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ORIGINAL ARTICLE

Clinical efficacy of a medically supervised outpatient high-protein, low-calorie diet program is equivalent in prediabetic, diabetic and normoglycemic obese patients

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OBJECTIVE: Type 2 diabetes mellitus (T2DM) affects approximately 10% of Americans, while 79 million Americans are estimated to have glucose intolerance or prediabetes (pre-DM). The present study was designed to determine whether obese patients with pre-DM or T2DM would lose weight as effectively as obese normoglycemic patients, in a medically supervised high-protein, low-calorie-weight management program.

METHOD: Patients enrolled in a self-paid, university-based, outpatient weight loss program using prescribed very-low-calorie diet (VLCD) (500–800 cal per day) or LCD diet (800–1200 cal per day), recommended exercise and group behavioral counseling were studied retrospectively. Patients entering the program for the first time and attending weekly clinic visits for more than 4 weeks were included in the analysis.

RESULTS: A total of 2093 obese patients, of whom 583 patients with pre-DM (fasting glucose $\geqslant 100$ and $<126\,mg\,dl^{-1}$), 367 patients with T2DM and 1143 normoglycemic patients entered the program from 1991 to 2010, who met all the inclusion criteria were included in the analysis. The body weight at baseline was 104.0 ± 20.0 kg for DM, 101.4 ± 18.4 for pre-DM and 99.0 ± 18.8 kg for non-DM. Weight loss and percent of weight loss within 12 months were analyzed using a linear mixed-effects model. There was no significant difference in weight loss between DM vs non-DM ($P = 0.4597$) and pre-DM vs non-DM ($P = 0.6006$) in 12 months. The length of enrollment in the program was positively correlated to weight loss rates in all patients ($P < 0.001$).

CONCLUSION: This study demonstrates that obese, pre-DM and DM patients all lost weight as effectively with VLCD or LCD over 12 months. Given the impact of weight loss on the progression of comorbid conditions, these data support the hypothesis that medically supervised diets, including VLCD and LCD, should be more widely used in the prevention and treatment of obese patients with pre-DM or T2DM.

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INTRODUCTION

The most significant comorbid disease associated with the global epidemic of obesity is type 2 diabetes mellitus (T2DM). This epidemic is driven by abdominal visceral and hepatic excess fat and affects both overweight and obese patients. While obesity with a body mass index (BMI) $>30\,kg\,m^{-2}$ was recently declared a disease by the American Medical Association,[1] many individuals around the world develop diabetes at a lower body mass index.[2] In the United States, women at a BMI of $27\,kg\,m^{-2}$ have an increased risk of T2DM, and the overall risk at a BMI of $30\,kg\,m^{-2}$ is 3000% or 30-fold. Although heart disease, hypercholesterolemia, gallstones and other comorbid conditions have a four- to sixfold increased risk, T2DM is linked to obesity in an intimate way that is has been termed 'Diabesity'.

It is now established that for 2–10 years, obese patients with pre-diabetes (pre-DM) put an extra burden on pancreatic beta-cells to secrete insulin, and to maintain or attempt to maintain euglycemia in the face of insulin resistance.[3,4] Two diabetes prevention studies in patients with hyperglycemia demonstrated that even a modest but labor-intensive lifestyle intervention resulting in a 5% weight loss prevented over half of new cases of diabetes in a 5-year period in comparison with a control group.[5,6] There have been publications supporting the concept that diet and lifestyle management should be the cornerstone of the prevention and treatment of T2DM[7,8] and reduce mortality in patients with T2DM and obesity.[9] The NIH Look AHEAD trial examining the impact of weight loss on cardiovascular mortality in patients with T2DM demonstrated significant weight loss in 1 year using a combination of dietary counseling, modest exercise recommendations and meal replacements. There were three predictors of successful weight loss: (1) use of meal replacements; (2) physical activity and (3) recording dietary intake.[10] Studies including a meta-analysis of weight loss interventions in adults with T2DM showed that multidisciplinary interventions including VLCD held promise for achieving weight loss.[11–15] We have previously shown that meal replacements are safe and effective in patients with T2DM.[16]

