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Lifestyle Modification with Diet and Exercise in Obese Patients with Heart Failure – A Pilot Study

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Abstract

Objective—There is a paucity of data regarding intentional weight loss in obese heart failure patients. This study sought to ascertain the safety and effectiveness of a lifestyle modification program in patients with systolic heart failure and metabolic syndrome.

Methods—Patients (n=20) with systolic heart failure (ejection fraction < 50%) and metabolic syndrome were randomized to standard medical therapy (Control) versus medical therapy and lifestyle modification (Lifestyle) and followed prospectively for 3 months. Lifestyle modification involved a walking program and reduced calorie diet with 2 meal replacement products (Slim Fast®) daily. Patients attended weekly meetings with a dietitian for 12 weeks. Endpoints were obtained at baseline and 3 months and included physical exam, laboratory values, quality of life questionnaire, 6 minute walk, and brachial ultrasound.

Results—At 3 months, 5 patients in each group had lost weight. Excluding 1 patient in each group who had increased diuretic dosing, the overall change in weight was −0.84 ± 3.82 and −0.50 ± 3.64 kg (p=0.85) in the control versus lifestyle groups respectively. No significant differences in the defined endpoints were noted. None of the patients had an adverse event that was related to weight loss or exercise.

Conclusions—This study is the first to assess the effects of a comprehensive program of dietary, behavioral, and exercise modifications in this population. Institution of lifestyle

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The authors have no conflicts of interest to disclose.

modification in patients with systolic heart failure and metabolic syndrome was well tolerated, but did not result in significant weight loss.

Keywords

Weight loss; Heart failure; Metabolic syndrome; Obesity

Introduction

The metabolic syndrome (MetS) affects approximately 68% of patients with heart failure (HF) [1]. Given the high prevalence of MetS in the HF population, its treatment may offer another method to improve the significant morbidity and mortality associated with heart failure. In the general population, treatment of the MetS involves addressing the underlying risk factors for its development, namely overweight/obesity, physical inactivity, diabetes and atherogenic diet [2]. First line therapy requires institution of lifestyle modification, specifically implementation of dietary modification and regular exercise to achieve intentional weight loss. Many different methods have been proposed to incur weight loss. In general, restriction of energy intake and increasing energy expenditure result in weight loss. A modest 5–10% weight loss improves the cardiovascular risk profile by decreasing hypertension (−9.5/5.3 mmHg) [3], dyslipidemias (−9% total cholesterol, −30% triglycerides) [4], and type 2 diabetes (58% reduction in incidence) [5].

The available data on weight loss in HF patients is controversial. Spontaneous weight loss regardless of baseline weight is not uncommon in HF, as in other chronic illnesses, and portends a poor prognosis. A retrospective analysis of the Studies of Left Ventricular Dysfunction (SOLVD) treatment study found that 36% of patients lost ≥6% or more from baseline weight during a mean follow-up of 35 months [6]. Weight loss, which is usually attributed to cardiac cachexia, is associated with reduced survival independent of age, sex, heart failure severity, and ejection fraction. The underlying etiology of cardiac cachexia may be related to a increased resting metabolic rate [7], reduction in total body fat and lean muscle mass, as well as increased levels of inflammatory cytokines and catabolic hormones [8].

However, intentional weight loss in overweight or obese HF patients may result in different consequences, or possibly benefits, than spontaneous weight loss. Intentional weight loss in obese/overweight patients with HF has not been extensively studied. Of the limited data available, a few small studies of bariatric surgery in HF patients (total n=28) have reported improvements in New York Heart Association (NYHA) functional class as well as systolic and diastolic cardiac function with weight loss [9–11]. Another study used orlistat to induce a 4.65 kg weight loss in 11 obese HF patients. This translated into an increase in 6 minute walk distance and lower total cholesterol and LDL levels [12]. Lastly, Evangelista et al. randomized 14 HF patients to a high protein, hypoenergetic diet, a standard protein, hypoenergetic diet, and a conventional diet [13]. At 12 weeks, those on the high protein diet demonstrated the greatest weight loss (−9.9 kg) as well as significant improvements in lipid profiles, functional status, glycemic control, and quality of life. Otherwise, there have been no randomized trials of purposeful weight reduction in HF patients.

The purpose of this study was to assess the feasibility, safety, and response to implementation of a lifestyle modification program to achieve intentional weight loss in patients with systolic heart failure already on maximal medical therapy.

