

Monogenic obesity prevalence and response to bariatric surgery in a cohort of Emirati patients

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Introduction

We have previously shown good short-term but variable long-term weight loss outcomes of bariatric surgery (BS) in a cohort of obese patients with MC4R deficiency. This study aims to elucidate the epidemiological landscape of Monogenic Obesity (MO) and quantify bariatric surgery's effectiveness in weight reduction among Emirati patients with severe obesity.

Methods

We selected a group of patients with extreme obesity ($\geq 50 \text{ kg/m}^2$) from our prospective BS cohort for genetic testing (MO genes including LEPR, PCSK1, POMC, MC4R and BDNF. Combined Annotation-Dependent Depletion (CADD) and Sorting Intolerant From Tolerant (SIFT) tools were used to measure variant deleteriousness. Relevant linked information including anthropometry, type (and number) of bariatric surgery, diabetes status and glycosylated haemoglobin were available from prospectively conducted questionnaires and patient records. Patients confirmed to have mutations (cases) with complete follow-up data ($n=14$) were compared to controls who were tested and in whom no mutations were found ($n=35$); relevant comparisons were made over 2 years (baseline, median of 3-, 6-, and 12-months post-surgery).

Results

The bariatric surgery cohort included 1089 patients (56% were males); 828 had recorded information on the type and number of surgeries (mean age of 38.6 ± 11.3 years). Diabetes status was identified as T2DM (64), IFG (54), IGT (17) and IFGC IGT (15). 129 (42%) patients were NGT; 41 patients had unrecorded diabetes status. 84 patients (11 %) underwent multiple (79 with two) surgeries. 190 morbidly obese patients (age 40.0 ± 5.1 years; BMI $54.73 \pm 10.49 \text{ kg/m}^2$) were selected and genotyped. 29 mutations (15.2 %, $n=26$) were found, of which four were novel polymorphisms of the UCP2 and MC4R genes. Baseline HbA1c was $6.02 \pm 1.25\%$. Compared to baseline, there were significant decreases in HbA1c, total weight and BMI at all time points over 24 months. The largest drop in weight occurred at 3 months post-surgery (172.10 ± 31.31 to $119.05 \pm 17.70 \text{ kg}$). There was a reduction in HbA1c to 5.14 ± 0.45 twelve months post-surgery. Percentage and excess weight loss were significantly less, compared to baseline, at all time points when comparing the cohort with mutations with controls without mutations.

Discussion

The prevalence of monogenic obesity is high (15.2% in our cohort, including four novel mutations) in patients with extreme obesity ($\geq 50 \text{ kg/m}^2$) undergoing bariatric surgery. Overall, the response to BS is acceptable but less than a comparator group without MO.