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ORIGINAL CONTRIBUTIONS

Presence of CC Genotype for rs17773430 Could Affect the Percentage of Excess Weight Loss 1 Year After Bariatric Surgery: Tehran Obesity Treatment Study (TOTS)

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Abstract

Background Morbid obesity could last for a long period of life and increase the risk of morbidity as well as premature mortality. Although bariatric surgery benefits patients by quick weight loss, not all bariatric patients lose the same percentage of weight after a long time from surgery, which may be the result of diet, physical activity, and genetic components.

Objectives In this study, we evaluated the association between the MC4R gene and both excess weight loss percentage (EWL%) and excess BMI loss percentage (EBMIL%) in a cohort of bariatric surgery patients after 6 and 12 months from surgery.

Methods A total of 424 bariatric surgery patients who had participated in the Tehran Obesity Treatment Study and had weight measurements after 6 and 12 months from surgery were included in the study. Four SNPs in the MC4R gene were selected for evaluating the associations.

Results We found that rs17773430 had a significant effect on both EWL% and EBMIL%, especially after 12 months of bariatric surgery. Furthermore, three other SNPs, rs17782313, rs476828, and rs11152213, did not show any significant association with EWL% and EBMIL%.

Conclusion This study was the first to report on the association of rs17773430 with both EWL% and EBMIL% in a cohort of patients after bariatric surgery. We found that weight loss after surgery is influenced by genetic factors, and there were significant differences between the distribution of EWL% and EBMIL% in morbid obese bariatric patients who have two minor alleles of the rs17773430 and other SNPs.

Keywords Association analysis · MC4R gene · Bariatric surgery · Cohort study · Obesity · Kernel machine

Introduction

Morbid obesity remains a significant medical and public health concern throughout the world and could last for a long period of life, while increasing the risk of metabolic disorders and premature mortality. It is claimed that bariatric surgery is the best available therapy to achieve and sustain significant weight loss in subjects with morbid obesity [1]. However, there is a wide interindividual variability in the operation-associated weight loss [1]. Studies assessing non-surgical strategies promoting weight loss have revealed a strong genetic influence on weight loss response [2].

However, relevance of genetic factors in operation-induced weight loss is unclear. Few studies confirmed that patients do not all lose the same percentage of weight after bariatric surgery, which could be the result of diet as well as genetic components. In fact, with regard to the genome-wide association studies, gene variants can affect long-term results of bariatric surgery [3]. One of the most important genetic loci in long-term energy balance regulation in severe obese patients is the leptin-melanocortin

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Table 1 Pre- and post-bariatric surgery characteristics of study participants

Follow-up	Variable[a]	GB surgery	SG surgery	*P* value[b]
Pre-surgery	Number of available individuals	144 (34%)	280 (66%)	-
	Weight (kg)	121 ± 1.5	122 ± 1.3	NS[c]
	BMI (kg/m^2)	46 ± 0.5	45 ± 0.3	NS
	TG (mg/dl)	160 ± 6.2	155 ± 5.0	NS
	TChol (mg/dl)	190 ± 3.1	189 ± 2.4	NS
	HDL (mg/dl)	47 ± 0.9	47 ± 0.7	NS
	LDL (mg/dl)	110 ± 2.8	113 ± 2.0	NS
	SBP (mmHg)	122 ± 1.0	124 ± 0.84	NS
	DBP (mmHg)	78 ± 0.7	79 ± 0.5	NS
Post-surgery (6 months)	No. of available individuals	131 (35%)	243 (65%)	-
	Weight (kg)	87 ± 1.2	89 ± 0.9	NS
	BMI (kg/m^2)	33 ± 0.4	33 ± 0.3	NS
	EWL%	64.5 ± 1.3	64.5 ± 1.2	NS
	EBMIL%	64.5 ± 1.2	64 ± 1.2	NS
	ΔW (kg)	34 ± 0.7	32 ± 0.7	NS
	ΔBMI (kg/m^2)	13 ± 0.2	12 ± 0.2	NS
	TG (mg/dl)	112 ± 5.2	104 ± 2.8	NS
	TChol (mg/dl)	167 ± 3.2	183 ± 2.3	< 0.001
	HDL (mg/dl)	43 ± 1.1	50 ± 0.7	< 0.001
	LDL (mg/dl)	99 ± 2.6	110 ± 2.0	< 0.001
	SBP (mmHg)	115 ± 1.0	114 ± 0.6	NS
	DBP (mmHg)	69 ± 0.9	69 ± 0.6	NS
Post-surgery (12 months)	No. of available individuals	126 (35%)	236 (65%)	-
	Weight (kg)	79.7 ± 1.1	82 ± 1.0	NS
	BMI (kg/m^2)	29 ± 0.4	30 ± 0.3	NS
	EWL%	79 ± 1.5	76 ± 1.2	NS
	EBMIL%	79 ± 1.5	76 ± 1.2	NS
	ΔW (kg)	42 ± 1.1	40 ± 0.9	NS
	ΔBMI (kg/m^2)	16 ± 0.4	15 ± 0.3	0.002
	TG (mg/dl)	94 ± 4.5	95 ± 4.0	NS
	TChol (mg/dl)	157 ± 3.4	180 ± 3.0	< 0.001
	HDL (mg/dl)	48 ± 1.2	53 ± 1.1	0.004
	LDL (mg/dl)	89 ± 3.0	104 ± 2.4	< 0.001
	SBP (mmHg)	115 ± 1.0	116 ± 0.7	NS
	DBP (mmHg)	71 ± 0.9	71 ± 0.7	NS