Methods and Procedures

Study population

Twenty patients with systolic HF (met modified Framingham criteria [14] for HF in past and ejection fraction ≤50%) and the MetS (based on the National Cholesterol Education Program III definition (NCEP III) [15]) were recruited from Ben Taub General Hospital, Houston, TX between March 2005 – November 2008. All participants were either overweight (Body mass index (BMI) 25–29.9 kg/m^2) or obese (BMI ≥ 30 kg/m^2) at their baseline non-edematous weight, NYHA class II – III, and on stable doses of standard HF therapy, such as beta-blockers and ACE inhibitors. All participants underwent an exercise stress test within 6 months prior to enrollment to exclude exercise-induced ischemia and dysrhythmias. Patients were excluded if they were NYHA class IV, blood pressure > 160/100 mmHg, still undergoing active titration of cardiac medications, had an acute coronary event or revascularization with the past 3 months, pulmonary artery systolic pressure >60 mmHg, weight loss of >10 pounds in past 3 months, or had other co morbid illnesses that limited lifespan or safety of participating in the lifestyle intervention. The study was approved by the Baylor College of Medicine Institutional Review Board.

Study protocol

After patient-informed consent and baseline evaluations were completed, all participants attended a one hour educational session. This session provided basic information about HF, with emphasis on aspects of self-care, such as exercise and nutrition, especially salt and fluid restriction. Thereafter, patients were randomized to continued usual HF management (Control) or HF management plus institution of a monitored diet and exercise program (Lifestyle) for 3 months. Throughout the trial, participants continued to receive their medical care, including medical management of their heart failure, from their usual physician. No patients received a device with cardiac resynchronization therapy during the study. Overall, 35% of participants had implanted cardiac defibrillators, one with resynchronization therapy, prior to beginning the study.

Lifestyle modification group

The goal of the combined diet/exercise intervention group was to induce a modest weight loss of 7% of baseline non-edematous body weight. The lifestyle intervention was modeled on the Look AHEAD (Action for Health in Diabetes) trial's behavioral program for diabetics [16,17] and included portion-controlled diet modification, behavioral techniques, physical activity, and social support.

Portion controlled diet

The portion-controlled diet was a structured diet consisting of two meal replacement products, one portion-controlled snack, and a self-selected meal each day. The calorie goal was 1200–1500 kcal/day for those who weighed <250 pounds, or 1500–1800 kcal/day for those whose weight exceeded 250 pounds [18]. The diet was also structured to meet a goal of 30% or fewer kcal from fat of which <10% kcal are from saturated fats. The meal replacement product, a SlimFast® beverage, was provided to participants. This beverage has 180 calories and contains 200 mg of sodium. Each participant was required to record his or her dietary intake in a weekly log as a tool for behavioral counseling.

Exercise

The physical activity program consisted of unsupervised walking. Participants were encouraged to walk at a level of moderate exertion based on the Borg Dyspnea scale (levels 3–5) for 10 minutes or longer each day. Participants were provided with a pedometer and

self-reported the duration of their exercise sessions as well as total steps/day in their weekly log. Home exercise was chosen as it was feasible in our low socioeconomic population as transportation, time, and expense were all considerations for participants in this study.

Behavioral modification

The lifestyle intervention involved weekly scheduled group sessions with a dietitian for 12 weeks. At each session, the participant's vital signs and weight were recorded. The sessions emphasized adherence to the diet, guided record-keeping, and performed additional lifestyle education. Topics such as portion-control, healthy eating choices/recipe modification, understanding food labels, taste-testing high fiber and low fat foods, stretching and strengthening exercises, and safe exercise principles were reviewed. In addition, the behavior list reviewed the diet and activity logs with the participant and assisted in tailoring the program to achieve the subject's individual goals.

Three days of dietary intake was extracted from logs of lifestyle participants at baseline and at the 3 month endpoint ± 2 weeks. Dietary composition was analyzed using software from the U.S. Department of Agriculture to summarize the daily calorie (kcal), fat (g), sodium (mg), and fiber (g) intake [19].

Clinical and laboratory endpoints

The following endpoints were assessed in all participants at baseline and 3 months. Height and weight measurements were obtained using the same professional beam scale. Height was measured to nearest 0.5 cm. Patients were weighed in clothing without shoes. These height and weight measurements were used to calculate the BMI. The waist-hip ratio was assessed as a measure of central obesity. The waist circumference was measured at the mid-point between the lower rib and pelvic rim. The hip circumference was measured at the greater trochanter. Blood pressure was measured manually in the seated position with an appropriate-sized cuff. The same arm was utilized throughout the study.

