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Weight Loss after Bariatric Surgery in Morbidly Obese Adolescents with *MC4R* mutations

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Abstract

Objective—To determine the frequency of Melanocortin4 Receptor (*MC4R)* mutations in morbidly obese adolescents undergoing bariatric surgery and compare weight loss outcomes in patients with and without mutations.

Design and Methods—In this prospective cohort study, 135 adolescent patients evaluated for bariatric surgery were screened for *MC4R* mutations; 56 had 12 month postoperative data available for analysis.

Results—*MC4R* mutations were detected in five of the 135 patients (3.7%); four underwent restrictive bariatric surgery. For the three patients with gastric banding, percent excess weight loss (%EWL) postoperatively was 36.0% at 5 years in one, 47% at 4 years in the second, and 85% at 1 year in the third. For the patient with gastric sleeve resection, %EWL of 96% was attained at 1 year postoperatively. The four *MC4R* cases had a higher, although non-significant, %EWL compared to 52 non-matched controls at 12 months postoperatively (48.6% vs. 23.4%; $p<0.37$). When matched by age, sex, and race to 14 controls, there was no significant difference in %EWL ($p < 0.31$), BMI change ($p< 0.27$), or absolute weight loss ($p <0.20$).

Conclusion—The frequency of *MC4R* mutations is similar to prior studies, with affected patients showing beneficial weight loss outcomes.

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Keywords

MC4R; Obesity; Adolescents; Bariatric surgery

Introduction

Over the past thirty years, the prevalence of adolescent obesity has more than tripled, with 4% now considered morbidly obese (BMI>99th percentile). (1, 2) Bariatric surgery is widely used in the morbidly obese adult population. Increasing evidence in the adolescent literature suggests that bariatric surgery may be the most effective treatment for weight loss in this population as well. (2, 3, 4, 5) It has been estimated that between 1000 and several thousand adolescents undergo bariatric procedures each year.(6, 7) A recent meta-analysis found that in adolescents, roux-en-Y gastric bypass (RYGB) and laparoscopic adjustable gastric banding (LAGB) procedures were associated with permanent weight loss and resolution of concomitant metabolic conditions, including diabetes and hypertension.(7) Vertical sleeve gastrectomy (VSG), originally performed as the first step in a staged weight loss procedure for severely obese adults, has also shown successful short-term weight loss in adolescence though long-term outcome data is lacking. (1, 8, 9, 10)

LAGB with the Lap-Band (Lap-Band System; Allergan Corp, Santa Barbara, CA) is a reversible surgical procedure in which food entry into the stomach is limited by placement of an adjustable belt-like band around the proximal portion. The band is connected to a subcutaneous port accessed percutaneously to adjust the inner diameter and the degree of gastric restriction.(1, 8) Sleeve gastrectomy is an irreversible procedure removing 75–80% of the stomach leaving a smaller, tubular stomach in its place. (7) Both of these restrictive surgeries produce weight loss by limiting food intake and causing early satiety, as opposed to combined restrictive and malabsorptive procedures, such as RYGB, which restrict intake but also limit intestinal contact with digested nutrients.

Genetic factors are estimated to account for 40% to 70% of the obesity predisposition of an individual. (11)The melanocortin 4 receptor (MC4R) is a seven transmembrane G protein coupled receptor expressed in the neurons of the paraventricular nucleus of the hypothalamus.(12) Proopiomelanocortin (POMC) is a key step in the anorexigenic signaling cascade of leptin with POMC derived peptides α-MSH and β-MSH binding the MC4R in the hypothalamus. Receptor activation by melanocortins causes a decrease in appetite and an increase of energy expenditure, both leading to weight loss.(13, 14)*MC4R* mutations, the most common monogenic form of obesity, account for between 2.5% and 5.8% of morbid obesity in pediatric and adult populations. (15, 16, 17)

Several mutations in *MC4R* have been characterized in humans. These mutations range from missense and nonsense to frame shift mutations (leading to both reduced and total loss of function) and are inherited in an autosomal dominant manner. Data on the effects of bariatric surgery in patients with monogenic obesity are limited. There are no studies that document the prevalence of *MC4R* mutations in adolescent patients undergoing bariatric surgery, nor are there any studies addressing long-term weight loss outcomes in adolescents with *MC4R* mutations post bariatric surgery. In this study, we describe five morbidly obese adolescent

patients with heterozygous *MC4R* mutations who underwent restrictive bariatric surgery at our institution and compare their postoperative weight loss outcomes with those of control patients without mutations. We hypothesized that *MC4R* mutations would decrease the effectiveness of restrictive bariatric surgery with less weight loss in affected patients.

