Obesity, Metabolic Syndrome

Benefit of Low-Fat Over Low-Carbohydrate Diet on Endothelial Health in Obesity

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Abstract—Obesity is associated with impaired endothelial-dependent flow-mediated dilation, a precursor to hypertension and atherosclerosis. Although dieting generally improves cardiovascular risk factors, the direct effect of different dietary strategies on vascular endothelial function is not known. The purpose of this study was to test the hypothesis that a low-fat (LF) diet improves endothelial function compared with an isocaloric low-carbohydrate (LC) diet. Obese (n=20; body mass index: 29 to 39; mean systolic blood pressure: 107 to 125 mm Hg) and otherwise healthy volunteers were randomly assigned to either the American Heart Association modeled LF (30% fat calories) diet or an isocaloric LC Atkins' style diet (20 g of carbohydrates) for 6 weeks (4-week weight loss and 2-week maintenance phase). Brachial flow-mediated dilation and dilation to nitroglycerin were measured with ultrasound using automated edge detection technology (baseline, week 2, and week 6). Blood pressure, weight loss, and cholesterol profiles were measured throughout the study. Weight loss was similar in LF (100±4 to 96.1±4 kg; $P<0.001$) and LC (95.4±4 to 89.7±4 kg; $P<0.001$) diets. Blood pressure decreased similarly in both groups (LF: 8/5 mm Hg; LC: 12/6 mm Hg) at 6 weeks. After 6 weeks, the percentage of flow-mediated dilation improved (1.9±0.8; $P<0.05$) in the LF diet but was reduced in the LC diet ($-1.4±0.6$; $P<0.05$) versus baseline. Dilation to nitroglycerin and lipid panels was similar at 0, 2, and 6 weeks. Despite similar degrees of weight loss and changes blood pressure, LF diets improved brachial artery flow-mediated dilation over LC diets. LF diets may confer greater cardiovascular protection than LC diets. (*Hypertension*. 2008; 51:376-382.)

Key Words: diet ■ weight loss ■ endothelium ■ obesity ■ blood pressure

Obesity is a risk factor for atherosclerosis, a major cause of morbidity and mortality throughout the world. In the United States, the incidence of obesity has risen dramatically in the past decade. Public awareness of the "obesity epidemic" has resulted in various dietary weight loss strategies, and it is estimated that 45% of American women and 30% of American men diet to lose weight.[1] However, the nutrient-specific effects of these diets on cardiovascular health are largely unknown.

Mounting evidence suggests that the integrity of the vascular endothelium is critical in the prevention of atherosclerosis, likely through release of endothelial-derived factors such as NO, which confer antiproliferative, anti-inflammatory, and antithrombotic properties, in addition to vasodilation.[2,3] Abnormal endothelial function marked by reduced dilation to an increase in flow (endothelium-dependent flow-mediated dilation [FMD]) is an early hallmark of cardiovascular disease and a strong prognostic factor for future cardiovascular events.[4–9] Most risk factors for coronary artery disease are associated with reduced FMD.[10]

Weight loss through conventional low-fat (LF) diets improve endothelial function[11,12]; however, some currently popular diets emphasize low-carbohydrate (LC) intake supplemented by high dietary fat and protein. Initial reports show sustained weight loss while on LC diets without detrimental effects on serum lipid levels.[13,14] Further benefit may be derived from the reduction in arterial pressure from either LF or LC diets. However, it is unclear whether these cardiovascular benefits of weight loss on a LC diet are negated by the known detrimental effects on endothelial function of even a single high-fat meal.[15–17] Weight loss is similar on LC and LF diets, but effects on cardiovascular health, a major anticipated benefit of most weight-loss regimens, may diverge. Therefore, the purpose of this study was to test the hypothesis that LF and LC diets have divergent effects on vascular endothelial function despite similar beneficial effects on weight, blood pressure, and lipid levels. Brachial artery FMD was used to test the net effect of these multiple parameters on an index of endothelial health.