Functional status was assessed using a 6-minute walk test. Vital signs were recorded before and after the exercise as well as the total distance walked and any symptoms during the test. Quality of life was assessed using the Kansas City Cardiomyopathy Questionnaire to track changes in HF symptoms, functional status, and emotional state [20].

Blood samples were obtained from participants in the morning after an overnight fast without administration of morning medications. Participants were supine in a temperature controlled room for >20 minutes prior to venipuncture. Blood was collected for analysis of lipid, glucose, insulin, and brain natriuretic peptide (BNP) levels. Samples were processed using standard automated methods with the lipid and glucose levels analyzed by spectrophotometry and the insulin and BNP, by immunoassay. Samples for adipocytokines, collagen markers, and inflammatory markers were obtained by centrifuging blood collected in EDTA tubes, extraction of plasma, and samples frozen at −80 degrees Celsius until assay processing.

Flow-mediated vasodilatation (FMD), a non-invasive measurement of endothelial function, was performed using a Sonosite Titan (Sonosite Inc.) ultrasound machine with a 10-MHz linear array transducer. The exam was performed according to the guidelines from the International Brachial Reactivity Task Force [21]. Participants were fasting, had not exercised, consumed caffeine or nicotine for 8 hours before the exam. The exam was performed in the opposite arm from venipuncture in a quiet, temperature controlled room with the patient supine. The internal diameter of the brachial artery was measured during systole in duplicate with the average of at least 5 measurements recorded. To create a stimulus for hyperemia, a blood pressure cuff was placed above the antecubital fossa and

inflated to approximately 50 mmHg above the systolic blood pressure for 5 minutes. Following cuff deflation, the maximal post-ischemic internal diameter was obtained (an average of several measurements during this period) and used to calculate the flow mediated dilatation. Approximately 10 minutes after this maneuver, a sublingual nitroglycerin tablet (0.4 mg) was administered. The maximal internal diameter of the brachial artery (an average of several measurements during this period) was recorded to assess endothelial-independent vascular function.

Statistical analysis

Data were analyzed using the STATA version 8 (College Station, TX). Continuous variables are presented as mean ± standard deviation if normally distributed or median (25^{th}, 75^{th} percentiles) if they required non-parametric assessment. Comparison analyses between the Control and Lifestyle groups or Weight Loss + and − were performed using the two-sample t-test or Wilcoxon signed-rank test depending on their baseline distribution (normal or non-parametric). Categorical variables were compared using the χ^2 test. The changes from baseline (defined as the 3 month value – baseline value) were also compared.

Results

Baseline characteristics of the 20 participants are shown in Table 1. Patients were on average 52 ± 10 years old, predominantly male (70%), and from a variety of ethnic/racial backgrounds. They had moderate to severe HF with 65% in NYHA class III, 35% with ischemic etiology, and a mean left ventricular ejection fraction of 26 ± 12%. Yet, despite this severity of HF, the median BNP was 54 pg/mL (23, 143). All participants were classified as overweight or obese with an average BMI of 39.0 ± 5.5 kg/m^2 and met 3 out of 5 of the NCEP criteria for the metabolic syndrome. The frequency of each criterion in descending order was: 95% increased waist circumference, 90% hypertension or blood pressure ≥ 130/85 mmHg, 70% elevated glucose or known diabetes, 45% low HDL, and 25% increased triglycerides. Participants were on stable, maximal medical therapy prior to enrollment. This included 90% on ACE inhibitors or angiotensin receptor blockers (ARB), 100% on beta-blockers (average carvedilol dosage: 39.2 ± 21.5 mg/daily, average metoprolol succinate dosage: 145.8 ± 68.5 mg/daily), 100% on diuretics (average furosemide dosage: 113.7 ± 68.5 mg/daily), 85% on statins, and 50% on aldosterone blockade. After randomization, the control and lifestyle groups remained similar except for a lower BMI (41.8±3.7 versus 36.3 ± 5.8 kg/m^2, p=0.02) and waist circumference (52 ± 4 versus 46 ± 7 inches, p =0.02) in the lifestyle group.

At the 3 month endpoint, 5 patients in each group had lost weight, with the lifestyle group losing slightly more weight than the controls (−1.2 ± 4.1 vs. −0.6 ± 3.7 kg, p=0.71). One patient in the lifestyle group had withdrawn from study. As detailed in Table 2, the small, non-significant change in weight translated into little change in metabolic parameters or biomarkers, except for slightly lower fasting glucose (Δ glucose 2.8 ± 19.1 mg/dL in controls, Δ −16.4 ± 63.3 mg/dL in lifestyle, p=0.37) and leptin level (Δ leptin 8.9 (−10.6, 21.4) in controls, Δ 1.7 (−28.0, 3.3) in lifestyle, p=0.19) in the lifestyle group. The only significant difference between the groups was an increase in waist circumference in the lifestyle group.

