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Clinical Efficacy of a Medically Supervised Low-Calorie Diet Program versus a Conventional Carbohydrate-Restricted Diet

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Abstract

Objective: To determine the effectiveness of a 6 month intensive medical intervention (IMI) with caloric restriction and high-protein meal replacements versus a conventional carbohydrate-restricted (CCR) diet.

Methods: This is an observational study designed to determine weight outcomes at 6, 12, 18 and 24 months after completing the IMI or CCR treatment. Patients were also required to participate in at least 5 miles of walking and 240 minutes of overall exercise per week. The primary outcome was percent body weight loss (BWL).

Results: A total of 604 patients with obesity or overweight were studied. Sixty-seven percent were in the IMI group, versus 33% in the CCR group. Initial BMI was similar in both groups (36.4 kg/m^2 (SD=7.7) vs. 36.0 kg/m^2 (SD=7.8), p=0.608). At 6 months, the IMI group had superior body weight loss (11.9% (SD=7.4) vs. 6.0% (SD=6.1), p<0.0001). However, the IMI group had greater weight regain than the CCR group, resulting in similar weight loss at two years (7.1% (SD=10.2) vs. 8.1% (SD=6.3), p=0.735). An adjusted analysis of outcomes averaged across 2 years demonstrated 2.8% greater BWL among the IMI group. Blood pressure significantly improved in both groups (p<0.001). Males (OR=1.77, 95% CI=(1.10,2.84), p=0.019) and patients with BMI ≥ 35 kg/m^2 (OR=3.32, 95% CI=(1.95, 5.65), p<0.0001) were more likely to achieve weight loss success with the IMI.

Conclusion: An Intensive Medical Intervention (IMI) characterized by high-protein meal replacements and caloric restriction can be highly effective in reducing body weight, even at two years post-intervention. This type of intervention should be strongly considered among obese patients who do not qualify for bariatric surgery, those with contraindications to weight loss medications, or those in need of weight loss prior to a medical procedure.

Keywords: Morbid obesity; Medical weight loss; Carbohydrate-restricted diet; Weight maintenance; Low-calorie diet; Meal replacement

Introduction

Obesity is a growing public health challenge, with more than two-thirds of the adult population in the United States either overweight or obese [1]. Medical weight management with caloric restriction, supplemented with behavioral support, pharmacologic agents, and exercise, is the cornerstone of obesity treatment. Yet there is minimal scientific consensus on the optimal dietary method for losing weight and preventing weight regain [2]. Although guidelines from the American Heart Association and National Institutes of Health emphasize the importance of low-fat, high-carbohydrate diets [3], carbohydrate-restricted diets have recently garnered substantial attention in the scientific community and general public alike, and many studies have confirmed that carbohydrate restriction results in greater weight loss compared with low-fat calorie-restricted diets [1,4,5].

The therapeutic benefits of all diets, however, are limited by their efficacy, tolerability, safety, compliance, and poor third-party pay or reimbursement, among other factors [6]. A proportion of patients are unable to respond, either with inability to lose weight initially, or with significant weight regain [7]. Because medical weight loss literature is dominated by short-term, heterogeneous studies with small sample sizes, the long-term effects of these diets are often unclear [8]. Bariatric surgery has become the primary insurance-covered intervention for obesity, whereas the costs of community-based diet programs often remain a burden on the patient. These costs can be prohibitive to uninsured or under insured populations. Thus, more effective medical treatments for obesity are needed to bridge the gap between these community-based programs and bariatric surgery.

The objective of this study was to design and evaluate an intervention based on elements of the most effective weight loss programs to induce significant initial weight loss and minimize weight regain. Our observational study assesses the short and long-term outcomes of a 6 month intensive medical weight management program with caloric and carbohydrate restriction using high-protein meal replacements and behavioral therapy. Patients enrolled in a conventional carbohydrate-restricted diet served as controls. To our knowledge, no studies to date have compared similar programs. We hypothesized that our 6 month intensive medical intervention would more effectively result in short and long-term weight loss, when compared to a conventional carbohydrate-restricted diet.

Methods and Procedures

This is an observational study of 604 men and women with obesity or overweight treated at an outpatient university hospital-based program. Inclusion criteria consisted of at least one visit with our medical weight loss physician (PI) and a minimum of 3 visits with either the PI or dieticians. Patients were required to have a BMI of 23 kg/m^2 or greater, or waist circumference greater than 35 inches for women and 40 inches for men. Patients younger than eighteen years were excluded. The university's institutional review board approved this study.