BMI, body mass index; *EWL%*, excess weight loss; *EBMIL%*, excess BMI loss; Δ*W*, delta weight (pre-surgery weight minus follow-up weight); Δ*BMI*, delta BMI (pre-surgery BMI minus follow-up BMI); *TG*, triglycerides; *TChol*, total cholesterol; *HDL*, high-density lipoprotein; *LDL*, low-density lipoprotein; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure

[a] *N* (%) or mean ± SE

[b] *P* value based on independent *t* test comparing two surgery methods in each follow-up time

[c] Not significant at 0.05 level

axis. This locus contains the melanocortin 4 receptor (MC4R), the major mediator of leptin's central effect that is expressed in neurons of the periventricular nucleus of hypothalamus (PVN). This expression can result in regulating food intake and maintaining long-term energy homeostasis [4]. Moreover, several mutations have been identified nearby or in the MC4R gene, have been identified in humans that can impair the hypothalamous, and do not allow the satiety hormone to be released [5, 6].

In this study, we analyzed the association between four candidate SNPs (rs476828, rs17782313, rs17773430, and rs11152213) and both excess weight loss percentage (EWL%) and excess BMI loss percentage (EBMIL%) after 6 and 12 months from bariatric surgery.

Table 2 Number of individuals in different excess weight loss (EWL%) categories 6 and 12 months after bariatric surgery based on a surgery type

Follow-up	Surgery type	EWL% category				Total	*P* value[a]
		< 30	30–50	50–70	≥ 70		
6 months	GB[b]	0	21 (16)	70 (54)	40 (30)	131	NS
	SG	2 (1)	57 (23)	118 (49)	66 (27)	243	
12 months	GB	0	6 (5)	25 (20)	95 (75)	126	0.02
	SG	1 (1)	22 (9)	72 (30)	141 (60)	236	

[a] *P* value for chi-square test between EWL% and surgery type in each follow-up time

[b] The values are presented as *n* (%)

NS, not significant at 0.05 level

Materials and Methods

Study Design and Participants The Tehran Obesity Treatment Study (TOTS) is a prospective cohort of patients with morbid obesity who undergo bariatric surgery. The type of surgery is mainly sleeve gastrectomy (creating a gastric tube over a 36-F bougie with exclusion of the 80% of the stomach) (SG) or one of the two types of gastric bypass procedures, Roux-en-Y (using an alimentary limb of 100–150 cm and a biliopancreatic limb of 50 cm) or mini-gastric bypass (a loop gastroenterostomy of 150–200 cm) (GB) [7].

All patients who were aged between 15 and 75 years with a BMI ≥ 35 kg/m^2 and had referred to our bariatric center from March 2013 were enrolled in the study, after providing a written informed consent. Details of the study protocol are

Table 3 Association analysis results for four SNPs located on chromosome 18 near MC4R gene, using linear and logistic regressions (adjusted for age, gender, and surgery type (SG/GB))

