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Changes in Lipid Profile and Insulin Resistance in Morbidly Obese Patients Following Laparoscopic Total Gastric Vertical Plication

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ABSTRACT

Background: Obesity has emerged as one of the most serious public health concerns in the 21st century. The consequences of this chronic disorder are serious. Bariatric surgery has been shown to eliminate comorbid conditions associated with obesity. Currently it is considered to be the only successful, long-term therapy for morbidly obese subjects.
Objectives: The aim of this study was to evaluate the effect of weight reduction following laparoscopic total gastric vertical plication on anthropometric indices, lipid profile and insulin resistance in morbidly obese patients.
Patients and Methods: 15 severely obese patients aged 32.4 ± 10 yr were enrolled in this prospective study. Body mass index (BMI), waist circumference, high-density lipoprotein cholesterol (HDL-c), total cholesterol (TC), low density lipoprotein cholesterol (LDL-c), triglycerides (TG), fasting glucose, fasting insulin and insulin sensitivity were measured before and 6 weeks after laparoscopic total gastric vertical plication (LTGVP). Insulin-sensitivity was estimated using the homeostasis model assessment of insulin-resistance (HOMA-IR).
Results: Anthropometric indices decreased significantly during the 6 week period after LTGVP. TG, LDL-c, fasting insulin, HOMA-IR and QUIKI also decreased but the changes in HDL-c, TC and fasting glucose were not significant. At baseline, we found a direct correlation between weight and TC, weight and fasting glucose, waist to hip ratio and TG and a negative correlation between waist to hip ratios and HDL-c.
Conclusions: LTGVP results in significant weight loss among morbidly obese subjects, and following weight reduction, lipid profile and insulin resistance improved.

Implication for health policy/practice/research/medical education:
Our findings shows that laparoscopic total gastric vertical plication results significant body weight reduction in morbidly obese subjects and it is associated with an improvement of the lipid and glucose metabolism, but it seems that we need further and longer time researches to clarify other metabolic changes after LTGVP. Our results may be useful for treatment of these high risk groups in practice.

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1. Background

Obesity is considered to be a chronic disease in which body fat stores are increased (1). It is a growing public health problem in developed and developing countries and in many countries it also appears to be responsible for substantial economic and health costs (2). In 2008,

the World Health Organization reported that 35% of adults aged +20 (34% men and 35% of women) were overweight (BMI ≥ 25 kg/m^2). The worldwide prevalence of obesity has more than doubled between 1980 and 2008. In 2008, 10% of men and 14% of women in the world were obese (BMI ≥ 30 kg/m^2). The first national survey of noncommunicable diseases in Iran reported that rates of obesity and overweight have reached a prevalence of approximately 11% and 29% respectively, among Iranian adults over 15 years (3). Esteghamati *et al.* also showed that obesity has grown rapidly in Iran. The rate of increase in the prevalence of obesity is even higher than in developed countries such as the United States, most European countries, and other Middle East countries (4). The consequences of this disorder are serious. Approximately 80% of obese adults have at least one, and 40% have two, or more associated diseases such as type II diabetes, hypertension, cardiovascular disease, cancers, dyslipidemia and/or insulin resistance (5, 6). For morbidly obese patients (BMI > 40 kg/m^2 or ≥ 35 kg/m^2 with significant co-morbidities (7)), bariatric surgery is currently the only reasonably successful, long-term therapy (8, 9). It has been proved to be the most reliable method of obtaining weight loss and long term weight maintenance (9). Buchwald *et al.* reported in a meta-analysis that resolution of type II diabetes was observed in 76.8% of patients, along with hyperlipidemia, hypertension, and obstructive sleep apnea in 70%, 61.7%, and 85.7% patients respectively after bariatric surgery (10). Overall it has been shown to eliminate between 85% and 95% of all co-morbid conditions associated with obesity with an acceptable low level of morbidity (11).

