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***Prospective Study***

**Effect of bariatric surgery on adiposity and metabolic profiles: A prospective cohort study in Middle-eastern patients**

Mazidi M *et al.* Adiposity and metabolic profiles following bariatric surgery

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**Abstract**

***AIM***

To investigate changes in adiposity and cardio-metabolic risk profile following Roux-en-Y gastric bypass in patients of Middle Eastern ethnicity with severe obesity.

***METHODS***

This prospective cohort study involved 92 patients who met the indications of bariatric surgery. Post-procedure markers of obesity and cardiometabolic profile were monitored regularly for a year.

### *RESULTS*

### Mean body mass index decreased by 29.5% from 41.9 to 29.5 kg/m2 between baseline and 12-mo follow-up, while mean fat mass decreased by 45.9% from 64.2 kg to 34.7 kg. An improvement was also observed in the gluco-metabolic profile with both fasting glucose and HbA1c substantially decreasing (*P* < 0.001).

### *CONCLUSION*

### The present study shows the short to medium term (1 year) health benefits of bariatric surgery for patients of Middle Eastern ethnicity.

**Key words:** Bariatric surgery; Anthropometric indices; Metabolic profile; Cardiometabolic risk

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**Core tip:** The present study obviously shows the health benefits of Roux-en-Y gastric bypass bariatric surgery for the patients of Middle Eastern ethnicity, particularly during the first twelve months of follow-up.

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**INTRODUCTION**

Obesity and related complications pose increasing health challenges worldwide[[1](#_ENREF_1)]. Obesity is associated with the development of various comorbidities including type 2 diabetes mellitus, hypertension, and dyslipidemia, which are well-documented risk factors for cardiovascular disease (CVD), as well as musculoskeletal disorders[[2-5](#_ENREF_1)].

 Dietary intervention, lifestyles modification and prescription of pharmaceuticals are the main methods of obesity prevention and control. However, nowadays there is growing attention to metabolic surgery/bariatric surgery, as a promising method to treat obesity. Roux-en-Y gastric bypass (RYGB) is a practical bariatric surgical procedure that has been shown to induce considerable weight loss in obese patients through restriction and malabsorption[[6](#_ENREF_1)]. Improvement in insulin secretion and sensitivity; and consequently improvement in type 2 diabetes mellitus control after bariatric surgery have been reported in the clinical investigations[[7,8](#_ENREF_1)]. Randomized controlled trials and observational studies support the medium-to-long term efficacy of RYGB in reducing body weight and fatness and controlling the major metabolic comorbidities of obesity[[9,10](#_ENREF_1)]. But there still remain some uncertainties about the effects of bariatric surgery on cardiometabolic profiles of obese individuals especially in the Middle East countries and available studies on the efficacy of bariatric surgery mostly originate from the West and predominantly involve Caucasian or African American patients, while a growing number of people with severe obesity is increasingly found in developing countries[[11](#_ENREF_1)]. Asian subjects have a different relationship between obesity and diabetes risk to Caucasians and hence the impacts of bariatric surgery in Asian populations may also differ from the effects reported previously in Caucasians. For example, Capella *et al*[[12](#_ENREF_1)] reported when they looked at patient sub-populations, they found that Afro-Americans lost significantly less weight than Hispanic Americans or White Americans. In addition, Hispanic American women lost less weight than White American women.

 To the best of our knowledge, there is no study to investigate the effect of bariatric surgery in Iranian and Middle Eastern ethnicity, hence the aim of the current study was to investigate the impact of the bariatric surgery on adiposity and metabolic profiles in the patients with Middle Eastern ethnicity.

**MATERIALS AND METHODS**

***Study design, setting, and participant***

This prospective observational cohort study was conducted between 2011 and 2015 at the Qaem and Imam Reza hospitals of Mashhad, Iran. A total of 92 participants (35 women, 38.0%) who had a body mass index (BMI) greater than 40 kg/m2 (or more than 35.40 kg/m2 with severe comorbidities due to obesity), aged between 25 and 65 years took part in the study. They all met the criteria for performance of bariatric surgery[[13](#_ENREF_1)]. Pregnant or breast feeding women, patients with known malignancies and those with any condition precluding surgery or general anesthesia were excluded from the study. None of the patients had previously undergone bariatric surgery.