Therapeutic weight loss in T2DM patients has been very difficult to achieve.[17,18] In practice, both primary care physicians and diabetes specialists focus on the control of hyperglycemia, while giving inadequate or no attention to weight management through changes in diet and lifestyle because of their belief that

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this is an exercise in futility.[19] As a result, obese diabetic patients are increasingly referred for bariatric surgery, an expensive option with significant side effects and the necessity of long-term medical management.[20] Recent meta-analysis reporting marked improvements in glycemic control in patients with T2DM after bariatric surgery at 1 year[21] reinforce these views.

This retrospective analysis of data from 2093 patients was designed to examine the efficacy of diet, exercise and lifestyle intervention programs in producing weight loss in obese patients with pre-DM or diabetes in comparison with normoglycemic obese patients enrolled in the same outpatient program.

PATIENTS AND METHODS

Subjects

This was a retrospective chart review of 2093 patients who participated in the weight loss program at the UCLA Risk Factor Obesity Clinic between 1991 and 2010. The study was approved by the Institutional Review Board of University of California, Los Angeles. Patients who met the following inclusion and exclusion criteria were included in the analysis. Inclusion criteria were an age of at least 18 years but <65 years, and BMI of at least 25 kg m^{-2} but <45 kg m^{-2},[22] enrolled in the program the first time and attended the weekly clinic visits at least for 4 weeks. Exclusion criteria were diagnosis of anorexia, binge eating disorder, bariatric surgery, adrenal insufficiency, myasthenia gravis, any chronic steroid use, any forms of cancer other than skin cancer and any kind of organ transplant.

The medically supervised meal replacement program

All study patients were enrolled in a medically supervised meal replacement weight management program (UCLA Risk Factor Obesity Program). The program has remained essentially the same since 1991. Participants were encouraged to attend seminars held during clinic hours including a series of weekly lectures and interactive meetings on diet, exercise and behavior modification. Dietitians and psychologists were available for consultation at each visit. Weight and vital signs were measured weekly and complete blood count and electrolytes were also recorded at baseline and at 2-week intervals. Every participant was seen on a bi-weekly basis by a physician to assess his/her success with the diet program, review laboratory tests, discuss any issues and adjust medications for any associated medical conditions and an exercise regimen, and also to participate in classes on behavior modification. Electrocardiograms were obtained at baseline and every 8 weeks and the QT interval was followed carefully. Bioelectrical impedance was measured every 8 weeks at the same time that an electrocardiogram was obtained. Target weights were estimated by bioelectrical impedance using preferred percent body fats based on age and gender, and discussed with patients.

Target calories were driven by desired rates of weight loss based on resting metabolic rate estimated using the Cunningham equation and fat-free mass (13.8 cal per day per pound fat-free mass). For the VLCD and LCD diet plans, specially prepared meal replacement products (R-Kane Inc., Pennsauken Township, NJ, USA) were used to provide between 500 and 1000 cal per day. Typical protein-rich powder formulas provided 100 cal with 15 g protein (60% protein, 40% carbohydrate), protein snack bars provided 150 cal and 10 g of protein, and soups provided 70 cal and 15 g of protein. All products were made with water or in some cases patients used sugar-free soft drinks. The protein was of high biological value including soy, casein and whey proteins. Patients were placed on combinations of five to eight servings per day of these products to reach their protein and calorie goals. In addition, after a period of time, many patients transitioned to a partial meal replacement program where four or five servings of meal replacements per day were combined with a defined meal of about 300 cal of lean protein and non-starchy vegetables. After the first 2 weeks in the program, patients were encouraged to exercise for 30 min per day and to add resistance exercise in those patients who were able to do so. Exercise was personalized based on the subject's ability, inclinations and comorbid orthopedic conditions. Exercise was delayed for the first 2 weeks in the program when diuresis owing to calorie restriction routinely occurred increasing the risk of electrolyte imbalances. Serum potassium was followed bi-weekly and complete metabolic panels including tests of liver and renal function were obtained at 4-week intervals.