Methods

Study Design and Participants

All of the protocols were approved by the institutional review board of the Medical College of Wisconsin. Twenty subjects were enrolled.

Participants were recruited via flyers and a television advertisement (3 to 4 enrolled at one time). Respondents underwent an initial screen by telephone for inclusion and exclusion criteria. Recruited subjects were 18 to 50 years old with a body mass index (BMI) of 29 to 39 and were not dieting. Exclusion criteria included eating disorder history, cardiovascular disease history, diabetes, elevated blood pressure (systolic blood pressure [SBP]: ≥150 mm Hg; diastolic blood pressure [DBP] ≥90 mm Hg; previous diagnosis of or current treatment for hypertension), elevated serum cholesterol or triglycerides (>200 mg/dL), pregnancy or plans for pregnancy, lactation, tobacco use within 6 months, use of diet pills, excessive alcohol use, use of illicit drugs, endocrine disease history, or preference for 1 of the 2 diets. Subjects arrived at the General Clinical Research Center after a 12-hour fast to obtain vital signs, urine for ketones and pregnancy testing, and a blood sample for serum lipids, insulin, and thyroid function after informed consent. A health history questionnaire was administered. Body fat and waist and hip circumference were measured. Prospective 3-day food histories and daily physical activity records were obtained.

Random assignment was accomplished with a 1:1 treatment assignment ratio using an envelope-based randomization. Envelopes containing diet assignments were prepared by nonstudy personnel, sequentially numbered, and identically sealed. When dropouts occurred after random assignment, the assignment was returned to the envelope system.

Baseline

Three days before diet initiation, vascular ultrasound (FMD) and blood testing were performed. Resting energy expenditure was measured (12-hour fast) by indirect calorimetry using a metabolic monitor according to published methods.[18]

Follow-Up

Every other day, participants retrieved food and reported dietary adherence, urine ketone results, and physical activity changes. At weeks 2, 4, and 6, anthropometric and vascular testing were conducted after a 12-hour fast. Urine samples were collected for pregnancy testing. Blood samples were obtained for measuring lipid, insulin, and glucose levels. Nutrition and weight loss counseling were offered to each participant at the end of the trial.

Diets

The LC diet provided 20 g of carbohydrates daily, supplemented with protein and fat content according to the Atkins' diet recommendation.[19] The LF diet provided 30% of the calories as fat, modeled after an American Heart Association diet.[20] Participants in both groups were given 750 calories less than their estimated weight-maintaining caloric requirement for 4 weeks, determined by resting energy expenditure and an activity factor, as described previously.[18] A 3-day dietary record and food preference questionnaire was used to assess usual eating patterns.[21] Dietary control and compliance were maximized by providing complete preprepared meals in the General Clinical Research Center bionutrition kitchen and a daily multivitamin, all distributed for 6 weeks. Participants reported daily urinary ketone test results and dietary deviations to assess compliance. Usual physical activity patterns were encouraged and daily activity monitored with a pedometer.

Blood Pressure Measurements

Blood pressure was measured with a Dinamap automated blood pressure device and appropriate cuff size in the supine and fasting states. Measurements were made on the nondominant arm after 5 minutes in the supine state, and 2 measurements made at 3- to 4-minute intervals were averaged for the blood pressure measurement at each visit. Blood pressure measurements were made at a similar time of day for each visit.

Measurement of Flow and Nitroglycerin-Mediated Dilation

Brachial artery ultrasound was performed using an 11-MHz probe and high-resolution ultrasound as described previously (please see the data supplement available at http://hyper.ahajournals.org).[22] Ultrasound images were video recorded and digitized using commercial edge detection software (Brachial Analyzer version 4.2.2, Medical Imaging Applications). Analysis was performed by trained readers who were blinded to the participant's diet. We have reported low interobserver and intraobserver variability with this procedure.[22,23] Our calculated coefficient of variation with this procedure is 3.1%, and this is consistent with others.[24]

Laboratory Analysis

Plasma glucose concentration was measured using the glucose oxidase procedure (Beckman II autoanalyzer). Serum insulin concentrations were measured by radioimmunoassay (Linco Research). Triglycerides (Stanbio), total cholesterol, and high-density lipoprotein and direct low-density lipoprotein cholesterol (LDL-c; Roche Diagnostics) were measured with spectrophotometric assays. High sensitivity C-reactive protein was measure with an enzyme immunoassay (MP Biomedicals).