Because weight loss in HF patients may be attributed to adjustments in diuretic dosage, we analyzed the change in diuretic doses from baseline to 3 months. Two patients, one in each group, had an increase in furosemide dosage from baseline to the 3 month endpoint. The control patient had a 20 mg increase in furosemide, yet gained 2.0 kg. The lifestyle patient had an 80 mg increase in furosemide with a 7.7 kg weight loss. Excluding these two patients, the overall change in weight at 3 months was −0.84 ± 3.82 kg and −0.50 ± 3.64 kg

(p=0.85) in the control versus lifestyle groups respectively. The exclusion of these two patients did not alter the results in Table 2. There were no significant differences in the functional parameters or biomarkers between the groups.

The impact of the lifestyle intervention on dietary intake and physical activity is summarized below. Lifestyle participants attended 8 ± 2 (out of 12 possible) visits with those achieving weight loss attending 9 ± 1 visits compared to those who did not lose weight, 8 ± 2 visits (p=0.37). The weekly diet and exercise logs for the lifestyle group were analyzed. Overall, baseline dietary intake (n=8) was 2779 (927, 6066) kcal, 98 (20, 198) g of fat, 4018 (1252, 9398) mg sodium, and 56 (15, 108) g fiber. At 3 months, the median values of fat (−26.1 vs. 2.5 g) and sodium (−2430 vs. −68 mg) intake were slightly lower with better maintained fiber intake (−7 vs. −39 g) in those who lost weight versus those who did not. The kilocalorie intake was slightly less in both groups (−189 kcal with weight loss versus −95 kcal cc without weight loss, p=0.83). The median overall steps/day as recorded by pedometer was 1259 (1028, 4519) at baseline (n=9). At 3 months, those who lost weight had increased their activity by 1434 (595, 3922) steps/day versus 862 (211, 1512) steps/day in those who did not (p=0.64).

To profile those who successfully lost weight, a comparison between baseline characteristics of those who lost weight and those who did not regardless of randomization group is demonstrated in Table 3. There were no significant baseline differences between those who lost weight and those who did not. The same analysis according to randomization group did not show any significant differences. The absolute change in study endpoints at 3 months by weight loss status is demonstrated in Table 4. While there are no statistically significant differences, those who lost weight had slight reductions in TNFα receptor 1 and leptin levels and less reduction in procollagen type I N-propeptide levels compared to those who did not lose weight.

Safety

An important component of this study was to assess the safety of patients with moderate to severe systolic HF participating in a lifestyle modification program with the goal of achieving intentional weight loss. One lifestyle patient withdrew from the study after 4 weeks. He had had frequent hospital admissions for volume overload and was readmitted after beginning the study and eventually underwent left ventricular assist device placement. He had not had any change in weight at time of last visit. Another lifestyle patient had known non-revascularizable coronary artery disease and was admitted for a non-ST elevation myocardial infarction during the study. This event did not occur while exercising. He was at his baseline weight at the time of this event. He underwent cardiac catheterization, but did not receive any revascularization or change in medication. There were no cardiac events in the control group. There were no events or hospitalizations due to hypoglycemia, metabolic or lactic acidosis. None of the patients had an adverse event that was related to weight loss or exercise.

Discussion

This is the first study to assess the effects of a comprehensive lifestyle modification program with diet and exercise in obese patients with systolic HF. Achieving significant intentional weight loss proved difficult in this population.

There is great debate over the optimal BMI for HF patients. Data suggest that obesity, classified as a BMI from 30–34 kg/m^2, portends an improved survival [22]. Recent HF care guidelines suggest that intentional weight loss is not recommended in HF patients unless the BMI exceeds 40 kg/m^2 (based on expert opinion, level of evidence C) [23]. This is in part

due to several studies that have demonstrated similar energy intake between HF patients and healthy adults, but an increased energy expenditure in HF patients leading to a negative energy balance [24]. The negative energy balance is driven by the activation of catecholamines and proinflammatory cytokines that not only increase the metabolic rate of tissue, but induce an anorectic response [25]. Yet, the fact remains that ~65% of heart failure patients are overweight or obese [26–30]. This substantial prevalence brings with it concomitant comorbidities such as diabetes, hyperlipidemia, and sleep apnea, aggravates symptoms of heart failure, and limits or excludes patients from transplant candidacy. Thus, there may be a role for instituting a moderate amount of weight loss in this population. We chose to implement a lifestyle modification program as it is a non-invasive, non-pharmacologic approach to intentional weight loss.