Management of dyslipidemia and insulin resistance is critically important in the prevention of many of these disorders including coronary artery disease in these patients (12). Increased serum levels of low density lipoprotein cholesterol (LDL-c) and/or serum triglycerides (TG) and decreased high-density lipoprotein cholesterol levels (HDL-c) are atherogenic and have frequently been reported in this population. Weight loss is associated with an improvement in fasting glucose, insulin resistance and impaired dyslipidemia (4, 11, 12). Thus, it appears very important to evaluate rapid and significant reductions of weight after new restrictive bariatric surgery techniques, such as laparoscopic total gastric vertical plication (LTGVP) on biochemical and anthropometric profiles in morbidly obese patients. The LTGVP method is a new surgical technique designed to reduce stomach capacity and its advantages remain under investigation.

2. Objectives

The aim of this study was to evaluate changes in lipid parameters (total cholesterol (TC), triglycerides (TG), LDL-c and HDL-c), fasting glucose, insulin, and insulin resistance (measured by the homeostasis model assessment (HOMA) and the quantitative insulin sensitivity check index (QUIKI)) in morbidly obese patients before and 6 weeks after LTGVP.

3. Patients and Methods

3.1. Study population

Between September 2009 and October 2010, 15 severely obese patients older than 19 years with a BMI of more than 35 kg/m^2 who agreed to undergo restrictive bariatric surgery were enrolled consecutively in this prospective study, which looked at the changes of different parameters before and after LTGVP. Exclusion criteria were as follows; diabetes mellitus, hypo- or hyperthyroidism, Cushing syndrome, a history of convulsions, liver and/or kidney disease, ischemic heart disease, rheumatoid arthritis, pregnancy, use of hormonal contraception, lipid-lowering drugs (statins, fibrates) and/or antidiabetic medications (e.g. metformin, thiazolidinediones, insulin). The study protocol was approved by the Tehran University of Medical Sciences' ethics committee and informed written consent was obtained from all subjects.

3.2. Study Protocol

Patients underwent a clinical assessment including; medical history, physical examination and co-morbidity evaluation by a multidisciplinary consulting team. In addition, for all patients, anthropometric measurements and blood sampling for biochemical assays were performed prior to, and 6 weeks after LTGVP.

3.3. Bariatric Surgery

All patients met the criteria detailed by the National Institutes of Health for patient selection to undergo bariatric surgery for morbid obesity (13). Patients underwent LTGVP and 11 patients were operated on by a single team. LTGVP was performed according to the techniques described by Talebpour and Amoli (14) briefly, patients were placed in the supine position with a 30-degree reverse Trendelenburg position. After the release of the greater curvature, continuous suturing from the fundus of the stomach to the antrum, making one or two layers of plication from the anterior wall of the stomach to its posterior wall, was performed.

3.4. Measurements of Anthropometric Indices and Blood Pressure

Qualified trained staff measured anthropometric indices and blood pressure before, and 6 weeks after surgery. Body weight was measured to the nearest 0.1 kg using a calibrated manual weighing scale (Seca 709, Les Mureaux, France). Height was measured to the nearest 0.5cm on a standardized wall mounted height board. Waist circumference (WC) was measured at the minimum circumference between the iliac crest and the rib cage at minimal respiration. Hip circumference was measured at the maximum protuberance of the

buttocks, and the waist-to-hip ratio (WHR) was calculated. BMI was defined as weight in kilograms divided by height in meters squared (kg/m^2). In order to accurately measure blood pressure, participants remained at rest for at least 15 minutes then the same staff member measured blood pressure on the right arm in the sitting position.

3.5. Laboratory Assays

Between 8:00 and 10:00 a.m., peripheral venous blood samples were collected from an antecubital vein after 10-12 hours overnight fasting. Blood samples were centrifuged at 3000g for 10 min and the plasma samples were stored at -80°C until further analysis. Fasting plasma glucose was measured by the glucose-oxidation method (Pars Azmoon, Tehran, Iran) and TC, TG, and LDL-c were determined by enzyme colorimetric assay (Pars Azmoon, Tehran, Iran) using an Eppendorf autoanalyzer (Eppendorf Corp., Hamburg, Germany). HDL-c was measured using a precipitation-based method. The serum insulin level was assayed by the immunoradiometric method (Biosource Europe SA, Belgium). Insulin sensitivity was determined by the HOMA index using the formula: HOMA-IR = fasting insulin (μU/mL) × fasting glucose (mmol/l)/22.5 (15). The QUICKI is derived using the inverse of the sum of the logarithms of the fasting insulin and fasting glucose: 1/(log (fasting insulin, μU/mL) + log (fasting glucose, mg/dL)) (16).