Statistical analysis

Summary statistics (mean, standard deviation and frequency distribution) were generated for demographic information and baseline clinical presentation to characterize the study population. Two-sample *t*-test, Wilcoxon's test or analysis of variance was used to compare continuous variables, and χ^2-test or Fisher's exact test was used to compare categorical variables among T2DM and pre-DM and non-DM patients. Wilcoxon's signed-rank test was used to evaluate the change of metabolic parameters from baseline to 6 and 12 months. To evaluate the association between weight loss and T2DM, or pre-DM, a repeated measurement mixed-effects model was used with the linear time trend to infer the average weight loss rate in the VLCD program. The fixed effects included time, T2DM, age, initial weight, sex, hypertension, hypothyroidism, obstructive sleep apnea, depression, low back pain, total number of comorbid conditions and interactions with time. For the random effect, autoregressive correlation was used to account for correlations of outcome within the same subject.

RESULTS

Study population

There were 3483 patients enrolled in our VLCD program between 1991 and 2010. A total of 2093 patients met the inclusion and exclusion criteria and were included in the analysis. There were 583 patients with pre-DM, 367 patients with DM and 1143 without DM (Figure 1). The baseline characteristics of the patients are demonstrated in Table 1. The mean age of all patients was 45.85 ± 11.15, with BMI of 35.19 ± 4.99 kg m^{-2}. The pre-DM and DM patients were older, had higher body weight and higher percentage of male than the non-DM patients. More patients with DM had obesity-related chronic medical conditions of depression ($P<0.0001$), degenerative arthritis ($P<0.0001$), dyslipidemia ($P=0.0132$), hypertension ($P=0.001$), hypothyroidism ($P<0.0001$) and obstructive sleep apnea ($P=0.0006$).

The mean enrollment time for all patients in the clinic was 213.10 ± 122.62 days. There were no statistical differences among the three groups ($P=0.7440$) (Table 2). The longer the patients enrolled in the weight loss program, the higher the average daily weight loss (Table 5). During the 12-month period, 51.08% of total patients attended the program for 6 months and 29.05% attended for 12 months. The retention rate for all the groups at any study time point during 12 months were the same (Table 2).

Effect of meal replacement program on body weight

The average mean total weight loss for all patients was 12.0 ± 5.6 kg at 3 months, 15.6 ± 8.4 kg at 6 months, 15.8 ± 10.0 kg at 9 months and 14.4 ± 10.2 kg at 12 months. The mean percent weight loss from baseline is shown in Figure 2. The percent weight loss from baseline for all patients was $9.88 \pm 4.33\%$ at month 3,

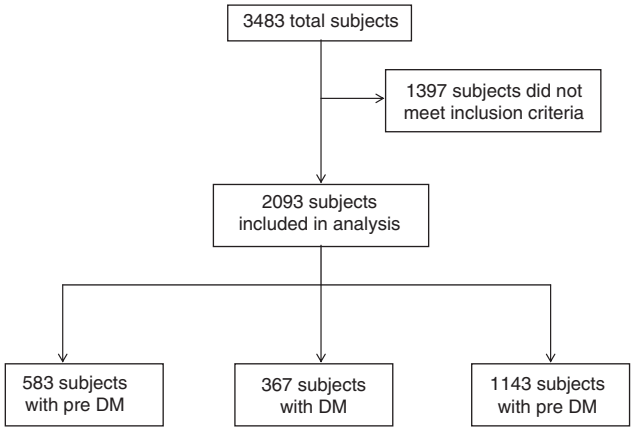

Figure 1. Scheme for study subject selection.