Methods and Procedures

Patients

Subjects were recruited from the weight management program at Columbia University Medical Center (CUMC) or referred by private pediatricians to the Center for Adolescent Bariatric Surgery (CABS) for restrictive bariatric surgery evaluation. Eligible subjects were adolescents 14–18 years of age who had BMI >40 kg/m^2 or >35 kg/m^2 and at least one co-morbidity. The BMI guidelines used were consistent with NIH criteria for bariatric surgery in adults. (18) Patients were required 1) to be Tanner stage 4 or greater (with a bone age of at least 13.5 yrs for girls and 14.5 yrs for boys) and 2) to have a history of obesity for at least 5 years, including failed attempts at dietary and medical management of obesity. After evaluations by a pediatric surgeon, a pediatric endocrinologist, a registered dietician, a nurse practitioner/exercise specialist, and a psychologist or psychiatrist, those who demonstrated understanding and willingness to incorporate dietary and exercise changes were offered restrictive bariatric surgery. A total of 135 patients considered appropriate candidates for restrictive bariatric surgery were screened for *MC4R* mutations between March 2006 and March 2011. Parents and patients 18 years old signed informed consents, and patients under 18 years old signed informed assents under CUMC Institutional Review Board approved protocols at time of entry into the CABS program and for gene studies.

Surgical Methods

Patients underwent LAGB or gastric sleeve resection procedures performed at the Morgan Stanley Children's Hospital of New York by a single pediatric surgeon (JZ). The technique for LAGB using the LAP-BAND® involves a silicone ring with an adjustable inner diameter positioned around the proximal stomach just distal to the gastroesophageal junction, creating a small proximal gastric pouch. The band is connected to a subcutaneous access port with band internal diameter adjusted by injection or withdrawal of saline. Placement of the LAP-BAND was performed laparoscopically with the patient under general anesthesia using 5 trocar sites according to the pars flaccida technique, described in detail elsewhere.(19) The LAP-BAND was left empty at the end of placement to allow for possible postoperative swelling. Contrast esophagram was performed to confirm band position and assess pouch emptying prior to discharge. Sleeve gastrectomy was performed laparoscopically as well. The sleeve resection was carried out using a multi-fire linear stapler with staple loads reinforced with Seamguard® (W.L. Gore & Associates, Flagstaff, AZ). Upper endoscopy was performed and demonstrated no staple line bleeding or evidence of a leak at time of procedure. The morning after surgery a contrast upper GI series was performed to assess sleeve anatomy and to check for gastric leak before starting oral fluids

Postoperative care

LAGB patients were instructed postoperatively to follow a standard restrictive dietary protocol including ingestion of a pureed diet in the first postoperative week, a blended diet for weeks 2–3, a soft diet for weeks 4–6, and a well-balanced low-fat diet for week 7 and beyond. Gastric sleeve patients were maintained on liquids for 2 weeks then advanced to puree for an additional 3–4 wks. Patients were instructed to return for follow-up visits for assessment of weight changes, for nutritional advice, and for postsurgical monitoring with adjustments as indicated at weeks 2, 4, 6, and 8, then monthly for the initial 12 months, with plans for follow-up at 15, 18, and 24 months, then semiannually for 5 years. (20) Nutritional supplements were prescribed as needed for documented deficiencies. Total weight loss (kg) and percentage of excess weight lost (%EWL) after surgery were calculated using Centers for Disease Control growth charts. Patient weights were plotted using Growth Analyser(Dutch Growth Research Foundation). Excess weight was defined as the weight above the 85th percentile of body mass index for age and sex. (21)