SNP	Position	MAF	Major/ minor	Phenotype	Beta (OR for case-control)	*Ci*	*P*
rs17782313	60183864	0.43	T/C	EWL% – 6M	4.7	(− 1.2, 10)	NS[a,b]
				BMIL% – 6M	4.4	(− 1.5, 10)	NS[a,b]
				EWL% – 12M	0.3	(− 7.0, 7.8)	NS[a,b]
				EBMIL%– 12M	0.4	(− 7.0, 7.8)	NS[a,b]
				EWL% – 12M (case-control)	1.1	(0.45, 2.7)	NS[a,b]
rs476828	60185354	0.43	T/C	EWL% – 6M	4.3	(− 1.6, 10)	NS[a,b]
				BMIL% – 6M	4.0	(− 1.9, 9.5)	NS[a,b]
				EWL% – 12M	− 0.2	(− 7.0, 7.8)	NS[a,b]
				EBMIL% – 12M	− 0.09	(− 7.0, 7.8)	NS[a,b]
				EWL% – 12M (case-control)	1.1	(0.45, 2.7)	NS[a,b]
rs11152213	60185715	0.43	A/C	EWL% – 6M	4.7	(− 1.2, 10)	NS[c]
				BMIL% – 6M	4.4	(− 1.5, 10)	NS[c]
				EWL% – 12M	.3	(− 7.0, 7.8)	NS[c]
				EBMIL% – 12M	0.4	(− 7.0, 7.8)	NS[c]
				EWL% – 12M (case-control)	1.1	(0.45, 2.7)	NS[c]
rs17773430	60295884	0.33	T/C	EWL% – 6M	6.6	(0.01, 12)	0.05[b]
				BMIL% – 6M	6.1	(− 0.5, 11)	0.07[b]
				EWL% – 12M	10.8	(2.7, 18)	0.009[b]
				EBMI%L – 12M	10.3	(2.4, 18)	0.010[b]
				EWL% – 12M (case-control)	4.0	(1.5, 10)	0.005[b]

EWL% – 6M, excess weight loss percentage after 6 months from surgery; *BMIL% – 6M*, excess BMI loss percentage after 6 months from surgery; *EWL% – 12M*, excess weight loss percentage after 12 months from surgery; *EBMIL% – 12M*, excess BMI loss percentage after 12 months from surgery