***Baseline evaluations***

Height (to the nearest 0.1 cm) was measured using a portable stadiometer (OTM, Tehran, Iran) in the upright position, without shoes, with the subject stretching to the maximum height and the head positioned in the Frankfurt plane. The weight and body composition were measured by a bio-impedance analyzer (BIA) (Tanita BC-418 MA, Tanita Corp., Japan) and participants were dressed in light clothing (*i.e.,* no shoes, sweaters or jackets, with 0.1 Kg accuracy, frequency range 50-60 Hertz) [[14](#_ENREF_1)]. The BIA was calibrated according to the manufacturer’s guidelines before each testing and the participants were informed in advance not to use any substance affecting their body composition (*e.g.,* alcohol and coffee) 24 h before the test[[14](#_ENREF_1)].

Body composition (weight, fat mass, free fat mass) was determined by bioelectric impedance using a Tanita Body Composition Analyzer (Tanita Corporation, Tokyo, Japan). Blood pressure was measured from the dominant arm, with subjects in a sitting position, after 10 min of rest. Measurements were repeated 3 times at 2-min intervals and the means of the 3 measurements were recorded.

For each participant, blood samples were drawn into serum-separating tubes after an overnight fast. Part of the sample was used immediately to measure fasting plasma glucose by the glucose-oxidase, GOD-PAP method[[15](#_ENREF_1)] and plasma lipids (cholesterol and triglyceride, high-density lipoprotein (HDL) and low-density lipoprotein (LDL)) were measured using enzymatic methods. Aspartate aminotransferase (AST), and alanine aminotransferase (ALT) were analyzed using standardized methods [spectrophotometry corresponding commercial kits (Pars Azmoon, Iran)][[16](#_ENREF_1)]. Total bilirubin and HbA1c were measured by commercially provided kits (Pars Azmun, Iran).

***Index surgical procedure and follow-up evaluations***

All 92 participants underwent a RYGB procedure following the same surgical technique performed by a single surgeon[[17](#_ENREF_1)]. Patients were NPO (Nil per OS) for three days after the surgery; thereafter, liquid diet was carefully started after a swallow test with gastrografin, and was maintained for two weeks. Upon discharge, patients were followed at the outpatient clinics of Qaem and Imam Reza hospitals, Mashhad, each 3 months for 12 mo with repetition of the assessments performed at baseline under the supervision of nutritionist and medical group.

***Ethical consideration***

All patients were completely informed about the surgical procedure offered including potential advantages, probable complications and cost-benefit ratio and completed a written informed consent to participate in the study. The study protocol was approved by the Mashhad University of Medical Sciences' Ethics Committee.

***Statistical analysis***

SPSS software (version 11.5, Chicago, IL, United States) was used for statistical analysis. Kolomogrov-Smirnov tests were used to evaluate the normality of data. Values are expressed as mean ± SD for normally distributed variables. For normally distributed variables paired t-test was used to compare the before and after surgery and equivalent test was used for the skewed variables. Change in adiposity markers and cardio-metabolic profiles during follow-up were investigated using the analysis of variance (ANOVA) and Kruskal-Wallis tests for repeated measures. *P*-value ≤ 0.05 was considered significant.

**RESULTS**

***Baseline adiposity and change during the first 12 mo of follow-up***

The mean BMI was 41.9 ± 4.5 kg/m2 at baseline and steadily decreased down to 29.5 ± 3.8 kg/m2 at 12 mo, giving a relative change of -29.5%. The relative change in BMI from baseline was -11.4% at 3 mo and -18.8% at 6 mo. The mean fat mass was 64.2 ± 11.0 kg at baseline and decreased by 45.9% down to 34.7 ± 8.2 kg at 12 mo. The relative change in fat mass was -21.0% at 3 mo and -37.5% at 6 mo (Table 1). In analyses stratified by gender, the patterns were very similar in men and women. For instance, the mean BMI decreased from 42.4 ± 5.2 kg/m2 at baseline to 29.4 ± 4.5 kg/m2 at twelve months in men, and from 41.1 ± 6.1 kg/m2 to 29.6 ± 3.3kg/m2 in women.

***Baseline cardiometabolic risk profile and trajectories during the first 12 months of follow-up***

HDL increased (*P* < 0.001) while other cardiovascular risk factors including total cholesterol, LDL cholesterol, triglycerides and Hs-CRP levels steadily decreased (*P* < 0.001) between baseline and 12-month follow-up, indicating an improvement of the cardiovascular risk profile (Table 1). An improvement was also observed in the gluco-metabolic profile with both fasting glucose and HbA1c substantially decreasing (*P* < 0.001) (Table 1). Both ALT and AST steadily decreased while total bilirubin increased during the first twelve months of follow-up (*P* < 0.001). Again, patterns were very similar in men and women taken separately.