Power Analysis

For an expected difference in FMV within each dietary group, the dietary effect was estimated to be 3.3%. With an α of 0.05 and a power of 80%, it was estimated that 7 to 10 subjects were needed per group.

Statistics

All of the data are presented as means±SEs. Comparisons of FMD between diets were made using a 2-way repeated-measures ANOVA. Normal distribution was tested with the Kolmogorov-Smirnov test. Where repeated-measures ANOVA showed a statistically significant effect for FMD, t tests were performed for individual differences between 2 time points (paired) or between diets at a single time point (unpaired). A paired t test was used to compare lipid profile results between baseline and 6 weeks within each diet. A 1-way repeated-measures ANOVA was used to determine whether there was an effect of each individual diet on insulin, glucose, and blood pressure. A $P<0.05$ was considered statistically significant.

Results

Subjects and Dietary Intervention

Fifty-six healthy subjects were screened for participation, and 26 were excluded because of exclusion criteria (elevated cholesterol: n=19; hypertension: n=1; BMI >39: n=2; BMI <29: n=1; smoking: n=1; hypotension: n=1; and dieting: n=1). Two subjects could not commit to all of the scheduled study visits and were excluded before random assignment. Eight volunteers were excluded after random assignment because of a loss in follow-up (no show: n=3), voluntary withdraw (nausea: n=1; unforeseen scheduling difficulties: n=1), and investigator withdraw (unreliability in data reporting and meal pick-up: n=3). Five African Americans (2 LF and 3 LC) and 1 Asian (LC) participated in the study. All of the other participants were white.

The treatment groups were balanced for demographics and clinical characteristics (Table 1). Subjects reported consuming 2227±176 (LC) and 2448±328 (LF) kcal/d before entering the study (*P* value not significant; please see Table S1). Throughout the first 4 weeks, daily consumption averaged 1855±100 (LC) versus 1755±202 (LF; *P* value not significant) kcal/d. During the weight maintenance phase (weeks 4 to 6), energy intake increased to 2522±277 and 2484±275 kcal/d in the LC versus LF diets, respectively (Table S1). Activity patterns were similar to prestudy levels

Table 1.   Patient Demographics and Clinical Characteristics

Characteristic	LC			LF		
	Baseline	Week 2/Week 4	Week 6	Baseline	Week 2/Week 4	Week 6
BMI, kg/m^2	34.0±0.9	32.7±0.9	32.0±0.8*	33.8±1.1	32.9±1.1	32.3±1.2*
Weight, kg	95.4±4.1	91.9±4.0	89.9±3.8*	100.2±3.7	97.9±3.7	96.1±4.0*
Lean body mass, kg	54.7±3.8	NT	51.3±3.3	60.7±3.5	NT	53.85±5.2
Total cholesterol, mg/dL	157.9±4.2	NT	163±6.1	152.7±8.7	NT	145.25±8.7
LDL, mg/dL	82.4±14.2	NT	95.4±13.7	93.8±6.8	NT	84.4±9.2
HDL, mg/dL	54.6±5.3	NT	54.5±5.0	49.9±4.29	NT	44.4±4.71
Triglycerides, mg/dL	77.9±14.1	NT	57.5±4.6*	60.6±6.9	NT	69.3±10.5
SBP, mm Hg	123.3±3.1	115.4±3.3*	112.6±2.7*	124.1±4.0	114.2±2.5*	115.2±3.0*
DBP, mm Hg	70.0±3.5	64±2.8*	65.8±2.6*	73.2±3.6	66.8±2.5*	66.8±3.3*
Insulin, mg/dL	18.2±3	14.04±1.97*	12.6±1.2*	17.05±3.92	14.04±2.0	14.46±2.09
Glucose, mg/dL	91.7±1.1	90.1±2.2	96±2.2	89.65±1.9	89.85±1.97	91.2±1.6
C-reactive protein, mg/L	5.7±1.3	6.7±1.2	6.2±1.1	4.9±1.5	5.5±2.3	5.3±1.9