3.6. Statistical Analysis

Data are presented as mean ± SD for numeric variables, and absolute frequencies with percentages in parentheses for categorical variables. Numeric variables were compared using the Wilcoxcon signed rank test. To determine the relationship between the various metabolic and anthropometrical parameters at baseline, Pearson's correlation was used. For the statistical analysis, the statistical package SPSS version 20 for Windows (SPSS Inc, Chicago, Illinois, USA) was used. All p values were 2-tailed with a statistical significance defined by ($P \leq 0.05$).

4. Results

Fifteen patients underwent LTGVP surgery. The mean age of the subjects was 32.4± 10 years and, 10 (66%) were female. The clinical characteristics of the study participants at baseline and 6 weeks after surgery are presented in *Table 1*.

Table 2 demonstrates the blood biochemistry profile of the study participants before and after LTGVP surgery. Patients lost an average 18.7 ± 5.2 kg (14.7%) of weight during the 6 week period after LTGVP. The mean preoperative BMI was 44.6 ± 5 kg/m^2 and it was significantly reduced to 38.1 ± 5.4 kg/m^2. When comparing post-surgery results with baseline the reduction of BMI, WC, weight, WHR, TG, LDL-c, and elevation of HOMA-IR were significant, but the changes in TC, HDL-c, fasting glucose, insulin levels and QUICKI were not significant. We computed Pearson correlations between all parameters at basal levels. We

Table 1. Clinical Characteristics of the Study Population at Baseline and 6 Weeks After Laparoscopic Total Gastric Vertical Plication (LTGVP)

	Before Surgery, mean ± SD	6 Weeks After Surgery, mean ± SD	*P* value
Age, y	32.4 ± 10	32.4 ± 10	
Weight, kg	128.4 ± 18.8	109.6 ± 18.3	0.001
Body mass index, kg/m^2	44.6 ± 5	38.1 ± 5.4	0.001
Waist circumference, cm	122.9 ± 14.3	107.8 ± 11.4	0.001
Waist-to-hip ratio	0.90 ± 0. 09	0.85 ± 0. 08	0.006
Systolic blood pressure, mmHg	117.8± 11.7	116.2 ± 12.9	0.857
Diastolic blood pressure, mmHg	74.5 ± 9.4	75.8 ± 10.8	0.779

Table 2. Serum Biochemistry Profile of Study Subjects Before and 6 Weeks After Laparoscopic Total Gastric Vertical Plication (LTGVP)

	Before Surgery, mean ± SD	6 Weeks After Surgery, mean ± SD	Difference (95% CI)	*P* value
LDL-C [a], mg/dL	113.2 ± 30.5	103.6 ± 24.8	1.4-17.6	0.041
HDL-C [a], mg/dL	38 ± 9.9	35.8 ± 5.6	-1.2-6	0.44
Total cholesterol, mg/dL	191.2 ± 38.9	181 ± 32.8	-5.2 -28	0.39
Triglycerides, mg/dL	199.7 ± 160	121.5 ± 35.8	27.5–153.9	0.001
Fasting glucose, mg/dL	97.6 ± 8.8	92.5 ± 6	-0.86–11.6	0.173
Fasting insulin, mu/L	16.1 ± 8.5	11 ± 2.9	0.76–8.7	0.06
HOMA-IR [a]	3.9 ± 2.1	2.5 ± 0.7	0.26-2.3	0.04
QUICKI [a]	0.3 ± 0.02	1.5 ± 0.12	0.01-0.2	0.08

[a] Abbreviations: LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance; QUICKI , quantitative insulin sensitivity check index

found a significant positive correlation between weight and total cholesterol (r = 0.56, *P* = 0.03), also with fasting glucose (r = 0.53, *P* = 0.03), and a significant negative correlation between waist to hip ratio with HDL-c (r = -0.63, *P* = 0.01) and a significant positive correlation between waist to hip ratios with TG (r = 0.63, *P* =0.01).