Treatment arms

Patients were offered one of two weight-loss treatments programs: an intensive medical intervention, and a conventional carbohydrate-restricted diet, which served as the control group. Designation of the treatment arm was based on patient preference. There was no crossover between treatment groups during the study period. The interventions are depicted in Table 1 and described below.

Intensive medical intervention (IMI)

After an initial visit with the PI, patients were seen every two weeks for 6 months of treatment by either a physician or a registered dietician. Patients were advised to consume 1,110 calories per day, as well as 30 grams of carbohydrates from nutritional supplements. The daily dietary program consisted of three medical grade Robard New Direction System® protein supplements, a 160-calorie protein bar, and one meal consisting of 350 calories. The Robard New Direction System® protein supplements were 200 calorie, high-protein, low-carbohydrate liquid meal replacements (1 serving: 200 calories, 6 g fat, 10 g carbohydrates including, 2 g fiber and 4 g sugars, 26 g protein). Patients purchased their own supplements and 350-calorie meals, and were instructed not to consume additional calories from fat, liquids, condiments, or other sources. Patients were provided written and verbal dietary instructions at their first visit, and given access to biweekly support groups, and email and phone interaction with a physician and dieticians. Patients were also instructed to engage in regular physical activity, including at least 5 miles of walking and a minimum of 240 minutes of overall exercise per week.

Conventional carbohydrate restriction (CCR)

Patients were seen monthly by the physician for 6 months of treatment and instructed in a carbohydrate-restricted diet consisting of protein at every meal and a snack. Patients were instructed to consume no more than 60 grams of carbohydrates total during the morning and midday meals and effectively no carbohydrates with dinner, other than the negligible amount found in non-starchy vegetables. Patients were instructed to avoid foods containing more than 30% of calories from fat. Calorie goals were based on the following equation: calories=((baseline weight lbs)(8) x 1.2)-500. Patients were provided written and verbal dietary instructions at their first visit and given access to email and phone interaction with a physician and dieticians. Patients were also instructed to engage in regular physical activity, including at least 5 miles of walking and a minimum of 240 minutes of overall exercise per week.

After the 6-month treatment period, all patients who completed either the IMI or CCR plan were placed on a conventional carbohydrate restriction plan for weight maintenance. The maintenance plan for both treatment groups was equivalent to the primary weight-loss treatment for the CCR group. Although follow-up during the weight maintenance period was not mandatory for study inclusion, every effort was made to encourage subjects to attend follow-up visits at monthly intervals, including frequent phone-calls and emails; patients were not, however, provided monetary stipends or cost-free meal replacements.

During maintenance therapy, as during the primary weight-loss intervention, all patients were instructed to engage in regular physical activity, including at least 5 miles of walking and a minimum of 240 minutes of overall exercise per week. Compliance with recommended dietary and exercise guidelines was assessed during follow-up visits with a physician and dieticians.

Data collection

Data were collected from March 2012 through July 2014. At intake, a detailed medical history that included assessment of comorbidities was obtained. Anthropometric data including height, weight, and waist circumference, Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) measurements, common laboratory values, and Beck Depression Inventory score were also collected (Table 1).

	Intensive Medical Intervention (IMI)	**Conventional Carbohydrate Restriction (CCR)**
Treatment Duration	6 months	6 months
Visits	Initial visit with the PI Biweekly visits with either a physician or registered dietician	Monthly visits with a physician
Calorie Goal	1,110 Calories/day	Calories/day=((baseline weight lbs)(8) x 1.2)-500
Carbohydrate Restriction	30 g/day*¥	60 g/day
Diet Structure	Three 200-calorie medical grade protein supplements per day One 160-calorie protein bar per day One 350-calorie meal per day, consisting of 150 calories from non-starchy vegetables and 200 calories from animal, dairy, or soy protein source	Three meals and a snack daily with protein at every meal At least two meals per day containing non-starchy vegetables

Adjunctive Treatment	Biweekly support groups Email and phone interaction with physician and dieticians	Email and phone interaction with physician and dieticians
Physical Activity	At least 5 miles of walking and 240 minutes of overall exercise per week	At least 5 miles of walking and 240 minutes of overall exercise per week
Weight Maintenance Plan$^{\Phi}$	Conventional carbohydrate restriction	Conventional carbohydrate restriction
*Other than the negligible amount found in non-starchy vegetables; $^{¥}$From nutritional supplements only; $^{\Phi}$Maintenance plan initiated after 6 months of either IMI or CCR treatment		

Table 1: Description of the intensive medical intervention and conventional carbohydrate restriction treatment groups.