Table 1. Demographic characteristics for all patients

	Pre-DM (n = *583*)		*DM* (n = *367*)		*Non-DM* (n = *1143*)		*Total* (n = *2093*)		*ANOVA*
Variable (continuous)	*Mean*	*STD*	*Mean*	*STD*	*Mean*	*STD*	*Mean*	*STD*	P-*value*
Age (years)	47.30	10.48	48.38	10.01	44.30	11.59	45.85	11.15	<0.0001
Weight (kg)	101.37	18.44	104.01	20.02	99.02	18.77	100.55	18.99	<0.0001
BMI (kg m^{-2})	35.73	5.04	35.98	4.93	34.67	4.93	35.19	4.99	<0.0001
Variable (categorical)	N	*%*	N	*%*	N	*%*	N	*%*	χ^2 P-*value*
Sex									
Female	440	75.47	256	69.75	885	77.43	1581	75.54	0.0120
Male	143	24.53	111	30.25	258	22.57	512	24.46	0.0120
Depression	192	32.93	218	59.40	427	37.36	837	39.99	<0.0001
Degenerative arthritis	37	6.35	29	22.34	29	2.54	148	7.07	<0.0001
Dyslipidemia	55	9.43	50	13.62	87	7.61	192	9.18	0.0025
Hypertension	183	31.39	155	42.23	373	32.63	711	33.97	0.0010
Hypothyroidism	172	29.50	129	35.15	212	18.55	513	24.51	<0.0001
Obstructive sleep apnea	180	30.87	152	41.42	355	31.06	687	32.82	0.0006

Abbreviations: ANOVA, analysis of variance; DM, diabetes mellitus. Wilcoxon's test was performed for two-sample comparison. ANOVA was performed for multigroup comparison.

Table 2. Enrollment time and retention rate

	Pre-DM (n = *583*)		*DM* (n = *367*)		*Non-DM* (n = *1143*)		*Total* (n = *2093*)		*ANOVA*
Variable (continuous)	*Mean*	*STD*	*Mean*	*STD*	*Mean*	*STD*	*Mean*	*STD*	P-*value*
Enrollment time (day)	213.30	121.63	208.74	124.50	214.39	122.59	213.10	122.62	0.7440
Retention rate	N	*%*	N	*%*	N	*%*	N	*%*	χ^2 P-*value*
Month 1	574	98.46	359	97.82	1115	97.55	2048	97.85	0.4705
Month 2	507	86.96	313	85.29	981	85.83	1801	86.05	0.7292
Month 3	446	76.50	276	75.20	862	75.42	1584	75.68	0.8599
Month 6	291	49.91	175	47.68	603	52.76	1069	51.08	0.1925
Month 9	218	37.39	120	32.70	436	38.15	774	36.98	0.1656
Month 12	162	27.79	109	29.70	337	29.48	608	29.05	0.7295

Abbreviations: ANOVA, analysis of variance; DM, diabetes mellitus. ANOVA was performed for multigroup comparison.