Data are presented as means±SEs. There was no significant difference between diets at each time point. For LC, sample size was 10 (1 male and 9 females; age (mean±SE): 33±2.3 years; for LF: sample size was 10 (4 males and 6 females); age (mean±SE): 38.0±2.6 years. Cholesterol (total, LDL, and HDL) and triglyceride values at week 6 are only for 18 subjects (10 LC and 8 LF). Insulin and glucose measurements are reported at week 4; all of the other values are week 2. LDL indicates low-density lipoprotein; HDL, high-density lipoprotein; BP, blood pressure; NT, not tested.

*Significant difference observed vs baseline ($P<0.05$).

as assessed by a pedometer. Positive ketone testing confirmed ketosis and compliance with the LC diet.

Effect of Diets on Weight Loss

Subjects in both diet groups demonstrated significant and similar reductions in weight at week 6 when compared with baseline (LF: −4.0±0.5 kg versus LC: −5.2±0.6 kg). As planned, subjects on the LC diet consumed significantly more grams of total fat, protein, dietary cholesterol, and saturated fatty acids compared with subjects on the LF diet (Table S1).

Brachial Artery Reactivity to FMD and Nitroglycerin

Brachial FMD did not change after 2 weeks on either diet; however, it improved significantly at week 6 in subjects on the LF diet (6.8±0.6% to 8.7±0.9%; 34% improvement; $P=0.043$; Figures 1 and 2). In contrast, FMD in subjects on the LC diet was reduced at 6 weeks versus baseline (8.2±0.7% to 6.8±0.6%; 14% reduction; $P=0.049$; Table 2; Figure 1). Baseline FMD was not different between the groups (Table 2). Nitroglycerin-induced dilation was similar
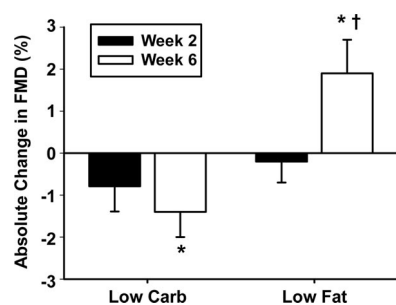

Figure 1. Mean absolute change in FMD at 2 and 6 weeks from LC and LF diets. Data are presented as means±SEs. *Significant difference from baseline in LC ($P=0.049$) and LF ($P=0.043$) diets (n=10 per group). †Significant difference in the absolute change in FMD at 6 weeks between diets ($P=0.003$).

in both diets over the course of the study (Table 2). Thus, the observed changes in FMD seem to represent alterations in endothelial, not smooth muscle, function.

Blood Pressure and Lipid Profiles

All of the subjects were normotensive at study initiation (SBP: 124±4 mm Hg; DBP: 69±3 mm Hg), but SBP and DBP decreased similarly at 2 and 6 weeks versus baseline (Table 1). By design, all of the subjects had normal cholesterol levels at baseline (Table 1), and there was no difference in total cholesterol, high-density lipoprotein cholesterol, and LDL-c within or between groups during the course of the study. Although triglycerides were similar at baseline, there was a reduction in triglycerides in LC dieters not observed in the LF group (Table 1; $P=0.02$). There was no relationship between the degree of weight loss and change in FMD in either diet (data not shown).

Insulin, Glucose, and C-Reactive Protein

Baseline fasting insulin and glucose were similar between groups. However, fasting insulin was significantly reduced at 4 and 6 weeks of dieting in LC (Table 1; $P=0.02$). There was no effect of either diet on C-reactive protein, a predictive marker of systemic inflammation (Table 1).