Weight and blood pressure measurements were obtained at 6 months for all patients who completed 6 months of treatment. Those who maintained follow-up during the weight maintenance period underwent weight and blood pressure measurements at 12, 18, and 24 months. At the end of the data collection period, information on adverse events, the total change in weight from baseline, and attrition rates were determined.

Statistical methods

Baseline categorical data (e.g. gender, race) were compared using chi-square tests. Continuous data (e.g. age, BMI) were described using means with standard deviations and were compared between groups using two-sample t-tests.

The primary outcome of percent Body Weight Loss (BWL) was compared at 6, 12, 18, and 24 months using two-sample t-tests. While easily comprehendible, these analyses may be biased towards patients with more follow-up. Therefore, an adjusted repeated measures linear regression model was also used to analyze weight loss outcomes, which accounts for the number of data points each patient contributes and the correlation within each patient, as well as baseline differences between groups. This model was used to determine if there was a difference in mean weight loss across all time points between groups. Similar analyses were performed for total weight loss, the percent of subjects with weight loss success (>10% BWL), and the percent with weight regain.

Repeated measures linear regression models were also used to evaluate for differences in blood pressure measurements within groups and between groups from baseline to 24 months. Subanalyses were performed for subsets of patients with baseline values that may be considered "at risk" (e.g. Systolic Blood Pressure (SBP) >130 mmHg at baseline).

Lastly, repeated measures multiple logistic regression models were designed to identify factors associated with weight loss success (>10% BWL) in each treatment group. All statistical analyses were performed using SAS version 9.4, with significance defined as a p-value of <0.05. In addition to p-values, the appropriate measures of substantive significance (i.e. Standard Deviation (SD) or 95% confidence intervals (CI)) have been included in the text and tables as well.

Results

604 men and women with obesity or overweight were enrolled. Baseline anthropometric and clinical data are listed in Table 2. The mean age of the study population was 48 years, and 78% were female. The mean BMI was 36.3 kg/m^2. At intake, thirteen percent of subjects had diabetes, 30% had hypertension, and 24% had dyslipidemia; comorbidities did not differ between treatment groups (p=0.981, p=0.946, p=0.620, respectively).

	Overall **N=604**	**IMI** **N=404**	**CCR** **N=200**	**p-value**
Gender, % female	78% (n=471)	75% (n=304)	84% (n=167)	0.021[1]
Age, mean years (SD)	48.0 (13.7)	49.0 (13.3)	46.2 (14.1)	0.017[2]
Race: White, % (n)	71% (n=427)	75% (n=304)	62% (n=123)	0.0015[1]
Black, % (n)	15% (n=90)	11% (n=46)	22% (n=44)	
Hispanic, % (n)	6% (n=37)	5% (n=21)	8% (n=16)	
Other, % (n)	8% (n=50)	8% (n=33)	9% (n=17)	
BMI, mean kg/m^2 (SD)	36.3 (7.7)	36.4 (7.7)	36.0 (7.8)	0.608[2]
Systolic BP, mean mmHG (SD)	121.5 (14.5)	121.7 (13.8)	121.1 (15.8)	0.626[2]
Diastolic BP, mean mmHG (SD)	78.5 (11.2)	78.3 (10.7)	78.9 (12.1)	0.557[2]

TSH, mean U/mL (SD)	2.40 (5.78)	2.5 (6.5)	1.9 (1.1)	0.167[2]
Insulin, mean µU/mL (SD)	11.9 (11.0)	12.0 (11.5)	10.9 (7.8)	0.555[2]
HbA1c, mean% (SD)	5.9 (0.7)	5.8 (0.7)	6.1 (0.9)	0.039[2]
LDL, mean mg/dL (SD)	109.5 (32.6)	110.2 (31.4)	107.1 (36.8)	0.420[2]
HDL, mean mg/dL (SD)	55.9 (16.2)	55.5 (16.4)	57.2 (15.7)	0.453[2]
BDI: Minimal depression (0-13)	74% (n=305)	76% (n=221)	71% (n=84)	0.761[3]
Mild depression (14-19)	15% (n=60)	14% (n=41)	16% (n=19)	
Mod depression (20-28)	8% (n=34)	8% (n=23)	9% (n=11)	
Severe depression (29+)	3% (n=12)	2% (n=7)	4% (n=5)	

[1]Chi-square test; [2]Two-sample t-test; [3]Wilcoxon rank sum test; BDI: Beck Depression Inventory; BMI: Body Mass Index; BP: Blood pRessure; CCR: Conventional Carbohydrate Restriction; HbA1c: Hemoglobin A1c; HDL: High-Density Lipoprotein; IMI: Intensive Medical Intervention; LDL: Low-Density Lipoprotein; SD: Standard Deviation; TSH: Thyroid Stimulating Hormone

Table 2: Profile of the study populations.