[a] *NS*, not significant at 0.05 level

[b] Comparing of CC carriers and TT/TC carriers

[c] Comparing of CC carriers and AA/AC carriers

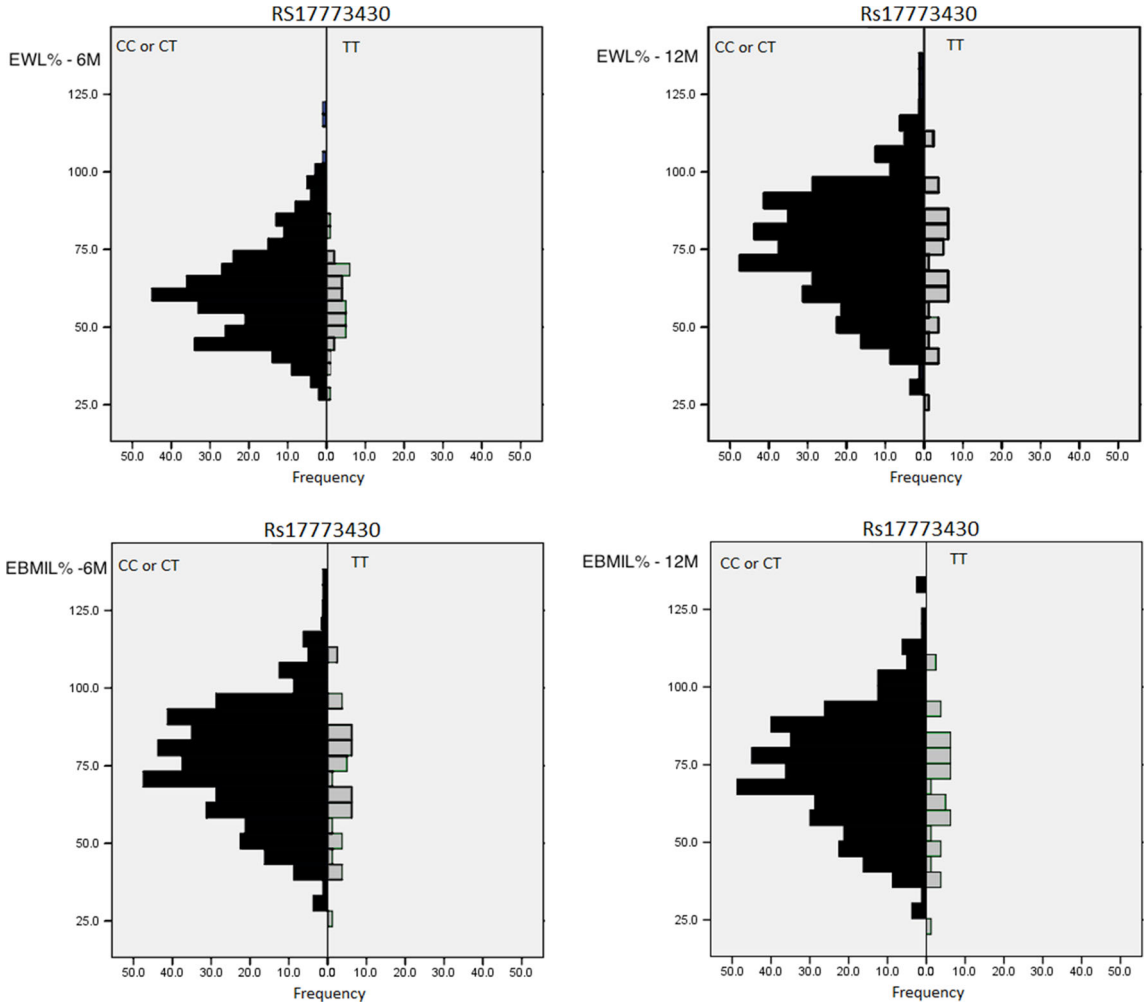

Fig. 1 Pyramid histogram of both EWL% and EBMIL% distribution, 6 and 12 months after bariatric surgery for individuals with none or one minor allele (TT or TC) and individuals with two minor alleles (CC) of rs17773430

available elsewhere [7]. Following surgery, patients underwent a strict post-op protocol, irrespective of their treatment group. Each patient underwent comprehensive assessments by our team after 1, 3, 6, and 12 months from surgery and then annually, to make sure they were following their schedule [7]. Regardless of surgery type, each patient underwent comprehensive assessments at 1, 3, 6, and 12 months after surgery by our post-op care team including an obesity expert, nutritionist, and exercise medicine physician. All patients received a similar calorie-restricted diet (with 10–35% protein) and were prescribed daily vitamin and mineral supplements up to 12 months. Moreover, all patients followed a physical activity program (at least 30 min/day, combined aerobic-resistive activity), postoperatively.

For the present study, we included 424 patients from the TOTS who had genotyped data and EWL% information 6 or 12 months after surgery.

Genomic DNA from 424 subjects were extracted from peripheral blood using the standard Proteinase K, salting out method [8]. DNA samples were genotyped with HumanOmniExpress-24-v1-0 bead chips (containing 654,333 SNP loci with an average mean distance of 4 kb) at the deCODE genetics company (Iceland) according to the manufacturer's specifications (Illumina Inc., San Diego, CA, USA) [7]. Among the genotyped SNPs, 4 markers that located on MC4R genes were selected for association analysis.

Calculating EWL and EBMIL% Regarding the weight and BMI measurements after 6 and 12 months from surgery, quantitative measures for EWL% and EBMIL% values were calculated as explained by Reinhold [9].

In addition to quantitative measurements for EWL% and EBMIL%, a case-control design was also considered in this study. In the case-control design, cases were defined as patients who had EWL < 70% and controls as patients who had EWL ≥ 70% after 12 months from surgery.