**DISCUSSION**

For the first time in a population of Middle East ethnicity, this study evaluated the effect of bariatric surgery on adiposity indices and cardio-metabolic profiles in severely obesity subjects. We found that surgical intervention had a marked effect on adiposity which was substantiated by the significant decrease in BMI and fat mass during the first twelve months of follow-up. This was paralleled by significant and gradual improvement of the cardio-metabolic profiles over the same time period.

 Consistent with our results, several studies have previously reported the beneficial effects of bariatric surgery on adiposity and cardio-metabolic profiles[[18-20](#_ENREF_18)]. A prospective study conducted on 1156 severely obese participants in Utah reported that patients lost 27.7% of their initial body weight six years after RYGB surgery[[21](#_ENREF_18)]. They also found that 94% of patients receiving RYGB surgery maintained at least 20% weight loss two years after surgery[[21](#_ENREF_18)]. Observed weight loss in the Utah study was similar to the results of the Longitudinal Assessment of Bariatric Surgery (LABS) study[[22](#_ENREF_18)]. Furthermore, in line with our findings, clinical studies with different age groups showed clinically meaningful weight loss and improvement in key health conditions among the participants who underwent bariatric surgery[[23,24](#_ENREF_18)].

 Considerable improvement of all lipid sub-fractions was observed during follow-up in our study, in line with other investigations[[20,25,26](#_ENREF_18)]. The Swedish obese subject (SOS) study indicated that the incidence rate of hypertriglyceridemia was significantly lower in the surgically treated group than in the control group after two years[[27](#_ENREF_18)]. In addition, significant post-operative improvement of gluco-metabolic profiles was observed during follow-up in our study. Improvement of HbA1C without medications has been reported in other studies[[1,21,28](#_ENREF_18)].

 In line with our findings, several pieces of evidence from clinical trials suggest that RYGB is associated with marked improvement in nonalcoholic fatty liver disease[[29-31](#_ENREF_18)]. The long-term effect of bariatric surgery on liver enzymes in the Swedish Obese Subjects (SOS) study[[32](#_ENREF_18)] indicated that bariatric surgery was related to lower serum ALT and AST levels at 2- and 10- year follow-up. In addition, analysis of the relation between changes in transaminase levels and changes in body weight indicated that weight gain was related to a substantial increase in transaminase levels.

In this study we have found that total bilirubin increased after the surgery, which is in line with other studies[[33-42](#_ENREF_18)]. Very recently, Mazidi et al have reviewed role of bile acids its subtractions on weight loss and glycaemic control after the bariatric surgeries[[43](#_ENREF_18)]. They have elaborated that there is a correlation between the concentration of the total bile acid and improvements in several key metabolic parameters after bariatric surgery[[43](#_ENREF_18)]. It has been reported that there was an inverse correlation between bile acid concentrations and postprandial glucose and triglycerides, and a positive correlation with adiponectin and peak GLP-1 levels following a mixed meal test[[33,44](#_ENREF_18)]. Moreover, augmented bile acid concentration (It has been suggested that changed upper intestinal tract structure after surgery might have an impact on the enterohepatic circulation of bile acids) could contribute to enhancements in insulin sensitivity, incretin secretion, lipid metabolism and postprandial glycemia after surgery[[33,45](#_ENREF_18)]. As mentioned above, the release of GLP-1 is correlated with bile acids[[43](#_ENREF_18)]. Therefore bile acid-dependent increases in postprandial GLP-1 concentrations may be somewhat responsible for the achievements of bariatric surgery in terms of both weight loss and glycaemic control[[46](#_ENREF_18)].

***Strengths and limitations***

This study has strengths. The study is sufficiently powered to test the associations. We have repeated investigations of a range of adiposity and cardio-metabolic markers at baseline and during follow-up, which allowed us to carefully characterize their trajectories up to 12 mo after bariatric surgery. Moreover, it is one of the biggest studies which have done in Middle East population. The findings from our study have to be considered in the context of some study limitations as well. We didn’t collect data on the lifestyle of participants and are therefore unable to determine their contribution to some of the observed effects. Moreover, for evaluating the body composition dual-energy X-ray absorptiometry would be a better choice which we did not use it.

The present study suggests health benefits of RYGB bariatric surgery for the patients of Middle Eastern ethnicity, particularly during the first twelve months of follow-up. Our findings suggest that RYGB bariatric surgery has favorable short and medium term effects on adiposity and cardio-metabolic profiles in this population.