Institution of lifestyle modification to achieve significant and sustainable weight loss is challenging in the general population, and plausibly more so in a HF population that is unable to achieve increased levels of exercise. In the general population, weight loss of >7% of baseline body weight is accepted as metabolically meaningful weight loss. This degree of weight loss has been associated with improved lipid profile and glucose control, lower blood pressure, as well as reduced inflammatory and prothrombotic factors [31]. Successful weight loss has been achieved with lifestyle modification programs that have utilized the following components: frequent interactive sessions with a registered dietitian that assisted participants with goal-setting, self-monitoring, stimulus control, and problem solving as well as provision of meal replacement products. Recent studies of such lifestyle programs in the general population have achieved ~10.7 kg weight loss with ~21% attrition [32]. Specifically, trials utilizing meal replacement products generally produce 6.19 – 6.5 kg weight loss with a 16% drop-out rate at 3 months [33]. Comparatively, the lifestyle group in this study lost only 0.50 ± 3.64 kg (after exclusion of 1 patient with increased diuretic dose) despite similar adherence to the intervention program. One possible explanation for the failure to achieve significant weight loss may be an inability to achieve adequate negative caloric balance secondary to failure to achieve a substantial increase in caloric expenditure (i.e. limited exercise tolerance) or actual non-compliance with diet despite apparent adherence with the lifestyle program. Yet, if HF is truly a negative energy state, any further tipping of the balance should result in weight loss. Another possibility is that there is a biochemical resistance to weight loss.

There is limited data regarding intentional weight loss in heart failure patients using other modalities, such as bariatric surgery or orlistat therapy. Ramani et al. [34] performed a retrospective analysis of 12 morbidly obese, HF patients who underwent bariatric surgery compared to 10 matched controls At 12 months, the bariatric surgical group had decreased BMI (from 53 to 38 kg/m^2), improved NYHA classification and increased left ventricular ejection fraction (from 21.7 to 35.0%) compared to baseline. The control group exhibited no significant change in BMI or ejection fraction and had a worsening NYHA class. The surgical group also had reduced heart failure hospitalizations compared to the controls (0.42 vs. 2.4 admissions). Twenty one obese, systolic heart HF patients were randomized to orlistat (n=11), a gastrointestinal lipase inhibitor, versus standard care. At 12 weeks, the orlistat group attained a 4.65 kg weight loss with accompanied improved lipid profile, a trend toward increased 6 minute walk distance, but no significant change in glucose, brain natriuretic peptide, or C-reactive protein levels [12]. There was one death in each group. Further research is necessary to assess various weight loss modalities and their impact on metabolic and cardiovascular outcomes in those with HF.

Other than restricting sodium to <2 g daily, there are no specific dietary HF guidelines. The U.S. Department of Health and Human Services and World Health Organization recommend sedentary adults over the age of 51 should have an estimated caloric intake of 1600 kcal for

females and 2000 kcal for males with a recommended fat intake of <65 g (or 20–37% of total calories), and fiber intake of >25 g [35,36]. The reported dietary intake in the lifestyle group suggests a wide variation in caloric intake (baseline range 640–7998 kcal/day). The sodium intake, 4018 mg (1252, 9398) and total fat intake, 98 g, (20,198) exceed the recommended amounts, but compare similarly to other studies reporting nutritional intake in HF populations [37–40]. Given the small study size and known variability in reporting dietary intake [41], it is difficult to ascertain an accurate difference in intake at 3 months. The degree of caloric reduction with lifestyle modification was not significantly different between those who lost weight versus those who did not. In general, institution of dietary changes in systolic HF patients, including use of meal replacement beverages, did not cause rapid or drastic weight loss or worsened heart failure. Despite the limitations of this data, the wide caloric intake would suggest that some participants would be in a negative energy balance, yet failed to lose weight, and were in fact obese. As well, the study by Lichtman et al. [41] demonstrated that the inaccuracies of dietary reporting are an under-reporting of dietary intake by 47%, if this is the case and then some participants' consumption greatly exceeds the recommended intake.