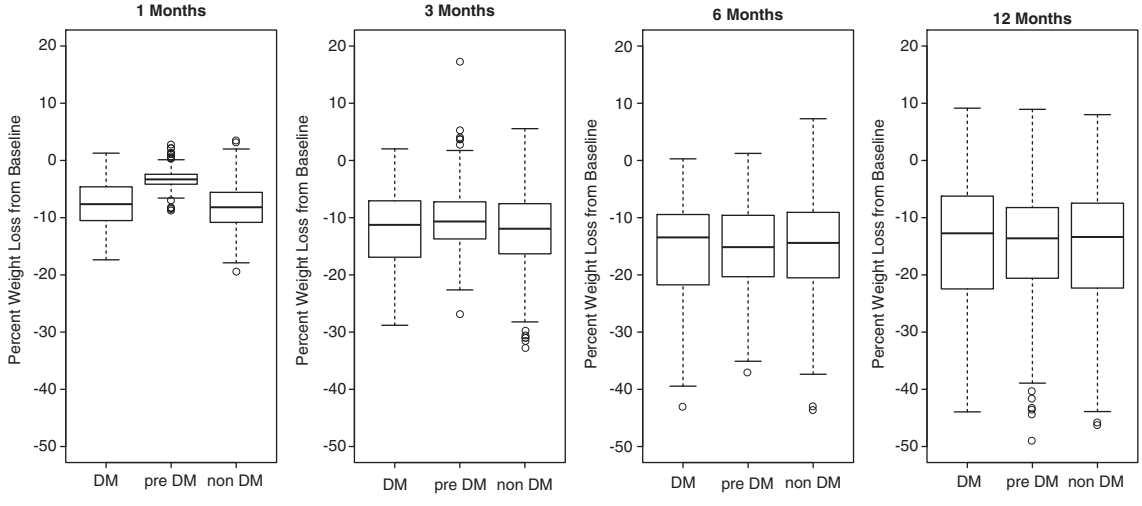

Figure 2. The boxplot for the percentage of weight loss from baseline.

15.35 ± 8.18% at month 6, 15.08 ± 10.23% at month 9 and 13.77 ± 10.38% at month 12. These percent weight losses were not different in the pre-DM, T2DM or normoglycemic patients. Using mixed-model regression analysis, weight loss rates were not statistically different among the patients with pre-DM, DM and normoglycemia.

Effect of meal replacement program on body composition

Body composition was measured by bioimpedance analysis every 8 weeks at the same time that an electrocardiogram was obtained. The average mean body fat percent at baseline was 40.86 ± 5.51 for pre-DM, 40.29 ± 5.77 for DM and 39.23 ± 5.60 for non-DM patients. The pre-DM and DM patients had statistically higher fat percentage than non-DM patients ($P < 0.0001$ pre-DM vs non-DM, $P < 0.01$ for DM vs non-DM) because of a lower fat-free mass. However, there was no significant difference in the reduction in percent fat among the above three groups of patients at any time point studied over the 12 months of participation in the program (see Table 3).

Age, gender and comorbidities on weight loss

In the analysis including all patients, aged 18–65 years, age was not a significant factor in weight loss rate ($P = 0.8138$). However, female gender did affect rates of weight as being female was associated with 8.99 ± 1.75 g greater average daily weight loss ($P < 0.0001$) (Table 4). Neither pre-DM nor T2DM was associated with differences in rates of weight loss. Patients with hypertension, hypothyroidism and obstructive sleep apnea had significantly less weight loss over time (Table 4). Dyslipidemia and degenerative arthritis were associated with more weight loss (5.14 ± 2.19 g, $P = 0.0192$ for dyslipidemia; 10.07 ± 3.53 g, $P = 0.0043$ for degenerative arthritis), while depression had no impact on average daily weight loss rates (Table 4).

Changes in weight-related comorbidities

The patients with DM had higher systolic blood pressure at baseline (DM patients 125.01 ± 22.56 mmHg vs non-DM patients 120.25 ± 11.35 mmHg, $P < 0.001$, vs pre-DM patients 122.77 ± 15.22 mmHg, $P < 0.0001$). There was significant reduction of systolic blood pressure at month 6 but not at month 12 for patients in all three groups. The diastolic blood pressure was significantly lowered for all patients at months 6 and 12 (Table 5).

The blood glucose level for DM patients at baseline was 118.60 ± 51.82 mg dl^{-1}, with a statistically significant average decrease of 8.39 ± 29.77 mg dl^{-1} ($P < 0.0001$) at month 6 and 6.29 ± 26.73 mg dl^{-1} ($P < 0.05$) at month 12. The blood glucose level at baseline for pre-DM patients decreased significantly at month 6 by 3.20 ± 10.68 mg dl^{-1} ($P < 0.0001$) and at month 12 by 2.21 ± 17.36 mg dl^{-1} ($P < 0.05$). The blood glucose level for non-DM patients increased at month 6 (1.61 ± 14.21 mg dl^{-1}, $P < 0.05$) and no change at month 12. Compared with patients without DM, the patients with DM and pre-DM had significantly more blood glucose reduction at months 6 and 12 ($P < 0.000$ at month 6, $P < 0.05$ at month 12). In the mixed-effect model analysis the weight change was significantly associated with a change in blood glucose ($P < 0.0001$) and there was no difference for the association between DM and pre-DM patients.