The IMI group consisted of 404 (66.9%) patients and the control group consisted of 200 (33.1%) patients. The groups were similar in initial BMI (36.4 kg/m^2 (SD=7.7) vs. 36.0 kg/m^2 (SD=7.8), p=0.608). There were, however, some baseline differences between the groups. Patients in the IMI group had a lower percentage of female patients (75% vs. 84%, p=0.021), a higher percentage of White race (75% vs. 62%, p=0.0015), and were slightly older (49.0 years (SD=13.3) vs. 46.2 years (SD=14.1), p=0.017).

Ninety-five percent of enrolled patients completed 6 months of treatment. At 12, 18, and 24 months, the percentage of eligible patients who were seen at office visits for maintenance therapy and weight measurements was 52.6%, 26.8%, and 19.6%, respectively. Follow-up did not statistically differ between treatment groups (p=0.111).

Weight loss outcomes

The mean %BWL and total weight loss were compared between groups at 6, 12, 18, and 24 months; results are listed in Table 3.

	Overall		**IMI**		**CCR**		**p-value**
%BWL	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	
6 months	10.0% (7.6)	576	11.9% (7.4)	392	6.0% (6.1)	184	<0.0001[1]
12 months	10.2% (10.1)	286	12.6% (9.7)	186	5.8% (9.2)	100	<0.0001[1]
18 months	8.5% (9.7)	99	10.5% (9.8)	53	6.2% (9.3)	46	0.028[1]
24 months	7.6% (8.7)	37	7.1% (10.2)	21	8.1% (6.3)	16	0.735[1]
WL (kg)							
6 months	10.3 (8.7)	576	12.4 (8.9)	392	5.9 (6.3)	184	<0.0001[1]
12 months	10.8 (11.5)	286	13.4 (11.7)	186	5.8 (9.3)	100	<0.0001[1]
18 months	9.1 (11.3)	99	11.5 (11.9)	53	6.4 (10.0)	46	0.024[1]
24 months	8.1 (11.2)	37	8.5 (13.5)	21	7.6 (7.5)	16	0.807[1]

[1]Two-sample t-test; BWL: Body Weight Loss; CCR: Conventional Carbohydrate Restriction; IMI: Intensive Medical Intervention; SD: Standard Deviation; WL: Weight Loss

Table 3: Mean %BWL and mean weight loss at 6, 12, 18, and 24 months.

At 6 months, the mean BWL was 11.9% (SD=7.4) in the IMI group and 6.0% (SD=6.1) in the CCR group (p<0.0001). The maximal mean %BWL in the IMI group was 12.6% (SD=9.7) and occurred at 12 months, versus 8.1% (SD=6.3) at 24 months in the CCR group. Both the mean %BWL and total weight loss were significantly greater in the IMI group at 6, 12, and 18-months, but not at 24-months. Weight loss was nearly equivalent in both groups at 24 months (IMI: 8.5 kg

(SD=13.5) vs. Control: 7.6 kg (SD=7.5), p=0.807). These results are illustrated in Figure 1.

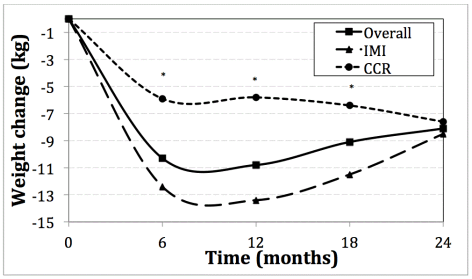

Figure 1: Mean Weight Loss at 6, 12, 18, and 24 Months. Mean weight loss was higher in the IMI group at 6, 12, and 18 months, but the difference between groups was not significant at 24 months.
*p-value < 0.05 for IMI versus CCR
IMI: Intensive Medical Intervention; CCR: Conventional Carbohydrate Restriction

Figure 1: Mean weight loss at 6, 12, 18, and 24 months. Mean weight loss was higher in the IMI group at 6, 12, and 18 months, but the difference between groups was not significant at 24 months. *p-value<0.05 for IMI versus CCR; IMI: Intensive Medical Intervention; CCR: Conventional Carbohydrate Restriction.