Sequencing

Patients had 5 mL of whole blood drawn for genetic analysis. Genomic DNA was isolated from peripheral leukocytes by cell lysis followed by DNA extraction and precipitation. Each subject's DNA was amplified by polymerase chain reaction for the coding regions and splice sites (primers and conditions available upon request) and sequenced by dideoxysequencing with the BigDye terminator kit using an ABI 377 sequencer (Applied Biosystems). Sequence was analyzed using Sequencher software. In addition, each electropherogram was visually reviewed to identify any heterozygous DNA variants not detected by the automated sequencing software. Variants classified as mutations have been previously reported as mutations or resulted in frame shift mutations and were absent from the 1000 genomes database (http://www.1000genomes.org/) and EVS database (http://evs.gs.washington.edu/EVS/). Mutations were confirmed with bidirectional sequencing.

Statistical Analysis

Subjects were divided based on the presence of *MC4R* mutations. The data are summarized with means ± standard deviations or counts and percentages while comparisons between subgroups are presented as means ± standard errors. The comparison of %EWL, absolute weight loss, and percent total weight loss at 12 months between *MC4R* mutation carriers (cases; n=4) and the cohort of 52 patients without *MC4R* mutations (non-matched controls) at 12 months postoperatively was performed using an independent, two-tailed t test. Each of the four cases were then matched (without replacement) with between two and five controls of the same race, sex and age within 2 years. The within-matched pair differences between *MC4R* cases and controls were tested with Analysis of Variance.

Results

Identification of MC4R mutations

135 patients evaluated for restrictive bariatric surgery were screened for *MC4R* mutations. The mean ±SD of age and BMI prior to surgery was 16.5 ±1.2 years and 54.4 ±8.6 kg/m^2,

respectively. Mutations in *MC4R* were detected in five of the 135 patients (3.7%) and included the heterozygous *MC4R* mutations: p.Cys271Arg, p.Asp146His, p.Phe202Leu, p.Ser139Cysfs*22, and p.Leu250Trpfs*34 (Table 1). Case 1 has functional studies that demonstrate loss of function. Case 2 is reported in the literature as a mutation but has one functional study demonstrating wild type activity, although this particular assay does not fully assess the function and all prediction algorithms suggest it is a pathogenic change (references in Table 1). Cases 3 and 4 are frame shift mutations resulting in premature termination and are strongly predicted to result in loss of function. Case 5 has another amino acid substitution at the same position that is a proven mutation, but our substitution has not been observed. All prediction algorithms predict the Asp146His variant to be pathogenic, and this allele is not observed in databases of normal individuals.

Weight loss after bariatric surgery

Four of the five *MC4R* mutation carriers underwent restrictive bariatric surgery (Figure 1). Of the 135 patients screened, 117 patients underwent bariatric surgery with LAGB performed in 113 patients. The remainder of patients (3 controls, 1 MC4R carrier) underwent GSR. Thirty-one patients (26.5%) missed the 12 month visit, but returned to clinic for continued postoperative care at subsequent visits. Thirty of the 117 patients who underwent bariatric surgery (25.6%), missed the 12 month postoperative visit and were lost to follow-up. Fifty-six patients of the original cohort had 12 month postoperative data available for analysis.

The mean age of the fifty-six subjects analyzed was 16.5 ±1.2 years with mean BMI 54.4 kg/m^2± 8.6 kg/m^2. Twenty-four patients (43%) were male. Patients were of diverse racial background (36% were Caucasian, 45% were Hispanic, 14% were African-American, and 5% were of mixed ethnicity). The mean %EWL of the entire cohort at 12 months equaled 25.0±24.9%, ranging from 95.2% of excess weight lost to 17.7% of excess weight gained.

