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ORIGINAL ARTICLE

Metabolic improvement of morbid obese patients following Roux-en-Y gastric bypass surgery: A prospective study in Mashhad, Iran

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Abstract

Background and Aim Obesity is one of the greatest public health concerns worldwide. Weight loss surgeries have been increased in recent decades due to the world's epidemic of obesity. The aim of this prospective study is investigating metabolic factors of morbid obese patients following Roux-en-Y gastric bypass surgery.

Methods This was a nonrandomized prospective cohort study conducted from 2010 to 2013 on 60 consecutive patients who had body mass index (BMI) of more than 40 kg/m^2 and met the surgical indication criteria of bariatric surgery. Upon discharge, patients were followed in outpatient clinic of Qaem Hospital, Mashhad, Iran, each 3 months for 12 months. Measurement of anthropometric and metabolic indices was done in each postoperative visit.

Results Mean BMI reduction was 15.26 ± 3.45 kg/m^2 in the patients with an average value of 28.84 ± 3.94 (range from 22 to 40 kg/m^2), which was significantly lower than the base value ($p < 0.001$). After a 12-month follow up, patients had lower low-density lipoprotein, triglycerides, and total cholesterol ($p < 0.001$ for all the variables), while achieving a greater high-density lipoprotein ($p = 0.004$). An improvement was seen in all of hypertensive patients after a 3-month follow up and blood pressure remained within normal limit in further follow ups. Complete remission was observed in all the patients with obstructive sleep apnea.

Conclusion It appears reasonable that multidisciplinary treatment including surgical alternatives should be concerned for all morbidly obese patients, considering high rate of failure of conservative medical therapy in this setting.

Keywords Metabolic improvement · Obese patients · Roux-en-Y gastric bypass surgery

Introduction

Obesity is one of the greatest public health concerns worldwide. The prevalence of obesity (body mass index of more than 30 kg/m^2) is doubled in the past 25 years in industrialized countries [1]. Based on the International Association for the Study of Obesity, there are 525 million adults with obesity worldwide and twice that number overweight [2], which means that there are almost 1.5 billion adult people worldwide that are at risk of chronic side effects of obesity. Obesity is associated with increased risk of type 2 diabetes mellitus (T2DM), dyslipidemia, hypertension, musculoskeletal disorders, cardiovascular diseases, and mortality [3, 4]. T2DM rate increases alongside with increment of obesity over the world. An estimate of 170 million people affected by T2DM worldwide was recently reported [5]. The

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first treatment of T2DM is surely lifestyle modification alongside with pharmacotherapy. However, surgical procedures have recently been considered as effective adjuvant therapy for patients with obesity and T2DM [6].

Weight loss surgeries have been increased in recent decades due to the world's epidemic of obesity. Many morbid obese patients around the world undergo variant bariatric surgical procedures such as gastroplasty, ring, gastric bypass, sleeve gastrectomy and laparoscopic adjustable gastric banding [7, 8]. Roux-en-Y gastric bypass (RYGB) is an effective bariatric procedure that results in sustained weight loss by means of restriction and malabsorption [7, 8].

RYGB consists of creating a small gastric pouch and a gastrojejunal anastomosis which leads to weight loss through both restriction and malabsorption. There are many techniques of gastrojejunal anastomosis with no consensus on which is the best [9]. Currently, bariatric surgery is recommended for individual with a body mass index (BMI) of more than 40 or more than 35 with severe comorbidities due to obesity [10].

Significant weight loss after bariatric surgery has been reported in the literature as well as improvement in T2DM, dyslipidemia, cardiovascular, and mortality risk. Waist circumference has also been reported to significantly decrease after bariatric surgeries in most of previous articles [11, 12].

Moreover, in some investigations, lipid profile and fatty liver disease have been shown favorable results in obese patients who have had bariatric surgeries compared with medically treated individuals [13].

Based on previous investigations, since RYGB induce a malabsorptive condition in patients compared to pure restrictive surgeries, for the same amount of weight loss, greater decrease of cholesterol level was observed with the former than with the latter technique [14]. Yet, there is insufficient result for recommending a bariatric surgical procedure for lipid lowering alone or risk reduction of cardiovascular disease alone, independent of BMI criteria [15]. Data are also insufficient to reach absolute conclusion about long-term survival [6].

Considering the growing number of this kind of surgery, post-surgical follow ups are important to determine long-term effects and efficacy. It is thus aimed in this prospective study, to investigate anthropometric changes as well as the improvement or remission of T2DM, hypertension, dyslipidemia, obstructive sleep apnea, and biochemical blood indices in a series of morbid obese patients submitted to RYGB surgical procedure through 1 year of follow up.