5. Discussion

In this study, we evaluated the short-term effects of LTGVP surgery on the changes of the main variables related to obesity, anthropometric indices and metabolic profile. We found some significant and non-significant metabolic changes during the 6 weeks following LTGVP. The significant reduction in BMI and weight six weeks after surgery indicated a decrease in obesity. This initial weight loss may be considered a successful first step, as several recent studies have shown that improvement in several health risk factors follows rapidly (17). Changes in the gastrointestinal tract following LTGVP is associated with a reduced food intake and decreased nutrient intake (due to a reduction in stomach size) and subsequently BMI, WC and WHR decreased significantly (18).

In our series, before LTGVP, we found a high percentage of patients with hypertriglyceridemia and low levels of HDL-c, but initial TC and LDL-c were not higher than desirable levels. Moreover, total cholesterol, which remained unchanged after laparoscopic adjustable silicone gastric banding (LASGB), was in fact nearly normal before surgery. However, our severely obese patients were relatively young and did not suffer from serious co-morbid conditions at baseline. Many studies have been published concerning changes in lipids and glucose metabolism regulation after different procedures of bariatric surgery. Changes in plasma lipid concentrations may predispose morbidly obese patients with or without impairment in glucose metabolism to a higher risk of many chronic diseases like cardiovascular disease (19). As mentioned in the previous studies, weight loss following bariatric surgery is associated with a significant improvement in insulin sensitivity and improvement of lipid profile based on different follow up periods from 3 to 12 months and different types of surgical procedures (20-23). In agreement with our results other authors also showed some significant and non-significant changes of these parameters. Shargorodsky *et al.* in 2006 reported an 18% weight loss 4 months after laparoscopic adjustable gastric banding (LAGB) in 41 subjects with a mean age of 40 years. TC, fasting insulin, TG and HOMA-IR changed significantly but there were no significant changes in fasting glucose, LDL-c and HDL-c (24). In 2004 Garrapa *et al.* studied 15 morbidly obese subjects aged 32 years. It was shown that 6 months after LASGB, fasting insulin, TG and HOMA-IR had changed significantly but they did not find any significant changes in fasting glucose, TC and HDL-c (25). Magdalena Vila *et al.* in 2009 also studied changes in lipid parameters, glucose, insulin, and insulin resistance before biliopancreatic diversion and 3, 6, 12, 18, and 24 months after surgery, in 115 obese patients with a mean age of 44.6 years. They reported that 3 months after Scopinaro biliopancreatic diversion, BMI, fasting insulin, TC and HOMA-IR, fasting glucose, and LDL-c improved significantly but they did not observe any significant changes in TG and HDL-c until 6 months after weight loss (26). In another study which was conducted with 68 women, mean age of 43 years in 2006 by Nguyenet *et al.* they showed that after a laparoscopic Roux-en-Y gastric bypass, TG, TC and LDL-c decreased significantly during the 3 month weight loss period, but significant changes in HDL-c levels were observed after 9 months (22).