**COMMENTS**

***Background***

Roux-en-Y gastric bypass (RYGB) is a type of weight-loss surgery, bariatric surgery. It’s often done as a laparoscopic surgery, with small incisions in the abdomen.

***Research frontiers***

This is the first and biggest study in middle-east subjects.

***Innovations and breakthroughs***

In this study they follow the subjects for 12 mo and through time, for each three months they have explore their adiposity and cardiometabolic factors.

***Applications***

Practical applications of our finding is that it can shed light on the post-operative side effct6s and changes after the bariatrics surgery for such a novel population.

***Peer-review***

The article "Effect of bariatric surgery on adiposity and metabolic profiles. A prospective cohort study in middle-eastern patients", by Mohsen Nematy *et al* is a clinical prospective study on a cohort of middle eastern obese patients treated by RYGB. The alleged main difference between this and other similar studies is that the population was of Middle Eastern ethnicity.

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**Table 1 Changes of anthropometrical and clinical factors from baseline to 12 mo follow up**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Factors** | **Baseline (91)** | **3 mo (86)** | **6 mo (83)** | **12 mo (80)** | ***P* value** |
| BMI (kg/m2) | 41.9 ± 4.5 | 37.1 ± 5.0 | 34.0 ± 4.6 | 29.5 ± 3.8 | < 0.001 |
| FM  | 64.2 ± 11.4 | 50.7 ± 9.2 | 40.1 ± 8.7 | 34.7 ± 8.2 | < 0.001 |
| FFM  | 68.3 ± 15.2 | 64.1 ± 15.8 | 60.7 ± 16.3 | 58.0 ± 16.6 | < 0.001 |
| LDL (mg/dL) | 162.2 ± 9.7 | 147.9 ± 11.3 | 139.7 ± 13.2 | 122.8 ± 19.5 | < 0.001 |
| HDL (mg/dL) | 35.7 ± 3.0 | 37.1 ± 3.4 | 36.9 ± 3.7 | 39.4 ± 5.3 | < 0.001 |
| TG (mg/dL) | 232.6 ± 26.1 | 208.5 ± 31.3 | 168.2 ± 28.7 | 132.6 ± 25.8 | < 0.001 |
| TC (mg/dL) | 244.1 ± 20.1 | 224.9 ± 24.8 | 198.2 ± 28.4 | 180.2 ± 42.7 | < 0.001 |
| FBG (mg/dL) | 142.5 ± 18.1 | 115.1 ± 15.8 | 102.5 ± 10.1 | 97.1 ± 8.2 | < 0.001 |
| HbA1c (%) | 6.8 ± 1.1 | 5.7 ± .92 | 5.5 ± 1.0 | 5.4 ± 1.2 | < 0.001 |
| ALT (IU/L) | 44.8 ± 8.5 | 33.0 ± 9.6 | 30.1 ± 9.4 | 25.1 ± 8.3 | < 0.001 |
| AST (IU/L) | 35.7 ± 7.0 | 28.1 ± 5.5 | 24.5 ± 5.2 | 23.5 ± 4.8 | < 0.001 |
| Total Bilirubin(mg/dL) | 5.0(3.2-6.1)  | 6.0 (4.1-8.5)  | 8.0 (5.5-9.5)  | 9.0 (6.1-11.8)  | < 0.001 |
| Hs-CRP (mg/dL) | 24.0 (19.0-26.0)  | 20.0 (14.5-27.2)  | 18.1 (12.1-26.6)  | 7.7 (4.6-10.8)  | < 0.001 |

Values expressed as mean ± SD for normally distributed data, and median and 25th-75th percentiles for non-normally distributed data. *P*-value is from the ANOVA or Kruskal-Wallis and it refers to total difference between follow up times. BMI: Body mass index; FBG: Fasting blood glucose; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol;TG: Triglyceride; TC: Total cholesterol; ALT: Alanine transaminase; AST: Aspartate transaminase; Hs-CRP: High-sensitivity C-Reactive Protein; FM: Fat mass; FFM: Fat free mass.



**Figure 1 Increased concentration of bile acids caused to activation of farnesoid X receptor A and G protein-coupled bile acid receptor, these two receptors have adverse impact on different tissues.** Activation of farnesoid X receptor A (FXRA) and G protein-coupled bile acid receptor (TGR5) can stimulate the secretion of glucagon-like peptide I and II (GLP), and GLP have positive effect on pancreas.