Methods

Patients and study design

This was a nonrandomized prospective cohort study conducted from 2010 to 2013 on 60 consecutive patients who had BMI of more than 40 kg/m^2 (or more than 35 with severe comorbidities due to obesity) and met the surgical indication criteria of bariatric surgery [16]. All patients were completely informed about the surgical procedure offered including potential advantages, probable complications, and cost-benefit ratio and filled the written informed consent.

Demographic characteristics as well as clinical history and anthropometric measurements were done and recorded in predesigned forms. Patients' measurements consisted of the following evaluations: a standard exam to assess height, weight and BMI, blood pressure, as well as history of diet, physical activity, and history of complications due to the obesity. Anthropometric measurements were also performed.

Patients were weighed using a digital load cell balance (Soehnle, West Germany) which had a precision of 0.1 kg. The heights of the patients were measured without footwear, by a vertically mobile scale (Holtain, Crymych, UK) and expressed to the nearest 0.1 cm. BMI was calculated as weight (kilograms) divided by height (square meters). Presence of hypertension was defined based on Mancia et al. criteria [17]. The criteria were systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg or current treatment with antihypertensive agents. Diabetes mellitus was defined according to the American Diabetes Association guidelines [18]. It was defined as two fasting plasma glucose of more than 125 mg/dL or current treatment with oral hypoglycemic agents or insulin.

All patients were preoperatively studied by a multidisciplinary team including psychiatrist, endocrinologist, nutritionist, anesthesia specialist, and surgeon. Blood sampling was obtained from all the patients prior to the surgery, after 12 h fasting for biochemical assays including fasting blood glucose (FBS) and glycated hemoglobin (HbA_1C) as well as lipid profile including total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglyceride.

Pregnant women or those on breast feeding, patients with lower 25 and over 65 years of age, patients with known malignancies, those who could not medically undergo surgery or general anesthesia, and disinclination to continue were excluded from the study. Patients with current coronary artery disease, history of arrhythmia, cerebrovascular accident or peripheral artery disease, current therapy with vasoactive drugs, active smoking, current or prior alcohol consumption of more than 60 g daily, and creatinine >2 mg/dL were also excluded from the study. Additionally, none of the patients had previously undergone bariatric surgery.

Surgical technique

The surgical technique was the same for all the patients (RYGB) and performed by the same team of surgeons. The surgical procedure was the similar for all the patient (RYGB)

[19]. During RYGB surgery, 50 cm from the proximal jejunum at 40–50 cm distal to the ligament of Treitz was dissected and a 150 cm antecolic Roux limb was created. A small 30–50 cm^3 proximal gastric pouch was also created. The Roux limb was anastomosed to alimentary limb 100 cm below the gastrojejunostomy.

Patients were nil per oral (NPO) for 3 days after the operation. Then, after a swallow test with gastrografin, liquid diet was cautiously started. Liquid diet continued for 2 weeks and patients were discharged as soon as they could drink, walk, and be free of important clinical complication.

Follow up

Upon discharge, patients were followed in outpatient clinic of Qaem Hospital, Mashhad, Iran, each 3 months for 12 months. Measurement of weight, waist and hip circumference, blood pressure, laboratory testing for fasting blood glucose, HbA_1c, total cholesterol, as well as HDL and LDL cholesterol and triglyceride level was performed in each postoperative visit.

In each visit, blood samples were collected after 12 h of fasting into non-anticoagulant tubes for biochemical tests and were centrifuged at 3000 rpm for 5 min and serum samples were harvested and kept at −70 until testing. Lipid profile was measured by an auto analyzer (Abbott analyzer, Chicago, IL, USA) in the biochemical laboratory of Qaem Hospital, Mashhad, Iran. Lipid profile as well as glucose and HbA_1c were drawn at baseline and at 3, 6, 9, and 12 months postoperatively.

Ethical considerations

The study protocol was approved by the Ethical Committee in Research of Mashhad University of Medical Sciences.

Statistical analysis

Before statistical analysis, normal distribution and homogeneity of the variances were tested. Data on qualitative characteristics are expressed as numbers and percentage values. Data on quantitative characteristics are expressed as mean±standard deviation (SD). Data were analyzed and figures were constructed using Statistical Package for Social Sciences computer software (SPSS version 11.5, Chicago, IL, USA).

Results

Of the 60 patients who participated in the study, 55 patients (91.7 %) were female and 5 patients (8.3 %) were male. Mean age was 34.5 ± 9.17 years at the beginning of the study. Patients were followed up each 3 months. Postoperative follow up was 1 year in all the patients. Postoperative complication did not occur in any of the patients during the 1-year follow up.