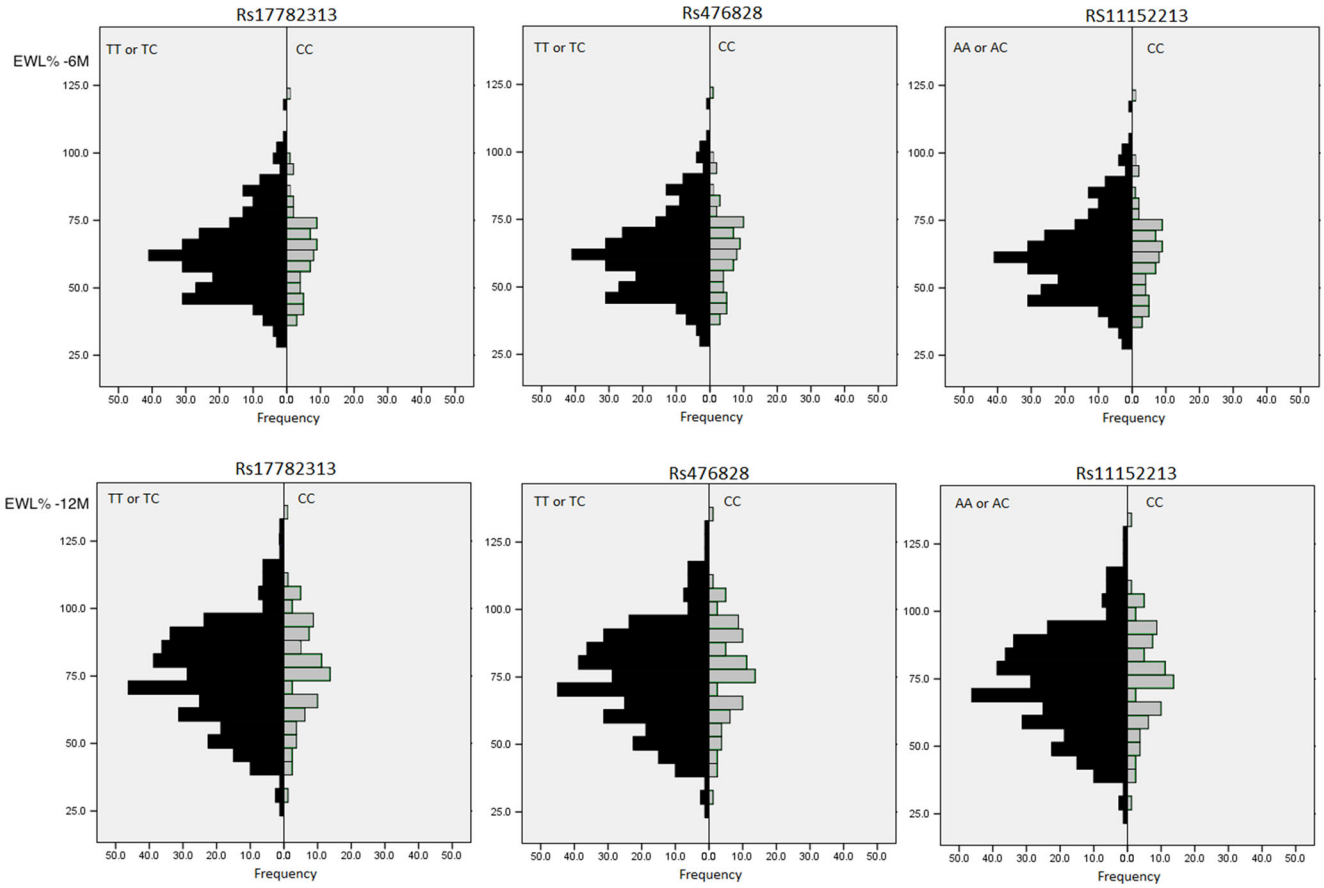

Fig. 2 Pyramid histogram of EWL% distribution, 6 and 12 months after bariatric surgery for individuals with none or one minor allele and individuals with two minor alleles for non-significant SNPs

Statistical Analysis For genotyped cleaning procedure, all four SNPs passed the cleaning control criteria including the Hardy-Weinberg equilibrium exact test at the 0.01 level, minor allele frequencies at 0.01, and genotyping call rates over 98%. Considering the wide range of age, significant linear relation between age and gender with both quantitative/qualitative measures of EWL% and EBMIL%, and the effect of different ethnicities or unrecorded familial correlations, 4 variables (i.e., age, gender, and two first principal components (PCs)) were considered as covariate in all association analyses. We also considered surgery type (SG/GB) as the covariate in association analysis.

Plink 2 was used for genotyped cleaning, principal component analysis, and association purposes. Significance level was considered as $P < 0.05$.

Genetic Risk Score Analysis A weighted IBS kernel machine regression model was used to assess the epistasis effect with significant SNP and the joint effect of four SNPs [10, 11]. Kernel machine model was conducted using SKAT package in R [12]. In these models, two first principal components, age, and gender were considered as the covariate effects.

Result

A total number of 424 patients participated in this study, of whom 79 (19%) were male with a mean (SE) age of 33.8 (1.1) and 345 (81%) were female with a mean (SE) age of 38.0 (0.6). Moreover, from the total number of patients, 144 (34%) underwent GB and 280 (66%) SG. The clinical and anthropometric data at pre- and post-surgery (after grouping based on surgery type) showed no difference in pre-surgery information; also, most characteristics had no difference between the two surgery groups after 6 and 12 months, except for HDL, LDL, and total cholesterol (Table 1).

Six months after surgery, about 79% of patients had EWL ≥ 50% and after 12 months, 65% had EWL ≥ 70%. Based on surgery groups, no significant difference was found in patients who had EWL ≥ 50% after 6 months. However, after 12 months, about 75% of GB and 60% of SG patients had ≥ 70% of EWL ($P = 0.02$) (Table 2).