The four *MC4R* mutation carriers were found to have a higher %EWL compared to the cohort of 52 non-matched controls at 12 months postoperatively (48.6% vs. 23.4%), although the difference in weight loss between the two groups did not reach statistical significance ($p<0.37$). For the three patients with LAGB, %EWL postoperatively was 36.0% at 5 years in one, 47% at 4 years in the second, and 85% at 1 year in the third. For the patient with gastric sleeve resection, %EWL of 96% was attained at 1 year. Of note, sex differences were observed with regards to weight loss at 12 months postoperatively among the entire cohort (Figure 2), but the slightly increased weight loss in females compared to males (26.6 ± 4.6% vs. 19.1± 3.6%) was not statistically significant ($p<0.23$).

The four *MC4R* mutation carriers were matched by age, sex, and race to 14 controls (Table 2). The 2 female cases were matched to 6 female controls (age 16.3 ± 0.3 vs. 16.4 ± 1.4 years, initial weight 125.8 ± 6.2 vs. 128.7 ± 4.9 kg, initial BMI 44.9 ± 3.1 vs. 44.6 ± 1.6 kg/m^2, respectively); 2 male cases were matched to 8 male controls (age 16.6 ± 1.1 vs. 16.3 ± 1.1 years, initial weight 178.4 ± 36.2 vs. 141.0 ± 7.1 kg, initial BMI 54.7 ± 7.8 vs. 46.0 ± 1.9 kg/m^2, respectively). There were no statistically significant between pair differences in %EWL ($p < 0.31$; females 0.10, males 0.60), BMI change ($p< 0.27$; females 0.13; males

0.79), or absolute weight loss (p <0.20; females 0.08; males 0.92) when comparing cases and controls at 12 months postoperatively (Table 3).

Discussion

To our knowledge, this study is the first to report the prevalence of *MC4R* mutations in a cohort of morbidly obese adolescent patients presenting for bariatric surgery. It is also the first to document successful weight loss after restrictive bariatric surgery procedures in patients with *MC4R* mutations suggesting that patients with these mutations are able to lose as much weight as patients without *MC4R* mutations. The overall pattern of results of the pair-matched analysis supports the findings from the general analysis. *MC4R* mutation carriers did not lose less weight than controls as had been hypothesized, although the difference in weight loss between the two groups did not reach statistical significance. Thus, carriers of MC4R mutations are expected to respond to bariatric surgery similarly to non-carriers, suggesting that the favorable effects of surgery on body weight are not mediated by MC4R activity variations.

Studies in animals and humans show a direct link between *MC4R* mutations and obesity. Rats with *MC4R* defects have decreased energy expenditure, hyperphagia, and early onset obesity.(22) Humans have similar symptoms in addition to hyperinsulinemia, increased fat mass, increased linear growth, and elevated bone mineral density.(23, 24, 25) MC4R agonists given to rats lead to decreased food intake and reduced body weight (26) and increased thermogenesis in brown adipose tissue.(27, 28)

Data on the effects of bariatric surgery in patients with monogenetic forms of obesity are extremely limited with little known regarding long term weight loss outcomes in adults or adolescents. It has been suggested that aberrant satiety signaling by the melanocortins could place individuals with *MC4R* mutations at higher risk for bariatric surgery failure, in particular after LAGB. (29) In a previous study of 300 adult gastric banding patients by Potoczna et al, *MC4R* mutation carriers (6.3%) were found to have poorer outcomes with less weight loss and fivefold more gastric complications than non-carriers.(30) Of note, the study by Potoczna et al included a large number of patients with binge eating disorders, which have been independently implicated in poorer outcomes post-surgery, possibly confounding the results of the study. A recent study focusing on adult patients with complications following banding requiring re-operation could not confirm this association between higher complication rates and *MC4R* mutation status following LAGB. (29)

Aslan et al published a case report of unsuccessful weight loss with postoperative weight gain following LAGB in an 18.7 year old with compound heterozygosity and complete functional loss of both alleles of the *MC4R*.(31) Although mutations in *MC4R* have been reported to be associated with up to 5.8% of the cases of severe obesity, less than 10 patients have been described in the literature with homozygous or compound heterozygous *MC4R* mutations. The presence of two mutations may make bariatric surgery ineffective in affected individuals.