Anthropometric characteristics

Preoperative mean weigh was 115.16 ± 16.41 kg in the patients which was decreased to 75.35 ± 10.78 kg after 1-year follow up. Mean weight loss was calculated as 34.57 % after 1-year post-surgery. Preoperative mean BMI was 44.20 ± 5.32 kg/m^2 (range 35–57.5). At 12-month distance follow up, mean BMI reduction was 15.26 ± 3.45 kg/m^2 in the patients with an average value of 28.84 ± 3.94 (range 22–40 kg/m^2), which was significantly lower than the base value ($p < 0.001$).

Preoperative mean waist circumference was 124.06 ± 11.71 cm (range 100–152) in the patients. Mean waist circumference reduction was 26.75 ± 8.60 cm after 12-month follow up (range 70–125 cm) with an average of 97.45 ± 12.65 cm, which had significant decrease in comparison with the baseline mean value ($p < 0.001$). Anthropometric characteristics of the patients at the baseline of the study and during the follow ups are presented in Table 1.

Clinical history and laboratory data

Of the 10 patients with T2DM at the beginning of the study, complete remission was observed in all the diabetic patients at 6-month post-surgery because both fasting blood sugar and hemoglobin A_1C were reached to normal levels, thus, medical therapy was discontinued after 6 months in all the diabetic patients (Table 2).

After a 12-month follow up, patients had lower LDL, triglycerides, and total cholesterol ($p < 0.001$ for all the variables), while achieving a greater HDL ($p = 0.004$). Total cholesterol dropped by 10.64 %, 9.45 %, 9.39 %, and 6.10 % at 3, 6, 9, and 12 months, respectively. LDL dropped by 12.19 %, 6.85 %, 5.69 %, and 9.3 % at 3, 6, 9, and 12 months, respectively. Triglyceride dropped steadily by 17.82, 16.21, 16.55, at 3, 6, and 9 months, respectively, and grossly dropped by 24.23 % after 12 months. HDL level increased by 0.56 %, 18.07 %, 9.56 %, and 0.87 % at 3-, 6-, 9-, and 12-month follow up, respectively. The evolution of lipid sub-fractions during 12-month follow up after bariatric surgery is given in Table 2.

Thirteen patients had chronic hypertension at the beginning of the study. An improvement was seen in all of hypertensive patients after 3-month follow up and blood pressure remained within normal limit in further follow ups.

Of the 10 patients who complained from obstructive sleep apnea (OSA), complete remission was observed in all the patients after 1 year of follow up.

Table 1 Changes in anthropometric parameters in 60 severely obese patients after Roux-en-Y gastric bypass surgery

	At baseline	Postoperative			
		3 months	6 months	9 months	12 months
Weight (kg)	115.16 ± 16.41	98.50 ± 12.83	88.69 ± 11.72	81.70 ± 11.35	75.35 ± 10.78
Height (cm)	161.43 ± 7.33	161.41 ± 7.56	161.43 ± 7.39	161.45 ± 7.42	161.51 ± 7.37
BMI (kg/m^2)	44.20 ± 5.32	37.83 ± 4.75	33.99 ± 4.27	31.30 ± 4.03	28.84 ± 3.94
Waist circumference (cm)	124.06 ± 11.71	116.61 ± 11.08	109.95 ± 10.63	103.81 ± 11.53	97.45 ± 12.65

Discussion

According to strong evidences, nonsurgical treatment, per se, is not enough among severe or morbid obese subjects [20]. Bariatric surgery especially gastric bypass achieves significant weight loss, reduces comorbidities, and improves quality of life. There is also explosive development of bariatric surgery reported in Iran [21]. Our study population was composed by a majority of women (91.7 %) in their early thirties. Prior studies were also formed by majority groups of young women [22].

Anthropometric indices including BMI and waist circumference significantly decreased after the surgery and sustained after 1 year of follow up. Rat models previously exhibited reduced food intake as well as avoidance of high-fat diets [23]. In human, RYGB leads to a selective reduction of the reward value of fatty and sweet tastes [24]. Previous studies showed postoperatively enhanced post-prandial satiation, which was associated with enhanced release of satiety gut hormones such as glucagon-like peptide 1 (GLP-1) and peptide tyrosine (PYY) [25]. The reduction in appetite and increase in satiety coupled with a shift in preferences for lower glycemic index foods are probably the major factors for sustained long-term weight loss after RYGB surgery.