The baseline total cholesterol was comparable in all patients. The triglyceride level for DM patients was significantly decreased at month 6 by 37.55 ± 76.13 mg dl^{-1} ($P < 0.001$) but not at month 12, while pre-DM and non-DM patients had significant reduction at both months 6 and 12. The high-density lipoprotein-cholesterol level for patients in all three groups was significantly increased in association with weight loss, but without any significant difference among groups. There was a significant decrease of low-density lipoprotein at month 6 only for DM and non-DM patients at months 6 and 12 but no change for pre-DM patients (Table 5).

DISCUSSION

Weight loss is often one of the first recommendations made to patients who have a new diagnosis of T2DM. However, therapeutic weight loss in T2DM patients has been very difficult to achieve and patients with T2DM have less success with maintaining their weight loss.[19] Many of the medications traditionally used to control blood glucose in diabetics, including insulin, thiazolidinediones and sulfonylureas,[22–24] can result in increased body fat over time. Among the above interventions, insulin is the one associated with the greatest amount of weight gain when used as monotherapy. Two of the largest studies to demonstrate this include the Diabetes Control and Complications Trial (DCCT) and United Kingdom Prospective Diabetes Study (UKPDS).[25,26] In the former study involving patients with T1DM, the intensive insulin group had an average weight gain of 4.6 kg more than those on conventional therapy.[26] The latter study in T2DM also demonstrated a mean weight gain of 4 kg in the intensive group as compared with a diet-controlled

Table 4. Effects of age, sex, enrollment time and comorbid conditions on weight loss rate (kg per week)

Effect	*Estimate*	*STD*	P-*value*
Age (years)	0.000015	0.000062	0.8138
Sex (M vs F)	−0.00899	0.001754	<0.0001
DM vs non-DM	0.002205	0.002229	0.3226
Pre-DM vs non-DM	−0.00032	0.001803	0.86
Depression	0.001719	0.001656	0.2992
Degenerative arthritis	−0.01007	0.00353	0.0043
Dyslipidemia	−0.00514	0.002193	0.0192
Hypertension	0.0036	0.001322	0.0065
Hypothyroidism	0.004181	0.001525	0.0061
Obstructive sleep apnea	0.002851	0.0014	0.0418

Abbreviations: DM, diabetes mellitus; F, female; M, male.

Table 3. Change of body composition

		Overall			*Pre-DM group*			*DM group*			*Non-DM group*			P-*values*		
		N	*Mean*	*STD*	N	*Mean*	*STD*	N	*Mean*	*STD*	N	*Mean*	*STD*	*DM vs non-DM*	*Pre-DM vs non-DM*	*DM vs DM*
Baseline fat%		1770	39.94	5.65	547	40.86	5.51	343	40.29	5.77	880	39.23	5.60	0.0045	<0.0001	0.1149
Fat% loss (month)	3	1432	2.52	3.99	446	2.74	4.07	276	2.27	3.82	710	2.48	4.01	0.3278	0.6352	0.3278
	6	729	5.05	5.25	219	5.31	5.10	136	4.92	4.98	374	4.94	5.43	0.7509	0.2977	0.7509
	9	452	5.11	5.70	136	5.75	5.95	84	5.25	5.80	232	4.68	5.50	0.5972	0.0805	0.5972
	12	320	4.70	5.95	97	5.67	6.17	71	3.50	5.58	152	4.64	5.89	0.1089	0.4202	0.1089

Abbreviations: ANOVA, analysis of variance; DM, diabetes mellitus. Wilcoxon's test was performed for two-sample comparison. ANOVA was performed for multigroup comparison.

