray, and E. Gakidou. 2014. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 384 (9945):766-781.
31. NHANES. 2000. National Health and Nutritional Examination Survey from 1988. 1994 (NHANES III) to (NHANES) 1999-2000.
32. Nordmann, A. J., A. Nordmann, M. Briel, U. Keller, W. S. Yancy, Jr., B. J. Brehm, and H. C. Bucher. 2006. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: a meta-analysis of randomized controlled trials. *Arch Intern Med* 166 (3):285-293.
33. Oberhauser, F., D. M. Schulte, M. Faust, H. Gudelhofer, M. Hahn, N. Muller, K. Neumann, W. Krone, and M. Laudes. 2012. Weight loss due to a very low calorie diet differentially affects insulin sensitivity and interleukin-6 serum levels in

nondiabetic obese human subjects. *Horm Metab Res* 44 (6):465-470.
34. Okazaki, T., E. Himeno, H. Nanri, H. Ogata, and M. Ikeda. 1999. Effects of mild aerobic exercise and a mild hypocaloric diet on plasma leptin in sedentary women. *Clin Exp Pharmacol Physiol* 26 (5-6):415-420.
35. Poyrazoglu, S., F. Bas, and F. Darendeliler. 2014. Metabolic syndrome in young people. *Curr Opin Endocrinol Diabetes Obes* 21 (1):56-63.
36. Rizk, N., M. Amin, and M. Yousef. 2011. A pilot study on metabolic syndrome and its associated features among Qatari schoolchildren. *Int J Gen Med* 4:521-525.
37. Rolland, C., M. Hession, and I. Broom. 2011. Effect of weight loss on adipokine levels in obese patients. *Diabetes Metab Syndr Obes* 4:315-323.
38. Samaha, F. F., G. D. Foster, and A. P. Makris. 2007. Low-carbohydrate diets, obesity, and metabolic risk factors for cardiovascular disease. *Curr Atheroscler Rep* 9 (6):441-447.
39. Smits, M. M., P. Woudstra, K. M. Utzschneider, J. Tong, F. Gerchman, M. Faulenbach, D. B. Carr, K. Aston-Mourney, A. Chait, R. H. Knopp, J. B. Meigs, E. J. Boyko, and S. E. Kahn. 2013. Adipocytokines as features of the metabolic syndrome determined using confirmatory factor analysis. *Ann Epidemiol* 23 (7):415-421.
40. Summer, S. S., B. J. Brehm, S. C. Benoit, and D. A. D'Alessio. 2011. Adiponectin changes in relation to the macronutrient composition of a weight-loss diet. *Obesity (Silver Spring)* 19 (11):2198-2204.
41. Trakhtenbroit, M. A., J. G. Leichman, M. F. Algahim, C. C. Miller, 3rd, F. G. Moody, T. R. Lux, and H. Taegtmeyer. 2009. Body weight, insulin resistance, and serum adipokine levels 2 years after 2 types of bariatric surgery. *Am J Med* 122 (5):435-442.
42. Van de Voorde, J., B. Pauwels, C. Boydens, and K. Decaluwe. 2013. Adipocytokines in relation to cardiovascular disease. *Metabolism* 62 (11):1513-1521.
43. Varady, K. A., L. Tussing, S. Bhutani, and C. L. Braunschweig. 2009. Degree of weight loss required to improve adipokine concentrations and decrease fat cell size in severely obese women. *Metabolism* 58 (8):1096-1101.
44. Vetter, M. L., A. Wade, L. G. Womble, C. Dalton-Bakes, T. A. Wadden, and N. Iqbal. 2010. Effect of a low-carbohydrate diet versus a low-fat, calorie-restricted diet on adipokine levels in obese, diabetic participants. *Diabetes Metab Syndr Obes* 3:357-361.
45. Volek, J. S., M. J. Sharman, A. L. Gomez, C. DiPasquale, M. Roti, A. Pumerantz, and W. J. Kraemer. 2004. Comparison of a very low-carbohydrate and low-fat diet on fasting lipids, LDL subclasses, insulin resistance, and postprandial lipemic responses in overweight women. *J Am Coll Nutr* 23 (2):177-184.
46. Westman, E. C., W. S. Yancy, Jr., J. C. Mavropoulos, M. Marquart, and J. R. McDuffie. 2008. The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus. *Nutr Metab (Lond)* 5:36.
47. Wing, R. R., M. K. Sinha, R. V. Considine, W. Lang, and J. F. Caro. 1996. Relationship between weight loss maintenance and changes in serum leptin levels. *Horm Metab Res* 28 (12):698-703.
48. Xenachis, C., E. Samojlik, M. P. Raghuwanshi, and M. A. Kirschner. 2001. Leptin, insulin and TNF-alpha in weight loss. *J Endocrinol Invest* 24 (11):865-870.
49. Yancy, W. S., Jr., M. K. Olsen, J. R. Guyton, R. P. Bakst, and E. C. Westman. 2004. A low-carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia: a randomized, controlled trial. *Ann Intern Med* 140 (10):769-777.

3/14/2015