When analyzed across the entire study period, the IMI group had an average of 5.7% greater mean BWL (95% CI=(4.6, 6.7), p<0.0001), which translates to approximately 6.5 kg greater weight loss. After adjusting for baseline differences between groups, the difference in weight loss between the IMI group and the control group remained significant, with 2.8% greater BWL in the IMI group (95% CI=(1.7,3.9), p<0.0001), corresponding to 3.4 kg greater weight loss.

Weight loss success was defined as >10% BWL. Among the IMI group at 6, 12, 18, and 24 months, 56.9%, 51.1%, 41.2%, and 28.6% of patients achieved weight loss success. In contrast, the corresponding values for the CCR group were, 25.0%, 29.0%, 28.3%, and 37.6% at 6, 12, 18, and 24 months, respectively. Overall, patients in the IMI group were 1.79 times more likely to have weight loss success than the control group (adjusted OR=1.79, 95% CI=(1.13, 2.84), p=0.013). The greater overall weight loss success among the IMI group was primarily attributable to weight loss success at 6 months (56.9% vs. 25%, p<0.0001) and at 12 months (51.1% vs. 29.0%, p=0.0003) (Figure 2).

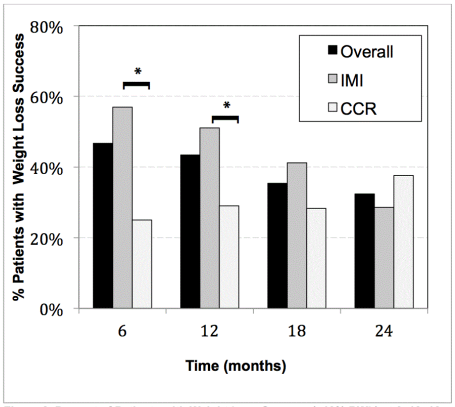

Figure 2: Percent of Patients with Weight Loss Success (>10% BWL) at 6, 12, 18, and 24 Months. The percent of patients with >10% BWL was higher in the IMI group at 6 months and 12 months, but differences between groups were not significant at 18 months or 24 months.
*p-value < 0.05 for IMI versus CCR
BWL: body weight loss; IMI: Intensive Medical Intervention; CCR: Conventional Carbohydrate Restriction

Figure 2: Percent of patients with weight loss success (>10% BWL) at 6, 12, 18, and 24 months. The percent of patients with >10% BWL was higher in the IMI group at 6 months and 12 months, but differences between groups were not significant at 18 months or 24 months. *p-value<0.05 for IMI versus CCR; BWL: Body Weight Loss; IMI: Intensive Medical Intervention; CCR: Conventional Carbohydrate Restriction.

Weight regain was measured by differences in body weight after completion of the intervention to 12, 18, and 24 months. Results are detailed in Table 4. The IMI group demonstrated greater weight regain at the 18-month time point (-3.1% (SD=6.4) vs. 0.6% (SD=5.9), p=0.007), but differences were not significant at 12 months (-0.2% (SD=4.9) vs. 0.6% (SD=4.1), p=0.162) or 24 months (-2.2% (SD=4.2) vs. -0.3% (SD=4.9), p=0.079). In an adjusted analysis, the IMI group had an average of 2.3% greater weight regain than the CCR group across the study period (95% CI=(1.1,3.4), p=0.0002).

	Overall		IMI		CCR		p-value
	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	
12 months	0.0% (4.6)	261	-0.2% (4.9)	175	0.6% (4.1)	86	0.1621
18 months	-1.4% (6.4)	85	-3.1% (6.4)	45	0.6% (5.9)	40	0.0071
24 months	-1.3% (4.6)	29	-2.2% (4.2)	15	-0.3% (4.9)	14	0.0791

[1]Two-sample t-test. *Analysis limited to subset of patients with 6-month %BWL (n=576); BWL: Body Weight Loss; CCR: Conventional Carbohydrate Restriction; IMI: Intensive Medical Intervention; SD: Standard Deviation

Table 4: Mean weight regain: Change in %BWL from 6-months to 12, 18, and 24 months*.

Blood pressure

Blood pressure values from baseline to 6, 12, 18, and 24 months were evaluated for changes within groups and between groups (Figure 3).