Linear model between EWL% and EBMIL%, as quantitative variables, with four SNPs after adjusting for age, gender, and surgery type showed that rs17773430 had an association with both EWL% and EBMIL% 12 months after surgery. A

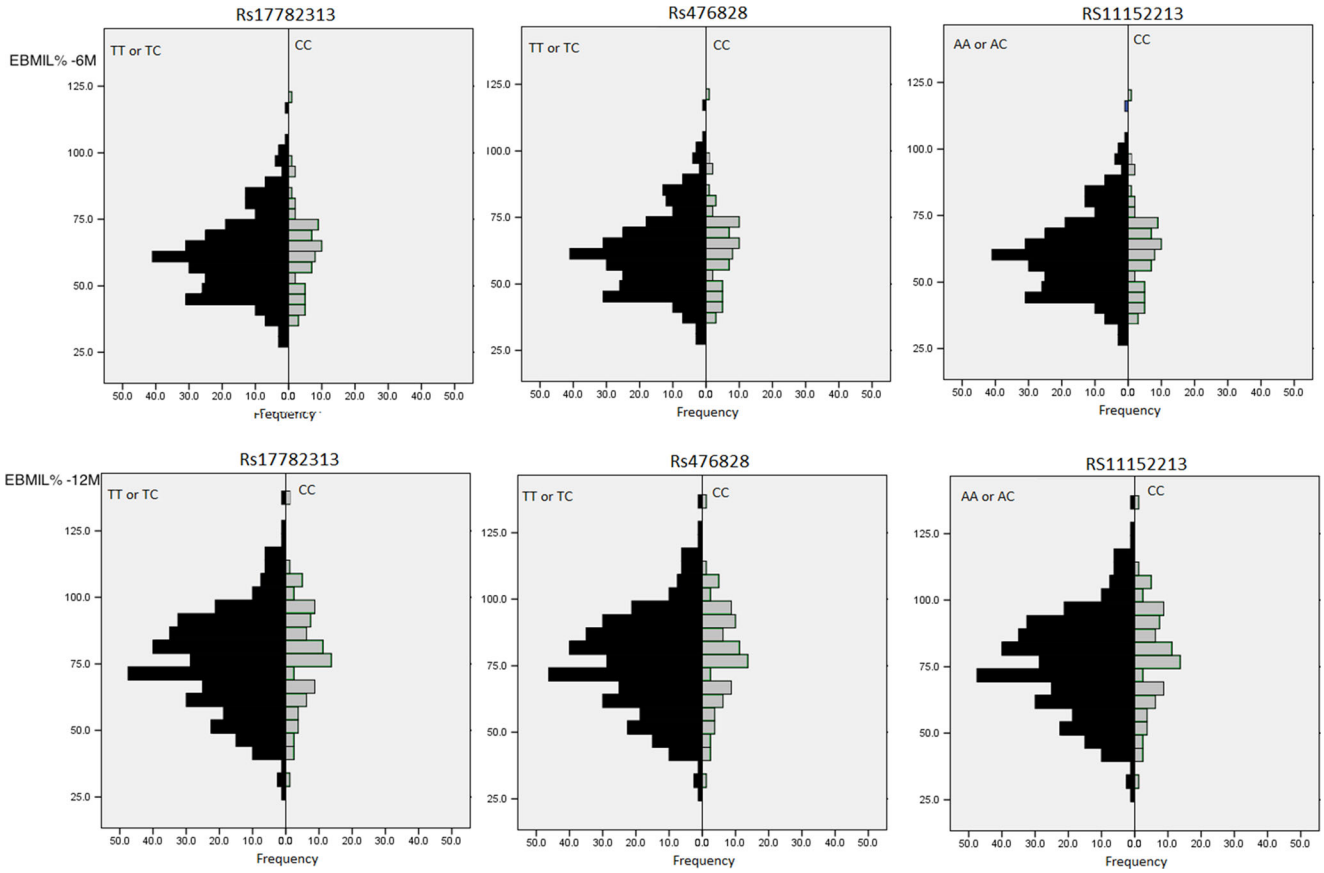

Fig. 3 Pyramid histogram of EBMIL% distribution, 6 and 12 months after bariatric surgery for individuals with none or one minor allele and individuals with two minor alleles for non-significant SNPs

case-control study showed a significant association between having EWL ≥ 70% after 12 months and two minor alleles ($P = 0.003$). The results of both linear and logistic models for association are presented in Table 3.

The chi-square test showed no significant difference between the distribution of C allele in rs17773430 among different surgery types ($P = 0.4$).