Table 5. Change of metabolic parameters

Variables	*Pre-DM group*			*DM group*			*Non-DM group*			P-*value*		
	N	*Mean*	*STD*	N	*Mean*	*STD*	N	*Mean*	*STD*	*DM vs non-DM*	*Pre-Dm vs non-DM*	*DM vs pre-DM*
Systolic (mm Hg)												
Baseline	583	122.77	15.22	367	125.01	22.56	1137	120.25	11.35	<0.0001	0	0
Change at month 6	266	−5.15†	19.23	156	−2.78*	13.13	536	−3.05†	10.81	0.74	0.13	0.22
Change at month 12	143	−2.27	13.94	93	−0.12	12.82	294	−0.92	11.64	0.7	0.42	0.34
Diastolic (mm Hg)												
Baseline	583	78.09	9.96	367	78.53	12.95	1137	77.68	15.64	0.01	0.02	0.43
Change at month 6	266	−2.58†	23.3	156	−1.76$^{\#}$	7.38	536	−3.84†	18.95	0.08	0.62	0.06
Change at month 12	143	−1.99$^{\#}$	8.27	93	−3.75*	22.76	294	−3.02†	21.97	0.95	0.47	0.55
Glucose (mg dl^{-1})												
Baseline	583	101.93	9.4	366	118.6	51.82	1091	91.58	10.73	<0.0001	<0.0001	0.81
Change at month 6	236	−3.20†	10.68	149	−8.39†	29.77	451	1.61*	14.21	<0.0001	<0.0001	0.15
Change at month 12	106	−2.21*	17.36	82	−6.29*	26.73	197	0.81	12.44	0.01	0	0.93
Uric acid (mg dl^{-1})												
Baseline	583	5.55	1.56	366	5.35	1.41	1091	5.31	1.69	0.25	0	0.08
Change at month 6	236	−0.84†	1.14	149	−0.85†	1.07	451	−0.79†	1.03	0.44	0.34	0.89
Change at month 12	106	−0.78†	1.12	82	−0.62†	1.07	197	−0.71†	1.6	0.84	0.11	0.22
Cholesterol (mg dl^{-1})												
Baseline	582	210.28	40.4	358	207.41	41.7	937	209.74	38.14	0.31	0.95	0.39
Change at month 6	128	−6.46	36.05	73	−3.13$^{\#}$	31.87	208	−1.04†	31.19	0.52	0.13	0.12
Change at month 12	64	−4.56	37.89	34	−1.51	45.37	85	−6.19*	26.3	0.91	0.63	1
Triglycerides (mg dl^{-1})												
Baseline	582	142.24	92.2	358	163.9	120.17	936	132.4	86.09	<o.0001	0	0
Change at month 6	128	−5.53†	76.48	73	−7.55†	76.13	208	−9.77†	79.97	0.19	0.15	0.9
Change at month 12	64	−3.35$^{\#}$	79.64	34	−7.75	113.73	85	−3.48†	72.48	0.63	0.22	0.62
HDL (mg dl^{-1})												
Baseline	582	60.19	27.84	357	59.16	16.08	935	61.4	15.61	0.01	0	0.99
Change at month 6	128	2.97$^{\#}$	9.12	73	3.00*	11.38	208	2.57†	10.16	0.28	0.52	0.62
Change at month 12	64	5.62$^{\#}$	12.74	34	4.35*	9.88	85	4.16†	11.66	0.87	0.62	0.75
LDL (mg dl^{-1})												
Baseline	582	121.64	40.39	357	115.55	36.8	935	122.02	32.78	0	0.89	0.01
Change at month 6	128	−2.32	30.71	73	−8.62	31.07	208	−7.66†	27.07	0.59	0.09	0.08
Change at month 12	64	−3.51	33.47	34	−4.32	43.82	85	−7.66$^{\#}$	22	0.72	0.63	0.58

Abbreviations: DM, diabetes mellitus; HDL, high-density lipoprotein; LDL, low-density lipoprotein. Wilcoxon's test was performed for two-sample comparison. Wilcoxon's rank-sum test for changes at months 6 and 12. Comparison with baseline value. *$P<0.05$, $^{\#}P<0.001$ and $^{\dagger}P<0.0001$.

treatment of DM. Insulin sensitizers such as thiazolidinediones and insulin secretagogues such as sulfonylureas also produce weight gain as monotherapy, but not to the same extent as that found with insulin.[22,27,28]