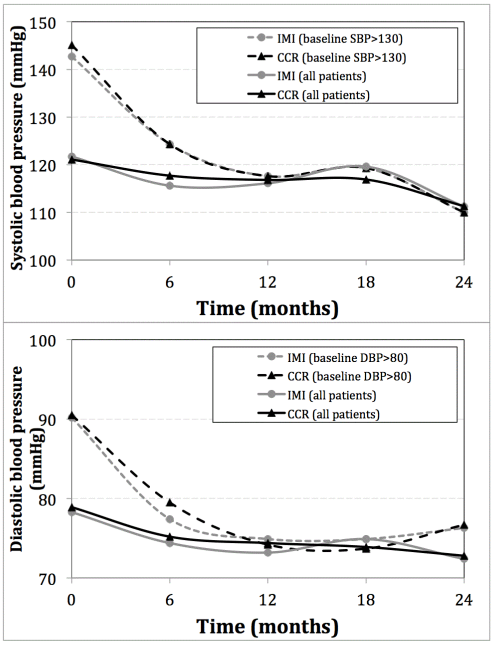

Figure 3: Change in Mean Systolic and Diastolic Blood Pressure From Baseline to 24 Months. Both SBP and DBP significantly improved from baseline to follow-up in the IMI and CCR groups. Improvements were amplified among those with SBP>130 & DBP>80 mmHg. IMI: Intensive Medical Intervention; CCR: Conventional Carbohydrate Restriction; SBP: systolic blood pressure; DBP: diastolic blood pressure

Figure 3: Change in mean systolic and diastolic blood pressure from baseline to 24 months. Both SBP and DBP significantly improved from baseline to follow-up in the IMI and CCR groups. Improvements were amplified among those with SBP>130 & DBP>80 mmHg. IMI: Intensive Medical Intervention; CCR: Conventional Carbohydrate Restriction; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure.

Both SBP and DBP significantly improved from baseline to 24 month follow-up in the IMI group (SBP: 121.7 mmHg (SD=13.8) vs. 111.2 mmHg (SD=12.4), p<0.001; DBP: 78.3 mmHg (SD=10.7) vs. 72.4 mmHg (SD=9.0), p<0.001) and CCR group (SBP: 121.1 mmHg (SD=15.8) vs. 111.3 mmHg (SD=7.2), p<0.001; DBP: 78.9 mmHg (SD=12.1) vs. 72.8 mmHg (SD=8.2), p<0.001), with no statistically significant differences between groups (p=0.493, p=0.719 respectively). The improvements for SBP and DBP were more pronounced for subjects with elevated blood pressure (e.g. SBP>130 mmHg, DBP>80 mmHg) at baseline, and these values are detailed in Table 5.

Independent predictors of successful weight loss

To evaluate factors predictive of weight loss success (>10% BWL) in the IMI and CCR groups, baseline parameters were evaluated with a repeated measures logistic model. In the IMI group, predictive factors included higher initial BMI and male gender. Results showed that patients with an initial BMI ≥ 35 kg/m^2 were 3.3 times more likely to achieve weight loss success than patients with BMI<35 kg/m^2 (OR=3.32, 95% CI=(1.95,5.65), p<0.0001). Males were 1.8 times more likely to achieve weight loss success than females (OR=1.77,95% CI=(1.10,2.84), p=0.019).

Factors predictive of weight loss success (>10% BWL) in the CCR group include higher initial systolic blood pressure and higher TSH laboratory values. Specifically, those with initial SBP of ≥140 mmHg were 4.4 times more likely to achieve weight loss success (OR=4.35, 95% CI=(1.8, 10.5), p=0.001). Additionally, those with TSH>4 U/mL were 4.1 times more likely to have >10% BWL (OR=4.10, 95% CI=(1.06, 15.76), p=0.040).

Other factors, including age, ethnicity, and presence of diabetes or hyperlipidemia, and baseline Beck Depression Inventory score were not associated with weight loss success in the either group.

Adverse events

Two patients from the IMI group (0.5%) developed symptomatic cholelithiasis requiring cholecystectomy during the study period. There were no mortalities. The rate of adverse events did not significantly differ between groups (0.5% vs. 0%, p=0.319).