Figure 1 shows the difference between the distribution of EWL% and EBMIL% between individuals with 2 minor alleles and the other SNPs. The distribution of EWL% and EBMIL% differs between individuals who had two minor alleles and those who had one or no minor alleles. Most of the individuals with two minor alleles for rs17773430 laid near the mean with less dispersion and none had high values of EWL% and EBMIL%. This means that individuals with TT or TC alleles for rs17773430 have a higher odds ratio to lose their weight than CC individuals. The pyramid histogram for the other 3 SNPs can be found in Figs. 2 and 3 for EWL% and EBMIL%, respectively.

Table 4 *P* values obtained from kernel machine regression model (the model adjusted for age, gender, and two first principal component effects)

Epistasis effect	EWL% 6 months	BMIL% 6 months	EWL% 12 months	EBMIL% 12 months	EWL% 12 months (case-control)
rs17773430 and rs17782313[b]	0.07*	0.11	0.30	0.22	0.07*
rs17773430 and rs476828[b]	0.98	0.06*	0.57	0.07*	0.92
rs17773430 and rs11152213[b]	0.29	0.92	0.34	0.92	0.07*
Joint effect of 4 SNPs[c]	0.09*	0.31	0.25	0.07*	0.34

EWL%, excess weight loss; *EBMIL%*, excess BMI loss

*Marginally significant

[b] Epistasis effect between two SNPs

[c] The joint effect of all four SNPs

The kernel machine result showed no association between joint effects of SNPs in all models (Table 4).

Discussion

In this study, the association of four SNPs, located on chromosome 18 nearby the MC4R gene, with EWL% and EBMIL% were assessed. We found that rs17773430 has a significant effect on both EWL% and EBML%, especially after 12 months from bariatric surgery. This variant is a C/T single nucleotide polymorphism located on the LOC105372155 gene, very close to and in the promoter of the *MC4R* gene, with GMAF of 0.1937 (according to NCBI database) [13] and MAF of 0.326.

To the best of our knowledge, no previous study has reported on the association between rs17773430 and EWL% in post-bariatric patients, and few studies have reported the weight loss evolution of patients carrying MC4R mutations [14–17].

However, some GWAS showed an association between rs17773430 with overweight and obesity [14, 18]. Melka et al. conducted a genome-wide association study for adolescent obesity and found that rs17773430 had an association with both BMI ($P = 5 \times 10^{-6}$) and total fat mass ($P = 9 \times 10^{-5}$) in the French-Canadian population [18]. Moreover, they showed that risk allele homozygotes vs. non–risk allele homozygotes had a higher BMI (by 2.4 kg/m^2) and more body fat (by 3.8 kg) but their blood pressure variations were almost identical [18].

In addition, in a case report study, Aslan et al. reported on a 17-year-old Caucasian male with severe obesity and abnormal weight gain since infancy, who showed a negative response to bariatric surgery. They claimed that having two non-functioning MC4R alleles had probably compromised his satiety response significantly [6].

Moreover, our study showed that three other SNPs, rs17782313, rs476828, and rs11152213, have no significant association with EWL% or EBMIL% after 6 and 12 months from bariatric surgery. The polymorphism rs17782313 is located near the MC4R gene and has a D' value of 0.47 with rs17773430; however, it showed no association with neither EWL% nor EBMIL%, after 6 and 12 months of bariatric surgery. The association results did not change after adjusting the effect of surgery type; however, a surgery-type matched study with longer follow-up is recommended for the future. The Resende et al. study did not confirm our results; they showed that the rs17782313 polymorphism was related to weight and BMI changes in females after 60 months of bariatric surgery [14]. There are many possible reasons behind the abovementioned inconsistency: ignoring male patients and the effect of age, difference in follow-up periods, and statistical analysis methods in their study.

We are aware that our study has some limitations. We did not assess pre-operative diet in our participants. Another limitation of our study was using different methods of bariatric surgery (SG or GB) with possibly different outcomes on participants. However, we overcame this pitfall by making sure that the patients undergoing each bariatric surgery method at baseline had statistically similar characteristics at baseline, and we also adjusted our results for this confounder by linear regression analysis. Finally, a 12-month follow-up was short, and in order to assess the impact of various SNPs on EWL% after bariatric surgery, longer follow-up studies are needed. Despite these limitations, our study has some noteworthy strengths too. To the best of our knowledge, this study is the first to report on the association between rs17773430 with both EWL% and EBMIL% in a cohort of patients after bariatric surgery. Another advantage of our study was the favorable follow-up rate (88% after 6 and 85% after 12 months).