Discussion

We observed a reduction in brachial artery FMD after 6 weeks of weight loss on an LC, Atkins'-style diet. In contrast, FMD improved during isocaloric weight loss with an LF American Heart Association–modeled diet. There was no change in endothelium-independent dilation to nitroglycerin at any time. Both diets favorably impacted cardiovascular risk factors, including SBP, DBP, and weight, suggesting that changes in endothelial function during weight loss with dietary interventions are macronutrient dependent. Thus, the composition of diet may be as important as the degree of
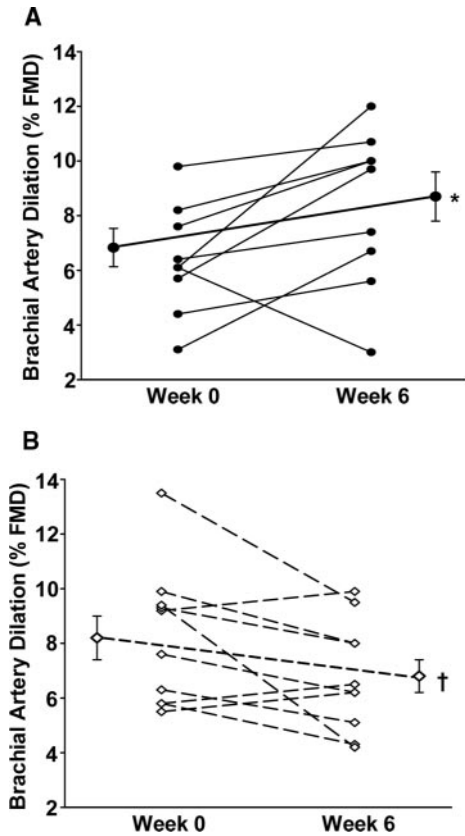
Figure 2. Individual subject %FMD at weeks 0 and 6. Solid lines represent the LF diet. Dashed lines represent the LC diet (B). Mean week 0 and 6 week FMD are represented as means±SEs in the LF (circles) and LC (triangles) diet. *Significant change in responses vs baseline LF diet. †Significant change in responses vs baseline LC diet.

weight loss in determining the effect of dietary interventions on vascular health.

Brachial artery FMD is an index of endothelium-dependent NO bioavailability and an early predictor of cardiovascular disease risk. We saw no change in the baseline or maximum diameter during hyperemia throughout the course of the study (Table 2). However, the most important comparison in this study that measured intrasubject responses over time is the percentage of change in diameter during, compared with before, diet initiation that is most reflective of NO release and endothelial responsiveness (Figure 2).

Obesity is an independent risk factor for the development of atherosclerosis. Weight loss strategies improve endothelial function in obesity and diabetes,[25,26] including weight loss from LF diets.[27] However, not all LF diets are similar. Keogh et al[28] observed that 3 weeks of reduced-fat background diet (36% fat calories), supplemented with high saturated fat (27 g/d), impaired endothelial function. Subjects on an LF, high-carbohydrate (≈93 g/d) diet demonstrated elevated triglycerides and total cholesterol with preserved FMD.[28] These subjects were not overweight, and the diets were not designed for weight loss. In our study the saturated fat content of the LC diet (75 g/d) was significantly higher than the LF diet (14 g/d; Table S1), possibly contributing to the difference in endothelial function.[29] Consistent with other studies,[14] LC dieting had no effect on total cholesterol, and triglycerides were reduced (Table 1).

One explanation for the adverse effect of an LC diet on endothelial function involves elevated dietary consumption of fat. Specifically, this diet recommends fat consumption (55% to 65%) as the primary macronutrient in place of carbohydrates (10%).[19] Whereas LC diet induces weight loss and improved body composition,[16] the endothelium may be damaged acutely by a high intake of cholesterol and fat.[15,30] The acute effects of a single high fat meal last ≥6 hours after ingestion.[17,31] Our subjects fasted for 12 hours before the study, presumably obviating the adverse acute postprandial effect of fat ingestion. In contrast, Focardi et al[32] reported an improved FMD in coronary arteries after 3 weeks of LC diet in the obese Zucker rat model of metabolic syndrome. Improved FMD was not associated with a reduction in weight in this model, and all of the animals had insulin resistance, suggesting that the vascular effects of LC may differ during diabetes.