		Baseline	6 months	12 months	18 months	24 months	p-value within group*	p-value between groups*
SBP, all patients								
IMI	N	396	263	136	33	17	<0.0001	0.493
	Mean (SD)	121.7 (13.8)	115.6 (11.3)	116.1 (12.2)	119.6 (12.8)	111.2 (12.4)		
CCR	N	197	172	95	44	16	0.0004	
	Mean (SD)	121.1 (15.8)	117.7 (11.4)	116.8 (11.9)	116.9 (10.8)	111.3 (7.2)		
SBP, baseline SBP>130								
IMI	N	75	49	30	7	4	<0.0001	0.158

	Mean (SD)	142.7 (8.0)	122.6 (13.2)	123.5 (12.8)	127.7 (15.3)	120.5 (14.2)		
CCR	N	37	31	20	9	4	<0.0001	
	Mean (SD)	145.1 (11.8)	124.3 (12.9)	117.6 (12.0)	119.3 (13.3)	110.0 (8.2)		
DBP, all patients								
IMI	N	396	263	136	33	17	<0.0001	0.719
	Mean (SD)	78.3 (10.7)	74.4 (8.7)	73.2 (9.4)	74.9 (7.9)	72.4 (9.0)		
CCR	N	197	172	95	44	16	<0.0001	
	Mean (SD)	78.9 (12.1)	75.2 (9.4)	74.4 (7.6)	73.9 (7.4)	72.8 (8.2)		
DPB, baseline DBP>80								
IMI	N	130	92	55	19	8	<0.0001	0.691
	Mean (SD)	90.2 (6.7)	77.4 (9.4)	74.9 (10.4)	74.9 (7.9)	76.3 (7.9)		
CCR	N	79	68	44	22	9	<0.0001	
	Mean (SD)	90.5 (7.7)	79.5 (8.2)	74.2 (7.9)	73.7 (5.8)	76.7 (7.1)		

*p-values based on linear regression modeling; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; CCR: Conventional Carbohydrate Restriction; IMI: Intensive Medical Intervention; SD: standard deviation

Table 5: Change in blood pressure values from baseline to 24 months.

Discussion

In this study, patients with obesity or overweight were placed on an intensive medical intervention or a conventional carbohydrate-restricted diet for 6 months; then, for up to two years, both patient groups were placed on a conventional carbohydrate-restricted diet thereafter. Results showed that the IMI group had superior initial body weight loss at 6 months (11.9% (SD=7.4) vs. 6% (SD=6.1), p<0.001). However, by 18 months, the IMI group had regained 3.1% of their post-intervention weight, whereas the CCR group continued to lose weight. Among those who completed 2-years of follow-up, weight loss was clinically significant in both the IMI and CCR groups, but the difference between groups was not significant (7.1% (SD=10.2) vs. 8.1% (SD=6.3), p=0.735).

The reason for similar weight loss at 2-years between the treatment groups is likely due to the 18 months of carbohydrate-restricted maintenance therapy, which was the same dietary plan for both groups. Patients who were initially on the IMI treatment and subsequently placed on CCR for maintenance therapy experienced an increase in overall caloric intake during maintenance therapy. This may be the cause of the greater weight regain in the IMI group, relative to the CCR group. Nonetheless, although the differences between the IMI and CCR groups were greatest initially and decreased over time, the differences between groups averaged across 2 years were substantial, with an adjusted 2.8% (95% CI=(1.7%,3.9%), p<0.0001) greater BWL among the IMI group.

In comparison to results from published trials on carbohydrate-restricted diets, the IMI treatment group demonstrated nearly twice the documented weight loss at 6 months (11.9% BWL (SD=7.4) vs. 6% BWL (SD=6.1), p<0.0001). As expected, the CCR arm demonstrated equivalent weight loss to similar carbohydrate-restricted dietary programs from other institutions [9,10].

When the results of our study are compared to commercially available nonmedical weight loss programs, both the IMI and CCR groups demonstrated superior weight loss results [11]. Based on the results of randomized controlled trials, participants who use nonmedical commercial weight loss programs, such as Weight Watchers and Jenny Craig, lose approximately 5% of their initial weight over 3 to 6 months, and maintain 3% BWL at 2 years [12-14]. It is important to note, however, that weight loss of this magnitude is not trivial and can be associated with reductions in obesity-related comorbidity and mortality [15].

Very low calorie diets (VLCD) provide a meaningful comparison to our study's IMI due to similarities in program structure. VLCDs involve a complete replacement of regular meals with food or formulations that provide 400-800 calories daily, which are typically used under medical supervision, and induce rapid weight loss [6]. In a study of 40 obese patients on VLCD of 800 kcal/day, participants who had meal replacements and one conventional meal per day lost 14.1% of their initial weight at 3 months and 8.4% at one year [16]. Another multicenter study evaluated 517 individuals who entered a commercially available 26-week VLCD program. Patients who completed treatment lost 21.8% of their initial weight. Of the 43% of patients who had 1-year follow-up, mean BWL was 9.0% [17].