The safety of exercise in HF is supported by Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training (HF-ACTION), a large randomized controlled clinical trial, as well as meta-analysis data [42–44]. Benefits of regular exercise in HF include reduced hospitalization/death, improved functional capacity and quality of life, as well as attenuation of LV remodeling and improved ejection fraction [45,46]. Our study documents the extreme limitation in activity in this population with only 1259 steps/day (1028, 4519). This is far below the recommended goal of 10,000 steps/day in the general population, but consistent with published data of pedometer-determined physical activity in populations with chronic illnesses [47,48]. The lifestyle modification program was successful in increasing participants' activity with those losing weight increasing to a greater degree than those who did not (Δ1434 vs.862 steps/day). No adverse events occurred while exercising.

The study was not adequately powered to detect significant differences in biomarkers. However, the baseline levels of biomarkers in our study are consistent with those reported in the literature for heart failure populations [49–54], except BNP levels fell within normal limits despite a mean EF of 26% and leptin levels were markedly elevated (median 52.3 ng/mL (30.6, 109.4)) consistent with levels reported for obese populations [55,56]. The TNFα receptor and leptin levels were highly correlated at baseline ($r_s = 0.82$) and there was a trend for reduction in both biomarkers in those who lost weight versus those who did not. Yet, it remains unclear what the overall effects of such elevated levels of leptin are as well as its subsequent reduction with weight loss. Leptin, a hormonal product of adipose tissue and cardiomyocytes [57], has been shown to be elevated in HF, with increasing levels correlating with worsening disease (lower VO_2 max) [58]. Leptin has been reported to decrease fatty acid oxidation leading to intracellular lipid accumulation [59], suppress myocyte peak shortening rate [60], alter extracellular matrix turnover [61], stimulate sympathetic activation [62,63], and is associated with increased proinflammatory cytokines (such as TNFα) [64] each of which may be detrimental in heart failure. Yet, leptin appears to exert cardioprotective effects such as attenuation of cardiomyocyte apoptosis [65], stimulation of cardiomyocyte hypertrophy [66], and nitric oxide mediated vasodilation [67,68]. In the general population, leptin levels are correlated with BMI and decline with intentional weight loss. There is some data that suggest that elevated leptin concentrations are associated with lower resting energy expenditure and may predict failure to maintain weight loss [55]. As leptin plays a role in appetite regulation, it has been proposed that obese individuals (obesity being a hyperleptinemic state) are resistant to the effects of leptin. Complicating the situation is evidence suggesting that this resistance may be to selective functions of leptin [66]. Given the paradoxical cardiovascular effects of leptin and the leptin

resistant state of obesity, it is difficult to interpret whether the trend toward a decreased leptin level with weight loss is beneficial or not [69].

This was a small pilot study to assess the feasibility and safety of a lifestyle modification intervention in systolic HF patients. While the intervention was well tolerated, it did not result in significant intentional weight loss. Given the small amount of weight lost, participants remained obese so it is expected that this would not result in a change in functional status, metabolic or hemodynamic parameters. A larger magnitude of weight loss is likely necessary to detect these changes. Further investigation is needed to define the metabolic and nutritional requirements of HF as well as the ideal body composition and weight in this population. A better understanding of the interaction of obesity and HF on the underlying cytokine milieu is critical to understanding this process. Following this, larger scale trials of lifestyle modification or pilot studies of other novel weight management modalities should be considered.

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Abbreviations

ACE	Angiotensin Converting Enzyme
ARB	Angiotensin Receptor Blocker
BMI	Body Mass Index
BNP	Brain Natriuretic Peptide
FMD	Flow-Mediated Vasodilatation
HDL	High Density Lipoprotein
HF	Heart Failure
MetS	Metabolic Syndrome
NCEP	National Cholesterol Education Panel
NYHA	New York Heart Association
TNFα	Tumor Necrosis Factor α

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Table 1

Baseline Characteristics of Participants.