In 2008, Botella-Carretero *et al.* showed that after a 30% weight loss following bariatric surgery in 41 morbidly obese women; BMI, fasting glucose, insulin, insulin resistance, LDL-c, and TG decreased significantly. No changes were observed in the WHR and in serum HDL-c levels (27). Fuentes *et al.* studied 53 morbidly obese subjects and showed a significant reduction in; TG, TC, fasting glucose and insulin levels (28). Swarbrick *et al.* reported that one month after bariatric surgery accompanied by a 10-12% weight reduction, the decrease in the BMI and improvement of HOMA-IR were significant, but the reduction of fasting glucose was not significant (12). These inconsistent data results are likely related to variations in follow-up intervals among the studies. It has been mentioned that improvements in lipid profiles occurring as early as 3 months and 6 weeks postoperatively may be too short a time to observe all of these changes (22). Pontiroli *et al.* have described favorable changes in lipids, with significant improvements in TG and HDL- c levels up to three years following gastric banding (29). Other researchers have reported a significant improvement in the overall lipid profile at the four year mark (30). As was mentioned earlier in the present study the follow-up may have been too short to fully evaluate the complete normalization of all abnormalities.

Another difference in this study compared with the others is the age of the participants. It appears that the average age of our participants was younger than in the other studies. Also other discrepant results may be related to the different surgery methods because LTGVP is a new restrictive technique and this was the first study that evaluated the changes of these parameters after the surgery. Other techniques of bariatric surgery are malabsorptive or consist of different restrictive or mixed procedures. It has been shown that different surgical procedures implement different physiological mechanisms (31). For example it has been demonstrated that malabsorptive procedures, result in the greatest weight loss (31). However, the degree of improvement varies not only with the type of procedure used, but the exact mechanisms of the metabolic and cardiovascular improvements associated with bariatric surgery are not yet clearly defined (32). Our data are comparable with those reported by Brolin *et al.* who found that HDL-C levels did not change significantly

during the period of rapid weight loss 6 months after surgery, but they increased substantially 12 months postoperatively (33). Because obesity and hyperlipidemia are independent factors for the development of cardiovascular disease, improvements in lipid profile and weight reduction observed after LTGVP surgery can reduce the risk in high-risk individuals (22). It is in agreement with our results that a direct correlation between weight with TC, WHR with TG and a negative correlation between WHR with HDL-c is found.

Insulin resistance is the principal cause of glucose intolerance, type II diabetes and it also induces the progression of atherosclerosis. HOMA-IR and QUIKI indexes are the most effective methods to evaluate insulin resistance and sensitivity (34). It has been shown that in addition to marked weight loss following bariatric surgery, insulin resistance ameliorates (10). Furthermore some studies have demonstrated specific differences among the several techniques of bariatric surgery. The changes in the metabolic outcomes are different when restrictive procedures or malabsorption approaches are used (35). The mechanisms involved in the improvement of insulin sensitivity are likely to involve the immediate reduction in food intake (accompanied by modulation of intestinal incretin hormones) (36), followed by the reduction of excess adiposity (37). Adipose tissue produces a number of hormones, known as adipokines, which signal changes in adipose mass and energy status (38). On the other hand, improvements in insulin resistance might be mediated by these adipocytokines, such as; adiponectin, leptin, and resistin (39). Weight gain and increased adipose tissue leads to insulin resistance and elevated blood glucose levels in obese individuals (197) and we found a direct correlation between weight and fasting glucose before LTGVP. It has been shown that by weight reduction, fat mass decreased significantly and levels of cytokines secreted from the adipose tissue changed (39). Through modification of the adipocytikines secreted from the adipose tissue, improvements in; fasting insulin, insulin resistance, and fasting glucose levels resulted (40).

In conclusion this study indicates that LTGVP is an effective therapeutic approach for obese patients because it reduces weight, insulin resistance and improves metabolic parameters. Weight reduction combined with an improvement in these parameters after weight loss can reduce the risk of developing co-morbid conditions in these high risk individuals. Some potential limitations of this study, and probably one of the main causes of discordance with other study results may have been the smaller number of patients that we studied.

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Authors' Contribution

Atefeh Golpaie contributed in designing and performing the study and wrote the article. Mohammad Javad Hosseinzadeh-Attar was the chief researcher and contributed in idea formation, designing and managing of the research project. Mostafa Hoseini was the statistical consultant and analyzed the data.Zohreh Karbaschian contributed in performing. Mohammad Talebpour performed the bariatric surgeries.

Financial Disclosure

All contributing authors declare that they have no conflicts of interest.

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