In conclusion, this report shows that weight loss after bariatric surgery is influenced by genetic factors; also, there are significant differences between the distribution of EWL% and EBMIL% in patients with morbid obesity undergoing bariatric surgery who have two minor alleles of the rs17773430 and the other SNPs. Moreover, there were no significant differences between EWL% and EBMIL% in patients with two minor alleles of the other three SNPs and patients with one minor or two major alleles of three SNPs.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Statement of Informed Consent Informed consent was obtained from all individual participants included in the study.

Human Rights/Ethical Approval This study has been approved by the Human Research Review Committee of the Endocrine Research Center, Shahid Beheshti University of Medical Sciences, No. 2ECRIES 93/03/13.

References

1. Sjöström L, Narbro K, Sjöström CD, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med. 2007;357(8):741–52.

2. Hainer V, Stunkard A, Kunešová M, et al. A twin study of weight loss and metabolic efficiency. Int J Obes. 2001;25(4):533.
3. Sun X, Li P, Yang X, et al. From genetics and epigenetics to the future of precision treatment for obesity. Gastroenterol Rep. 2017;5(4):266–70.
4. Rottembourg D, O'Gorman CS, Urbach S, et al. Outcome after bariatric surgery in two adolescents with hypothalamic obesity following treatment of craniopharyngioma. J Pediatr Endocrinol Metab. 2009;22(9):867–72.
5. Adan R, Tiesjema B, Hillebrand J, et al. The MC4 receptor and control of appetite. Br J Pharmacol. 2006;149(7):815–27.
6. Aslan I, Ranadive SA, Ersoy BA, et al. Bariatric surgery in a patient with complete MC4R deficiency. Int J Obes. 2011;35(3):457.
7. Barzin M, Hosseinpanah F, Motamedi MA, Shapoori P, Arian P, Daneshpour MA, et al. Bariatric surgery for morbid obesity: Tehran Obesity Treatment Study (TOTS) rationale and study design. JMIR research protocols. 2016;5(1).
8. Daneshpour MS, Fallah M-S, Sedaghati-Khayat B, et al. Rationale and design of a genetic study on cardiometabolic risk factors: protocol for the Tehran Cardiometabolic Genetic Study (TCGS). JMIR research protocols. 2017;6(2):e28.
9. Reinhold R. Critical analysis of long term weight loss following gastric bypass. Surg Gynecol Obstet. 1982;155(3):385–94.
10. Javanrouh N, Daneshpour MS, Soltanian AR, Tapak LJG. Kernel machine SNP set analysis provides new insight into the association between obesity and polymorphisms located on the chromosomal 16q.12.2 region: Tehran Lipid and Glucose Study. 2018;658:146-51.
11. Wu MC, Maity A, Lee S, Simmons EM, Harmon QE, Lin X, et al. Kernel machine SNP-set testing under multiple candidate kernels 2013;37(3):267-275.
12. Lee SS, Lee MSS. Package 'SKAT'. 2017.
13. Coordinators NR. Database resources of the national center for biotechnology information. Nucleic Acids Res. 2016;44(Database issue):D7.
14. Resende CMM, Durso DF, Borges KBG, et al. The polymorphism rs17782313 near MC4R gene is related with anthropometric changes in women submitted to bariatric surgery over 60 months. Clin Nutr. 2018;37(4):1286–92.
15. Elkhenini H, New J, Syed A. Five-year outcome of bariatric surgery in a patient with melanocortin-4 receptor mutation. Clin Obes. 2014;4(2):121–4.
16. Klampfer L, Huang J, Sasazuki T, et al. Inhibition of interferon γ signaling by the short chain fatty acid butyrate[1]1Montefiore Medical Center New Research Initiative Award to LK and the American Cancer Society Institutional Research Grant to LK (ACS IRG# 98-274-01), UO1 CA88104 (to LA), and P30-13330 from NCI. Mol Cancer Res. 2003;1(11):855–62.
17. Goergen M, Manzoni D, De VB, et al. Influence of obesity-susceptibility loci (MC4R and INSIG2) on the outcome of weight loss and amelioration of co-morbidity in obese patients treated by a gastric-bypass. Bulletin de la Societe des sciences medicales du Grand-Duche de Luxembourg. 2011;2:7–24.
18. Melka MG, Bernard M, Mahboubi A, et al. Genome-wide scan for loci of adolescent obesity and their relationship with blood pressure. J Clin Endocr Metab. 2012;97(1):E145–E50.