The effort to drive hemoglobin A1c down to prevent complications can reduce the effectiveness of weight management interventions. There is most likely no one specific reason why weight gain is an associated side effect of these hypoglycemic medications. Current proposed mechanisms include: (1) reduction of glycosuria resulting in retention of calories; (2) anabolic effects of insulin; (3) increased appetite; (4) decreased leptin production; and (5) fluid retention.[19] Of these, increased appetite and reduction of glycosuria appear to have the greatest effect on weight gain. A reduction in basal metabolic rate has also been examined to explain weight gain with glycemic control. However, several studies investigating basal metabolic rate before and after therapy with insulin, thiazolidinediones or sulfonylurea have not been able to confirm a reduced basal metabolic rate as the cause for weight gain.[29–31]

Several studies reported significantly less weight loss in T2DM than in non-DM patients.[32–34] Our study has tested the hypothesis that diabetes or pre-DM would lose weight less effectively than non-diabetic obese patients. It should be noted that all three groups have insulin resistance, while only the pre-DM and DM groups have abnormalities of insulin secretion. In a study explicitly designed to compare the weight loss of T2DM and non-DM with age- and weight-matched patients, Guare *et al.*[35] found that obese T2DM patients can lose as much weight as controls during a 16-week behavioral weight loss program, but had difficulty maintaining their lost weight. In a more recent study, Baker *et al.*[36] found near-identical weight change between DM vs non-DM patients in a 24-week VLCD weight loss clinical trial (diabetes: 8.5 ± 1.3 kg vs control: 9.4 ± 1.2 kg, $P = 0.64$). In the current study, we have examined the weight loss of a large number of pre-DM, DM and non-DM patients in a real-world outpatient program and found VLCD to be clinically effective in inducing weight loss in patients with pre-DM and T2DM as in obese patients without diabetes.

Owing to the widely held perception that diets cannot produce and maintain adequate weight loss for pre-DM and DM patients, there has been increased interest in recommending bariatric surgery as the only practical weight loss modality for patients with

T2DM. Our data demonstrate that pre-DM and DM patients can lose about 15% of initial body weight at 6 months and patients remaining in the program for 12 months maintained a 14% weight loss. One of the reasons that bariatric surgery has been preferred is that dietary adherence is viewed as uniformly poor. However, over 50% of the patients enrolled for 6 months and 30% of patients enrolled for 12 months were adherent in our medically supervised program. The diet program was well tolerated without metabolic complications or serious adverse events, and is an alternative to bariatric surgery for a significant subset of patients with obesity and hyperglycemia or T2DM.

Although VLCD has previously been shown to result in weight loss in patients with and without T2DM[14,37] and to induce rapid improvements in glycemia and dyslipidemia in patients with type 2 diabetes,[15,34] our study demonstrated beneficial changes in blood pressure, blood glucose and lipids. Most of our patients were taking medications for their T2DM and for comorbid medical conditions, and our practice protocols call for real-time adjustment of all the medications, especially hypoglycemic agents. The change of medications was not captured in the electronic data entry and we may have underestimated the effects of weight loss on glucose control as a result. Similarly, patients on statin drugs for hypercholesterolemia also discontinued their use of drugs when low-density lipoprotein-cholesterol levels declined below the optimal levels suggested by their doctors.

The limitations of the study include: retrospective study design; pre-DM and DM were defined by fasting blood glucose values instead of oral glucose tolerance test and hemoglobin A1c; lack of information on changes of medications over time.

Our results indicating successful weight loss can be achieved in patients with DM, but the approach to weight loss in obese diabetic patients will need to be more aggressive and comprehensive. A successful program requires more than educational sessions with dietitians and a manual of instruction on weight loss.[17,18] A comprehensive program with multidisciplinary team members engaged with patients on a regular basis can help a significant subset of obese T2DM patients to achieve a metabolically meaningful weight loss. Comparative effectiveness research initiatives to assess and identify those obese patients with pre-DM or DM who do not require bariatric surgery are needed.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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