In contrast to the above findings, studies in adults with heterozygous *MC4R* mutations demonstrate sustained weight loss in response to gastric bypass. Aslan et al was the first to document weight loss after RYGB in adults with heterozygous *MC4R* mutations.(32)They screened 92 patients finding 4.3% with *MC4R* mutations and noted similar weight loss between those with and without *MC4R* mutations at 12 months postoperatively.

A recent study by Hatoum et al also documented sustained weight loss in patients heterozygous for hypomorphic *MC4R* alleles after RYGB. (31) Of 972 patients sequenced preoperatively, 62 (6.4%) had at least one heterozygous mutation. Patients heterozygous for *MC4R* mutations exhibited the same magnitude and distribution of postoperative weight loss as patients without *MC4R* mutations. Hatoum et al also studied male age- and litter mate-matched *MC4R* knockout (*MC4R*−/−), heterozygous (*MC4R*+/−), and wild type mice. They reported *MC4R*−/− mice having substantially less weight loss after surgery than wild-type animals, with *MC4R*+/− mice remaining fully responsive to gastric bypass. The authors concluded that two normal copies of the *MC4R* gene are necessary for normal weight regulation, but a single normal copy of the *MC4R* gene may be sufficient to regulate the weight loss effects of RYGB.(33)

Mul et al analyzed the effect of VSG on body weight, food intake and glucose sensitivity of wild-type and MC4R-deficient (*MC4R*(+/−) and *MC4R*(−/−)) rats compared with sham-operated controls. Results showed reduced body weight and fat mass and improved glucose metabolism postoperatively independent of MC4R activity. In 46 adult human subjects who underwent VSG and were screened for MC4R mutations, BMI, body weight, and HbA1c levels 12 months postoperatively were unaffected by the genetic variations in the coding sequence in five subjects suggesting that the beneficial effect of VSG on body weight and glucose metabolism were not mediated by MC4R activity alterations.(34)

In our study, one male *MC4R* mutation carrier (case 1) lost a similar percent EBW (15.3%) to the male noncarrier cohort (17.7%) at 1 year postoperatively. It appeared that female *MC4R* mutation carriers lost more EBW (84.4 and 95.2%, respectively) at 12 months compared to the group of female non-matched control patients (26.6%) and the male cohort (17.7%). However, five additional females in the non-matched control cohort also lost greater than 70% of their EBW. In addition, although one male carrier (case 3) gained 0.6% EBW, four non-matched control patients also had a net weight gain at 12 months postoperatively and nine patients lost less than 10% of their EBW. By 48 months postoperatively, case 3 had lost 30.7 kg from baseline with total %EWL of 46.7%.

The limitations of our study include the small sample size of *MC4R* mutation carriers limiting the ability to draw definitive conclusions due to the lack of power. The intermittent follow-up of our four *MC4R* mutation carriers made it difficult to compare weight loss at different time points. A visit frequency of 5 total visits during the first 12 months postoperatively was anticipated. The actual visits of the 4 MC4R carriers averaged 3.8 visits versus 4.0 in the 52 patient control group. Possible explanations for the insufficient weight loss and weight gain in our patient population at 12 months postoperatively have been discussed in a previous paper published by our group.(20) These include lack of social support, failure to change eating habits, and failure to incorporate recommended exercise.

Degree of adherence to follow-up appointments could have further contributed to disappointing outcomes in certain patients. Patients were encouraged by their surgeon, dietician, and endocrinologist to attend all recommended postoperative appointments and received telephone reminders in order to maximize care and weight loss outcomes. Despite these limitations, our experience indicates that restrictive bariatric surgery with laparoscopic adjustable gastric banding or sleeve gastrectomy may result in significant long term weight loss for patients with heterozygous *MC4R* mutations comparable to a cohort of patients without mutations.