Parameter	Overall n=20	Control n=10	Lifestyle n=10	p value between Control & Lifestyle
Age, years	52 ± 10	55 ± 9	49 ± 10	0.20
Sex, % male	70%	70%	70%	1.0
Race, n, W,B,H,O	3,12,3,2	2,6,1,1	1,6,2,1	0.88
Ejection fraction, %	26 ± 12	27 ± 12	25 ± 11	0.80
Etiology, % non-ischemic, ischemic, other	50%, 35%,15%	50%, 40%,10%	50%, 30%,20%	0.37
Body mass index kg/m^2	39.0 ± 5.5	41.8 ± 3.7	36.3 ± 5.8	0.02
Metabolic Parameters				
Blood pressure, mmHg	120±16/75±13	121 ± 15/73 ± 8	119 ± 18/77 ±16	0.79/0.54
Glucose, mg/dl	115 ± 49	127 ± 52	103 ± 45	0.28
Triglycerides, mg/dl	126 ± 43	125 ± 51	127 ± 35	0.91
High density lipoprotein, mg/dl	46 ± 11	46 ± 12	45 ± 10	0.85
Waist circumference, in	49 ± 6	52 ± 4	46 ± 7	0.02
Biomarkers				
Brain natriuretic peptide pg/mL	54 (23, 143)	59 (25, 127)	54 (21, 234)	0.82 *
Procollagen Type III N-peptide, μg/L	5.4 (4.2, 6.4)	5.7 (4.2, 6.4)	4.5 (4.2, 6.0)	0.76 *
Procollagen Type I N-propeptide, μg/L	39.1 (21.2, 69.0)	63.3 (32.9, 69.0)	33.0 (21.2, 43.2)	0.31 *
Tumor necrosis factor -α, Receptor 1 pg/mL	1374 (1182, 1825)	1369 (1270, 1778)	1391 (1174, 3003)	0.89 *
Interleukin-6, pg/mL	4.8 (2.9, 10.1)	8.1 (3.97, 10.3)	3.0 (2.3, 5.4)	0.13 *
Leptin, ng/mL	52.3 (30.6, 109.4)	55.8 (44.9, 59.6)	34.8 (24.0, 154.2)	0.69 *
Functional Parameters				
6 min walk, feet	1189 ± 333	1112 ±323	1267 ± 342	0.31
Kansas City Cardiomyopathy Questionnaire, overall score	63.6 ± 21.5	60.4 ± 24.6	66.6 ±19.1	0.55
Flow mediated vasodilation %	6.1 ± 6.2	7.0 ± 5.1	5.2 ± 7.4	0.56

* non-parametric analysis, presented using median (25th, 75th percentiles)

Abbreviations: W = white, B = black, H = Hispanic, O = other

Table 2

Change at 3 months by Randomization Groups.

Parameter	Overall n=19	Control n=10	Lifestyle n=9	p value between Control & Lifestyle
Metabolic Parameters				
Weight, kg	−0.88 ± 3.8	−0.56 ± 3.7	−1.2 ± 4.1	0.71
Body mass index, kg/m^2	−0.35 ± 1.2	−0.23 ± 1.1	−0.49 ± 1.3	0.64
Blood pressure, mmHg	−3 ± 18/−2 ± 13	−4±21/−2±14	−2±15/−2±13	0.78/0.89
Glucose, mg/dl	−6.3 ± 45.4	2.8 ± 19.1	−16.4 ± 63.3	0.37
Triglycerides, mg/dl	8.6 ± 35	5.7 ± 42	11.8 ± 27	0.87*
High density lipoprotein, mg/dl	−1.5 ± 8.6	−0.5 ± 9.1	−2.7± 8.3	0.6
Waist circumference, in	0.6 ± 2.7	−0.7 ± 2.0	1.8 ± 2.8	0.05
Biomarkers				
Brain natriuretic peptide, pg/mL	−1.5 (−39, 18)	4 (−39, 18)	−5 (−28.5, 20.5)	1*
Procollagen Type III N-peptide, μg/L	−0.68 (−2.50, 1.04)	−0.85 (−2.50, 0.51)	−0.36 (−2.49, 1.47)	0.64*
Procollagen type I N-propeptide, μg/L	−4.7 (−16.9, −1.4)	−3.6 (−24.3, −1.4)	−5.4 (−14.1, 0.1)	0.91*
Tumor necrosis factor-α Receptor 1, pg/mL	76.1 (−332.1, 182.9)	131.5 (−140.0, 472.4)	72.2 (−413.9, 163.8)	0.3*
Interleukin-6, pg/mL	−0.39 (−1.85, 0.9)	−0.85 (−2.52, 1.01)	0.10 (−0.96, 0.80)	0.63*
Leptin, ng/mL	1.7 (−11.8, 12.9)	8.9 (−10.6, 21.4)	1.7 (−28.0, 3.3)	0.19*
Functional Parameters				
6 min walk, feet	124 ±333	84 ± 411	169 ± 235	0.59
Kansas City Cardiomyopathy Questionnaire, overall score	3.9 ± 14.6	1.7 ±10.0	6.1 ± 18.6	0.55
Flow mediated vasodilation, %	−0.4 ± 7.2	0.3 ± 7.9	−1.2 ± 6.9	0.73

* non-parametric analysis, presented using median (25th, 75th percentiles)

Table 3

Baseline Characteristics of Those Who Lost Weight versus Those Who Did Not (Regardless of Randomization Group).