Dietary weight loss strategies have blood pressure–lowering effects.[16] Foster et al[14] demonstrated modest reductions (1 to 2 mm Hg) in SBP in a randomized trial of LC dieting for

Table 2.   Hemodynamic Characteristics

Hemodynamic Characteristics	LC			LF			P, LC vs LF
	Baseline	Week 2	Week 6	Baseline	Week 2	Week 6	
Baseline diameter, mm	3.42±0.21	3.48±0.25	3.58±0.23	3.94±0.25	4.05±0.28	3.85±0.28	0.317
Peak diameter, mm	3.77±0.24	3.73±0.26	3.82±0.24	4.29±0.30	4.43±0.26	4.26±0.27	0.722
Maximum FMD, %	8.2±0.7	7.4±1.0	6.8±0.6*	6.8±0.7	6.3±0.7	8.7±0.9*	0.003
Baseline peak velocity, cm/s	60.8±5.9	76.43±10.1	65.7±3.2	54.0±3.0	62±3.0	53±3.7	0.278
Baseline mean velocity, cm/s	36.2±3.7	44.5±5.3	38.5±2.5	32.3±1.7	38.6±2.0	31.5±2.0	0.466
RH peak velocity, cm/s	105.2±10	133.8±11	116.9±6.3	104±7.0	109.7±7.7	115.1±7.0	0.955
RH mean velocity, cm/s	58.6±6.0	58.7±5.5	67.7±3.2	59.4±6.15	65.7±4.4	61.4±3.5	0.391
Peak change in flow velocity, %	76.0±12	86.0±13	80.0±8.0	83.8±9	70±7	101±10	0.246
Maximum NTG Dilation, %	20.9±0.02	19.8±0.03	20.6±0.02	21.30±0.023	16.20±0.02	19.30±0.02	0.305

Data are presented as means±SEs. There was no difference observed versus the other diet. *P* value represents an independent *t* test evaluating the changes between diets at 6 weeks. RH indicates reactive hyperemia; NTG, nitroglycerin.

*Significant difference observed vs baseline (*P*<0.05).

1 year. In contrast, another study showed no blood pressure effect after 6 months of LC versus LF dieting. We observed a sustained reduction in SBP and DBP at 2 and 6 weeks of dieting (Table 1). This could serve as a confounder in our assessment of brachial FMD,[33] except that the blood pressure lowering was similar in both diet groups, indicating that the differential effect on endothelial function was independent of blood pressure.

Several previous studies have evaluated the effect of weight reduction on endothelium-dependent vasodilation. Surgical and medical weight reduction showed improved FMD, regardless of the method of weight loss.[25] Endothelial function correlated strongly with fasting glucose but not other cardiovascular risk factors, such as body weight or BP. The medical weight loss program included behavioral and dietary regimens based on the National Heart, Lung, and Blood Institute guidelines for weight management ($\leq$30% of total calories from fat). Unlike other studies,[34] our study used individuals without coronary artery disease risk factors, thereby eliminating confounders in the assessment of endothelial function, making changes in FMD most likely related to the dietary intervention.

Multiple mechanisms may account for improved endothelial function during weight loss on an LF diet, including changes in inflammatory cytokines and oxidative stress.[12] Human obesity is associated with a chronic inflammatory state involving serum adipokines and cytokines produced by fat that adversely affect endothelial cell function either directly or through oxidative mechanisms.[12,35] Loss of fat mass is associated with reduced inflammation, thereby improving endothelial function.[12] In obese women, sustained dieting with weight loss reduced inflammatory cytokines (eg, tumor necrosis factor-α) to nonobese levels.[12] Whether this reduction occurs during the early stages of dieting (ie, 6 weeks) is unknown. Before dietary initiation, study subjects demonstrated FMD values that tended to be low (Figure 2) but were similar to those reported in other studies of normal subjects[36] and in studies of patients with elevated BMI.[26,37] Weight loss and waist circumference were similar between groups, arguing against fat mass as a possible confounder. The inflammation blood marker C-reactive protein levels in our subjects were at levels associated with an increased risk of developing hypertension[38] and were not altered by dietary intervention (Table 1). However, the overall inflammatory status of our population may not have been sufficient to reduce baseline FMD and may reflect the otherwise healthy status of these subjects.