In conclusion, the frequency of *MC4R* mutations in our morbidly obese adolescent patient population who underwent bariatric surgery appears to be similar to other studies. Studies in the adult literature indicate sustained weight loss in patients with heterozygous *MC4R* mutations following RYGB and VSG, with poor outcomes suggested for patients homozygous for loss-of-function mutations. Our study is the first to document weight loss after bariatric surgery in adolescent patients with heterozygous *MC4R* mutations and provide preliminary information on outcomes of mutation carriers after restrictive bariatric surgery. These findings support considering patients heterozygous for MC4R mutations as appropriate candidates for restrictive, in addition to malabsorptive, bariatric surgery procedures.

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Abbreviations

MC4R	Melanocortin4 Receptor
%EWL	percent excess weight loss
Wt	weight
LAGB	laparoscopic adjustable gastric banding
RYGB	Roux-en-Y gastric bypass
POMC	Proopiomelanocortin
CABS	Center for Adolescent Bariatric Surgery
EBW	excess body weight

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What is already known about this subject

- *MC4R* mutations are associated with up to 5.8% of severe obesity in pediatric and adult populations.
- Studies in animals and humans show *MC4R* defects to be associated with decreased energy expenditure, hyperphagia, and early onset obesity.
- Limited data on outcomes to bariatric surgery interventions in patients with MC4R mutations, do not address long-term weight loss outcomes in adolescents.

What this study adds

- This is the first study to document successful weight loss after restrictive bariatric surgery procedures in patients with *MC4R* mutations.
- Preliminary results suggest that patients with these mutations are able to lose as much weight as patients without *MC4R* mutations.
- These findings support considering adolescent patients with heterozygous *MC4R* mutations as appropriate candidates for bariatric surgery procedures.

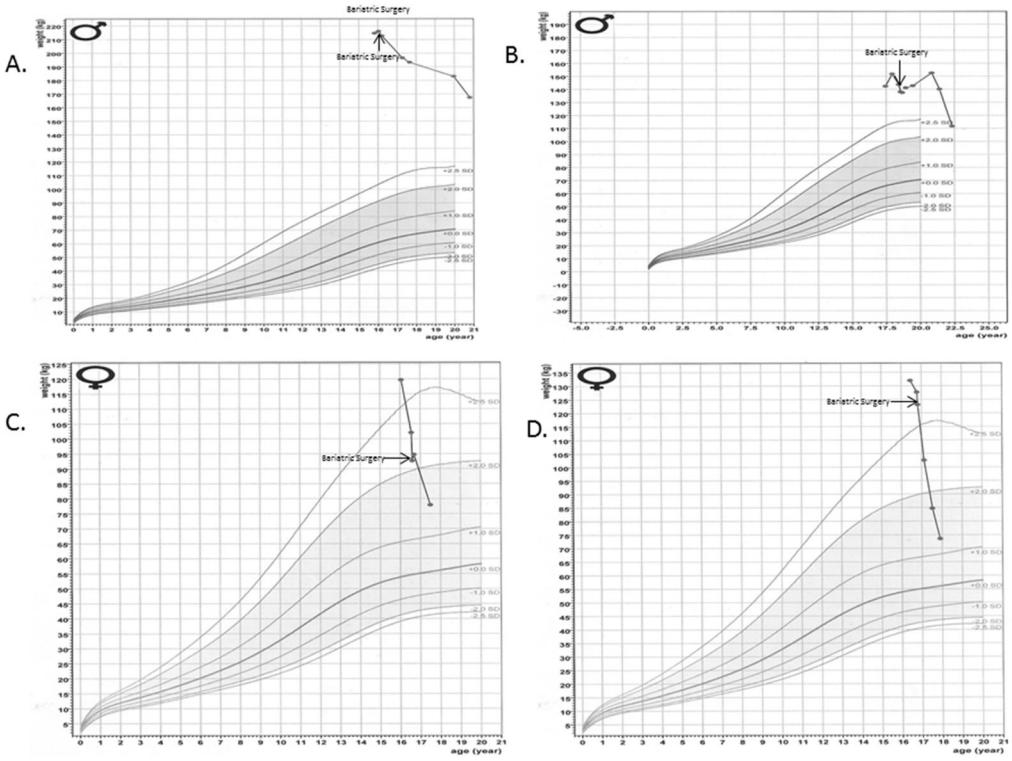

Figure 1.