FBS and HbA_1C, as insulin resistance parameters, were decreased by 64 mg/dL and 2.5 %, respectively during the study. Medical therapy was discontinued after 6 months in all the diabetic patients due to normalization of FBS and HbA1C. Significant postoperative improvement of Hb1Ac has been reported in previous studies [12, 26]. After 2 years of follow up, FBS was also reported to be lower in patients who had RYGB compared with those who receive medical therapy [12, 26]. Decreased levels of FBS were also reported with other types of bariatric surgeries [27, 28]. Also, serum bile acid levels will increase and balance in the postoperative state after RYGB which are associated with improvement of glucose profile [29, 30]. Bile also improves glycemia by stimulating GLP-1 and PYY incretion [31]. Kashyap et al. in a prospective trial on 60 subjects with uncontrolled T2DM and moderate obesity reported improvement of pancreatic β cell function after RYGB surgery but not after sleeve gastrostomy [32]. Additionally, plasma concentration levels of insulin had been reported to reduce after RYGB, but the post-prandial response had been exaggerated [33]. In aggregate, the authors want to emphasize that combining surgery with medical therapy are suggested for severely and morbidly obese patients who suffer from T2DM.

Significant reduction of all lipid sub-fractions was reported during follow up. Since dyslipidemia is a main risk factor that explains the excessive mortality rate in severely obese patients, it should be noticed as a noteworthy outcome of RYGB surgery. According to Benaiges et al. in a prospective cohort study, LDL cholesterol fell significantly in RYGB group while no significant changes were recorded in the sleeve gastrectomy group, after 1-year follow up [34]. The study noted that RYGB surgery produces a clear benefit in all lipid fractions [34]. In contrast, previous studies with restrictive surgery techniques have reported no significant difference in total cholesterol levels [35–37]. We observed mean decrease of 71.1 mg/dL in total cholesterol after 1 year of

Table 2 Changes in insulin resistance parameters and lipoprotein profile in 60 severely obese patients after Roux-en-Y gastric bypass surgery

	Baseline	3-month follow up	6-month follow up	9-month follow up	12-month follow up
FBS (mg/dL)	146 ± 33.92	109 ± 25.40	96 ± 7.12	88.5 ± 10.17	82 ± 11.46
HbA_1C (%)	7.7 ± 0.4	5.8 ± 0.16	5.5 ± 0.26	5.3 ± 0.19	5.2 ± 0.13
Total cholesterol (mg/dL)	228.5 ± 25.00	204.2 ± 24.70	184.9 ± 15.4	167.5 ± 16.3	157.4 ± 19.5
LDL-C (mg/dL)	160 ± 12.67	140 ± 8.16	130 ± 6.6	123 ± 11.1	111.5 ± 15.4
HDL-C (mg/dL)	35.6 ± 0.44	35.5 ± 6.1	41.8 ± 3.4	45.8 ± 6	46.2 ± 3.8
Triglyceride (mg/dL)	216 ± 27.1	177.5 ± 25.1	148.7 ± 27.8	124 ± 24.3	94 ± 22.2

Data are expressed as mean±standard deviation

LDL low-density lipoprotein, *HDL* high-density lipoprotein

follow up in our patients. It is in accordance with previous studies [35, 38, 39] and is caused by a similar reduction in LDL cholesterol level.

HDL cholesterol was increased by 10.6 mg/dL after 1 year of follow up. Most of the previous studies have reported significant HDL increment after RYGB surgery [35, 39, 40]. In our study, mean triglyceride level dropped by 122 mg/dL after 1-year follow up. As previously described, bariatric surgery results in 30 % to 40 % reduction in triglyceride concentration [38, 41]. We want to emphasize that the benefit on improvement of cholesterol fractions of RYGB surgery are greater than those obtained with available pharmacological strategies for severely obese patients.

The current study sheds light on the evolution of anthropometric parameters and lipid profile as well as insulin tolerance indices after RYGB surgery which induced weight loss in a series of severely obese patients displaying a high range of BMIs. The magnitude of weight loss (34.57 %) and its persistency are considered as major contributors in glucose control after bariatric surgery. Understanding main mechanisms of diabetes remission after the surgery can help develop new therapeutic medical or surgical interventions in diabetic patients with severe obesity.

Multidisciplinary treatment including surgical alternatives should be considered for all morbidly obese patients, considering high rate of failure of conservative medical therapy in this setting. Further clinical prospective studies with larger number of patients and longer follow ups are needed to design end- point in terms of long-term metabolic and cardiovascular effects and life expectancy.

Compliance with ethical standards

Ethical considerations The study protocol was approved by the Ethical Committee in Research of Mashhad University of Medical Sciences.

Conflicts of interest SF-s, MM, AT, PR, FR, SH, ED-M, ZSSS, MS, MGM, MTR, AN, SMRP, SA, ST, FF, and MN declare that they have no conflict of interest.

Ethics statement The study was performed in a manner to conform with the Helsinki Declaration of 1975, as revised in 2000 and 2008, concerning human and animal rights, and the authors followed the policy concerning informed consent as shown in springer.com.

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