Improvements in lipid profiles may also contribute to differences in endothelial function between LF and LC diets. Endothelial function improves with lowering of LDL-c in patients with hypercholesterolemia.[39] In our study, there was an $\approx$16% increase in LDL-c in LC dieters (Table 1). Patients with LDL-c levels <80 mg/dL have better FMD compared with levels of 80 to 100 mg/dL.[40] However, in our study there was no relationship between LDL-c and FMD ($r=1.03$), suggesting that the magnitude of dietary influences on LDL-c were not sufficient to account for the altered FMD in patients with relatively normal cholesterol profiles.

The LF and LC diets may contain specific antioxidants that influence endothelial cell function. For example, the LC diet contained significantly less daily folic acid (LF: 0.4 mg/d versus LC: 0.006 mg/d; with multivitamin supplementation), suggesting an antioxidant mechanism for improved FMD during an LF diet. Previous studies indicate that folic acid doses of 5 mg/d are required to improve endothelial function. Similarly, dietary supplementation with L-arginine improves NO synthase function and NO-dependent vascular function.[12] However, in our study, arginine intake was greater in the LC than LF diet (Supplemental Table S1). Thus, accounting for any effect of this amino acid would augment our observed differences in vascular function. On the other hand, it is also unlikely that the antioxidants, vitamins C and E, found in our multivitamin supplement had any impact on the observed difference in FMD, because the doses provided (60 μg and 30 IU) were well below oral dosages known to alter endothelial function.[41] Future studies are warranted to better discern the relationship among inflammatory cytokines associated with oxidative stress, antioxidant enzyme function, and endothelial function during dieting.

There are several limitations of this study. First, unlike other studies,[14,28] we eliminated risk factors to focus our analysis of dietary effects on vascular function, thereby making it difficult to generalize these findings to all of the obese patients who typically have other risk factors. Second, there was an age and gender difference between groups such that the average age and the number of men were lower in the LC than in the LF group (Table 1). These observations may explain the tendency toward a higher baseline FMD in LC versus LF subjects, because men tend to have reduced FMD responses at an earlier age than women.[42] However, in a subanalysis there was no correlation between age and FMD at baseline or the magnitude of FMD change, arguing against an effect of age on endothelial function. We recruited men and women between 18 and 50 years of age before most age-dependent declines in endothelial function have been reported.[42] Third, there were 8 and 0 dropouts in the LC and LF groups, respectively, suggesting that the LC diet is less tolerable. It is difficult to determine tolerability of LC dieting in a relatively small sample size. Fourth, our study represents a short intervention in a small number of subjects. Because we were able to control the confounding effects of disease and diet in this trial by administering every meal to each subject, the required sample size necessary to detect changes in our primary end point (FMD) was relatively small. However, a corresponding limitation of this small sample size is the inability to make conclusions regarding secondary effects of age, gender, and racial interactions on weight loss, FMD, and cardiovascular health. The long-term consequences of dieting are not known, and future investigations evaluating the long-term effects of effective weight loss strategies on endothelial function in health and disease necessitate larger trials.

Perspectives

Endothelial-dependent brachial artery FMD is reduced after 6 weeks of weight loss in obese subjects on an LC, Atkins'-like diet but is improved on an isocaloric LF diet, similar to the

one recommended by the American Heart Association. This differential effect on endothelial function transcends associated changes in weight and blood pressure. Taken together, these studies in this relatively small cohort suggest that weight loss with a traditional LF diet may be a more effective intervention to preserve vascular health than an interventional diet with LC content. Larger clinical studies are required to investigate the duration and magnitude of dietary effects on endothelial health.

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