Weight loss (kg) status post bariatric surgery in case 1 (A), case 2 (B), case 3 (C), and case 4 (D).

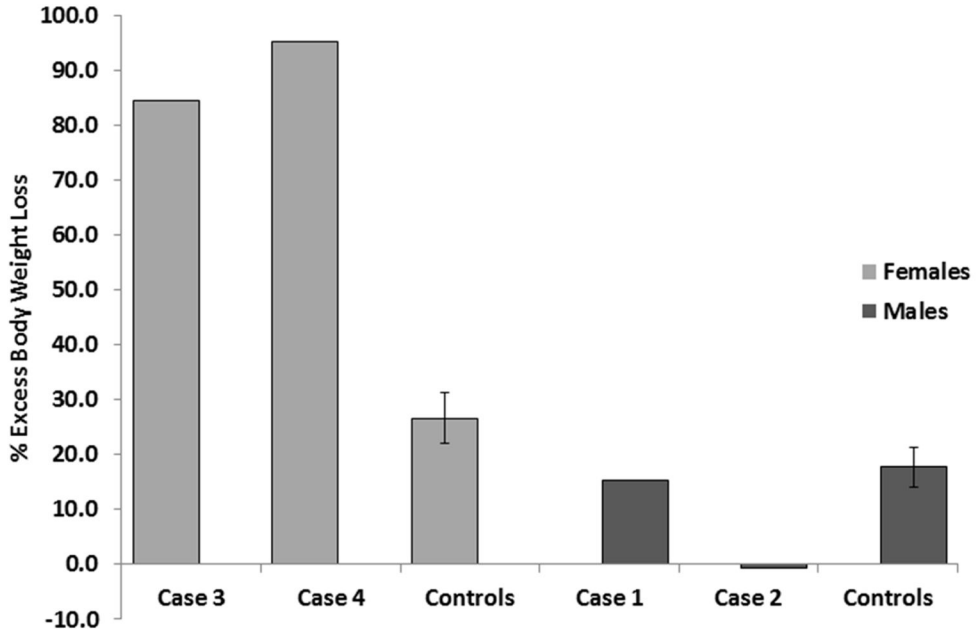

Figure 2.
Percent excess body weight loss 12 months post bariatric surgery

Table 1

Clinical data from patients heterozygous for *MC4R* mutations

Case	*MC4R* mutation	Activity	Reference	Sex	Age (yrs)	Ethnicity	Initial Wt (kg)	BMI Z- score	Surgery	Absolute Wt Loss (kg)	Maximum %EWL	FHx of Obesity
1	p.Cys271Arg	No activity	(17)	M	15.92	AA	214.6	3.25	LAGB	47.3	36% †	Father, mother, MGF, sibling
2	p.Phe202Leu	Normal activity	(35)	M	17.42	H	142.3	3.03	LAGB	30.7	46.7%‡	PGF, PGM
3	p.Ser139Cysfs*22	Predicted loss of function mutation	—	F	16.08	C	119.6	2.47	LAGB	41.7	84.4%*	Father, sibling, paternal aunt, uncle; maternal uncles, aunt
4	p.Leu250Trpfs*34	Predicted loss of function mutation	—	F	16.5	C	165.8	2.61	GSR	58.4	95.3%*	Mother, father, siblings
5	p.Asp146His	No data available	—	F	17.08	AA	142.3	2.47	_	_	_	Mother, MGM, sibling

AA African-American, H Hispanic, C Caucasian,

† 60 months postoperatively,

‡ 48 months postoperatively,

* 12 months postoperatively; Wt weight, %EWL percent excess weight loss, FHx Family history, MGF maternal grandfather, MGM maternal grandmother, PGF paternal grandfather, PGM paternal grandmother

Table 2

Clinical data from patients heterozygous for *MC4R* mutations and fourteen matched controls