Parameter	Weight Loss − n=9	Weight Loss + n=10	p value
Age, years	51 ±10	55 ± 9	0.39
Sex, % male	67%	70%	0.88
Race, n, W,B,H,O	1,6,2,0	2,5,1,2	0.44
Ejection fraction, %	25 ± 13	28 ± 11	0.60
Body mass index, kg/m^2	40.2±5.0	38.3±6.3	0.46
Blood pressure, mmHg	122±15/80±14	119±19/70±10	0.73/0.07
Glucose, mg/dl	117±58	115±44	0.93
Triglycerides, mg/dl	126±52	121±33	0.79
High density lipoprotein, mg/dl	47±13	44±9	0.67
Waist circumference, in	49±7	49±7	0.93
Biomarkers			
Brain natriuretic peptide, pg/mL	54 (21, 127)	49.5 (25, 92)	0.93*
Procollagen Type 3 N-peptide, μg/L	5.72 (5.21, 6.22)	4.18 (4.16, 6.44)	0.40*
Procollagen Type 1 N-propeptide, μg/L	57.1 (35.0, 69.0)	30.3 (16.0, 52.0)	0.09*
Tumor necrosis factor-α Receptor 1, pg/mL	1270.3 (1182.3, 1824.6)	1378.4 (1346.8, 1499.2)	0.83*
Interleukin-6, pg/mL	5.08 (3.55, 8.08)	3.85 (2.30, 20.59)	0.82*
Leptin, ng/mL	59.6 (34.8, 109.4)	44.9 (30.6, 55.8)	0.45*
Functional			
6 min walk, feet	1192±404	1164±288	0.86
Kansas City Cardiomyopathy Questionnaire, overall score	68.8 ± 19.5	59.2±24.6	0.37
Flow mediated vasodilatation, %	8.5±4.9	3.7 ± 6.7	0.1

* non-parametric analysis, presented using median (25th, 75th percentiles)

Abbreviations: W = white, B = black, H = Hispanic, O = other

Table 4

Absolute Change in Parameters at 3 Months by Weight Loss Status.

Parameter	Weight Loss − n=9	Weight Loss + n=10	p value
Metabolic Parameters			
Weight, kg	2.1 ± 1.8	−3.6 ± 3.1	0.0001
Body mass index, kg/m^2	0.54 ± 0.72	−1.15 ± 0.89	0.0003
Blood pressure, mmHg	−4.2 ± 13.1/−4.2± 11.8	−2.4 ± 22.3/0 ± 14.2	0.83/0.49
Glucose, mg/dl	−8.8 ± 45.4	−4.1 ± 47.8	0.83
Triglycerides, mg/dl	5.4 ± 39.3	11.4 ± 32	0.72
High density lipoprotein, mg/dl	0.33 ± 7.9	−3.2 ±9.2	0.38
Waist circumference, in	1.5 ± 2.9	−0.175 ± 2.4	0.20
Biomarkers			
Brain natriuretic peptide, pg/mL	4.5(−28.5, 16.5)	−5.5 (−39, 26)	1.0 *
Procollagen Type III N-peptide, μg/L	−0.76 (−1.86, 0.45)	−0.48 (−3.76, 1.90)	0.82 *
Procollagen Type I N-propeptide, μg/L	−14.14 (−20.68, −2.49)	−4.13 (−5.98, 4.32)	0.16 *
Tumor necrosis factor-α Receptor 1, pg/mL	139.5 (−31.97, 250.98)	−56.3 (−453.9, 180.14)	0.16 *
Interleukin-6, pg/mL	−0.26 (−2.52, 0.80)	−0.52 (−0.96, 1.01)	0.81 *
Leptin, ng/mL	10.0 (−4.9, 20.0)	−3.8 (−30.0, 5.33)	0.12 *
Functional			
6 min walk, feet	26.2 ± 276.4	212.4 ± 368.1	0.23
Kansas City Cardiomyopathy Questionnaire, overall score	5.4 ± 11.3	2.5 ± 18.0	0.69
Flow mediated vasodilatation, %	−1.9 ± 7.5	2.1 ± 6.7	0.35

* non-parametric analysis, presented using median (25th, 75th percentiles)