Based on these data, some investigators argue in favor of VLCD, noting that it induces excellent initial weight loss [18]. However, weight regain is significant, with approximately 8-9% BWL at 1 year, and only 5% at 4 years [11,19]. The IMI utilized in our study induced less initial weight loss at 6 months relative to a VLCD, but superior weight loss at one year and beyond, presumably due to increased dietary compliance with the carbohydrate-restricted maintenance therapy.

It has been suggested that rapid weight loss, when achieved in conjunction with an appropriate long-term weight management

program, is successful in maintaining clinically significant weight loss over time [20]. Yet, because weight regain is a common cause of long-term failure among successfully treated patients with obesity or overweight, the choice of maintenance therapy is paramount. In this study, the choice of a carbohydrate-restricted diet as maintenance therapy was based on multiple large randomized trials demonstrating that diets moderately high in protein content improved the likelihood of weight loss maintenance [21-24]. The underlying physiology of weight loss due to carbohydrate restriction with increased protein consumption involves rebalancing the insulin-glucagon ratio in favor of lipolysis [1,6], but the long-term effectiveness of carbohydrate-restricted maintenance therapy is likely multidimensional-involving changes in thermogenesis, satiation, and sustainability, rather than a dietary shift in macronutrient composition alone.

Overall, our study demonstrated significant weight reduction at 24 months regardless of the treatment arm (IMI: 7.1%, CCR: 8.1%). However, based on our results, males and those with higher BMI achieve more weight loss under the IMI plan. Bischoff et al. also found that males fared better with their low calorie diet intervention, and speculated that males may have done better because they initially had higher BMI, and also because daily calorie restriction means more pronounced restriction for males than females [7]. Being that males have high rates of success; such intensive medical interventions may be considered as an alternative to surgical weight loss for males with higher BMI. Additionally, the IMI may be considered as a safe and effective choice for preoperative weight loss prior to bariatric surgery, or other interventions that benefit from preoperative excess weight loss, such as transplant and orthopedic surgery. The IMI may also be beneficial among patients who are resistant to induction of weight loss or unable to tolerate weight loss medications.

The significance of factors predictive of weight loss success in the CCR group, namely higher initial SBP and TSH, is less evident. An interpretation may be that patients with increased medical comorbidity may have greater motivation to lose weight and therefore succeed with a conventional carbohydrate-restricted diet.

Strengths of this study include the duration, sample size, and assessment of a novel weight management program. All body measurements were obtained by trained professionals and not through patient self-reporting. The study assessed both primary weight loss and maintenance of weight loss.

Limitations include the single center nature of the study. Patients were not prospectively randomized to treatment arms and therefore the study may be subject to more biases and confounding than a randomized controlled trial; on the other hand, it has been speculated that adherence and clinical outcomes improve when participants are able to freely select their weight-loss program, and thus randomization may underestimate the true effect of medical weight management programs [9,25,26].

Attrition rates were also significant, although the attrition rates reported in this study are similar to many other published medical weight loss studies [7,9,27], highlighting dropout and attrition as an area of much needed improvement in medical weight management. Lastly, we did not analyze our data by using a baseline-carried forward analysis because this would artificially inflate the power of our long-term data and dampen the true effect of our intervention. Certainly, a future assessment of the IMI should include randomization, improved long-term follow-up, and a full assessment of amelioration of co-morbidities with thorough laboratory assessment.

In 2013, the American Medical Association changed its classification of obesity from "a major public health problem" to a disease. One of the objectives of this change was to encourage third-party payers to increase coverage for obesity treatment. Presently, reimbursement for medical management of obesity is minimal, whereas coverage for bariatric surgery is increasing. Hopefully, as medical management continues to evolve with improved weight loss and maintenance outcomes, increases in reimbursement for medical management will follow suit.

Conclusion

This study demonstrates that an intensive medical intervention with caloric and carbohydrate restriction results in superior short-term weight loss versus carbohydrate restriction alone, but similar weight loss at two years. Short-term results of the IMI are comparable to medically supervised VLCD programs; however IMI weight loss is superior in the long term due to less weight regain when paired with a carbohydrate-restricted diet for weight maintenance. An intensive medical intervention program as described in this study is safe and effective, and may be used preferentially in patients who are resistant to induction of weight loss and in those who have contraindications to bariatric surgery or weight loss medications.

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