Pair	*MC4R* mutation	Sex	Age (yrs)	Ethnicity	BMI (kg/m^2)	DLD	HTN	IFG	IGT	OSA	PCOS
Pair 1											
Case 1	**p.Cys271Arg**	**M**	**15.92**	**AA**	**62.6**	**−**	**+**	**−**	**−**	**−**	**−**
Control		M	16.22	AA	47.10	+	−	+	−	+	−
Control		M	16.44	AA	46.80	−	−	−	−	−	−
Control		M	16.55	AA	50.30	−	−	−	−	−	−
Pair 2											
Case 2	**p.Phe202Leu**	**M**	**17.42**	**H**	**49.4**	+	+	**−**	**−**	**−**	**−**
Control		M	14.56	H	47.20	+	−	−	−	+	−
Control		M	15.14	H	44.90	+	−		−	−	−
Control		M	16.01	H	48.30	+	−	+	+	+	−
Control		M	17.76	H	35.30	+	+	+	+	−	−
Control		M	17.87	H	47.80	+	−	−	−	+	−
Pair 3											
Case 3	**p.Ser139Cysfs*22**	**F**	**16.08**	**C**	**41.9**	**−**	**−**	**−**	**−**	**−**	**−**
Control		F	16.21	C	45.60	+	−	−	−	−	−
Control		F	17.64	C	42.30	+	−	−	−	−	+
Pair 4											
Case 4	**p.Leu250Trpfs*34**	**F**	**16.50**	**C**	**48.0**	**+**	**−**	**−**	**+**	**+**	**+**
Control		F	14.15	C	41.50	+	−	−	−	−	−
Control		F	15.5	C	47.00	+	−	−	−	−	+
Control		F	17.35	C	46.30	+	−	−	−	−	+
Control		F	17.49	C	44.80	+	−	−	−	−	+
Case 5	**p.Asp146His**	**F**	**17.08**	**AA**	**44.4**	**+**	**−**	**−**	**−**	**−**	**−**

AA African-American, H Hispanic, C Caucasian; DLD dyslipidemia, HTN hypertension, IFG impaired fasting glucose, IGT impaired glucose tolerance, OSA obstructive sleep apnea, PCOS polycystic ovarian syndrome, + presence of comorbidity, - absence of comorbidity

Table 3

Matched Pair Analysis Results (n=18)

	Females			Males		
	MC4R Cases (n=2)	**Controls (n=6)**	**p-value within pair**	**MC4R Cases (n=2)**	**Controls (n=8)**	**p-value within pair**
Age	16.3 ± 0.3	16.4 ± 1.4	0.69	16.6 + 1.1	16.3 + 1.1	0.69
Wt at baseline (kg)	125.8 ± 6.2	128.7 ± 4.9	0.98	178.4 ± 36.2	141.0 ± 7.1	0.36
BMI at baseline	44.9 ± 3.1	44.6 ± 1.6	0.86	54.7 ± 7.8	46.0 ± 1.9	0.35
Wt at 12 months (kg)	75.7 ± 11.1	107.2 ± 6.8	0.27	168.6 ± 10.5	133.6 ± 5.4	0.28
% Wt loss	39.6 ± 13.0	14.7 ± 5.9	0.09	4.6 ± 2.5	6.0 ± 1.3	0.79
Wt loss (kg)	50.1 ± 15.4	18.4 ± 7.6	0.08	9.9 ± 4.0	8.8 ± 2.1	0.92
EBW (kg)	55.4 ± 5.5	58.2 ± 3.4	0.86	99.0 ± 11.8	67.6 ± 6.1	0.38
% EWL	89.8 ± 21.8	35.2 ± 13.3	0.10	7.3 ± 4.4	12.4 ± 2.3	0.60
BMI at 12 months (kg/m^2)	27.1 ± 5.0	37.5 ± 3.1	0.12	51.8 ± 2.3	42.7 ± 1.2	0.24
BMI change (kg/m^2)	−17.9 ± 3.9	−7.0 ± 2.4	0.13	−2.9 ± 1.3	−3.7 ± 0.7	0.79

Means ± SEM; p-value for average within matched-pair difference by ANOVA