Postprandial Triglyceride, Glucose and Insulin Levels 10 Years After Bariatric Surgery in Women With Severe Obesity – A Pilot Study: Part 2 – Biliopancreatic Diversion

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Summary

Obesity significantly increases the risk of developing metabolic and cardiovascular diseases. The most effective management tool for both obesity and type 2 diabetes (T2D) is bariatric/metabolic surgery. Delayed postprandial plasma triglyceride clearance contributes to the development of atherosclerosis in patients with T2D. Biliopancreatic diversion (BPD) was shown to be the most effective procedure in long-term T2D remission. However, the effect of BPD on postprandial metabolic profile has not been studied so far. In this pilot study, we therefore examined the changes in postprandial glucose, insulin, and triglyceride in women with severe obesity and T2D before surgery and then two and ten years after BPD. The studied cohort included 7 women (mean age at baseline=49.3±8.2 years) with severe obesity (mean BMI= 45.7±2.9 kg/m²) and T2D. A standardized liquid mixed-meal test was carried out in all subjects and the mean postprandial levels of plasma glucose, insulin, and triglyceride were analyzed by standard laboratory procedures. For statistical evaluation, ANOVA with Bonferroni multiple comparisons was used. Ten years after BPD not only a significant reduction of an average BMI ($F=32.9$, $p<0.001$) but also significant declines in mean postprandial plasma levels of glucose ($F=155.3$, $p<0.001$), insulin ($F=69.8$, $p<0.001$), and triglyceride ($F=139.9$, $p<0.001$) were demonstrated. The observed changes in postprandial metabolic profile may contribute to improved cardiometabolic health after bariatric surgery.

Keywords

Type 2 diabetes mellitus • Severe obesity • Bariatric surgery • Biliopancreatic diversion • Postprandial glucose • Triglycerides

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Introduction

Obesity is associated with increased morbidity (type 2 diabetes /T2D/, arterial hypertension, cardiovascular diseases, and certain cancers) and mortality, decreased quality of life, and a considerable increase in health care costs [1]. Bariatric surgery is the most effective tool for the treatment of obesity in terms of both weight loss and the reduction of cardiometabolic health risks, particularly T2D [2,3,4]. Bariatric surgery plus intensive medical therapy was shown to be more effective than intensive medical therapy alone in decreasing or resolving hyperglycemia [5]. In patients with severe obesity and T2D, bariatric surgery reduced body weight and improved overall metabolic control to a greater extent than medical treatment which included glucagon-like peptide-1 (GLP-1) agonist liraglutide [6]. In the study of Khorgami *et al.* (2019), more than 50 % of patients with T2D exhibited remission two years after bariatric surgery [7]. Mingrone *et al.* (2015) also showed that 37 % of patients in a gastric bypass group and 63 % of patients in a biliopancreatic diversion (BPD) group had a remission of T2D 5 years after surgery [8]. According to a network meta-analysis of randomized controlled trials that covered six bariatric surgeries, BPD was the most effective procedure in long-term diabetes

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remission [9]. Bradnova *et al.* (2014) described statistically significant weight loss and improvement in metabolic parameters in women with T2D 6 months after surgery [10]. In the same cohort, Vrbikova *et al.* (2016) described similar improvements in insulin sensitivity after three surgical procedures (laparoscopic adjustable gastric banding LAGB, BPD, and laparoscopic greater curvature plication LGCP) introduced in their study [11].

Prolonged postprandial triglyceride clearance significantly contributes to the increased cardiovascular risks in patients with T2D [12]. According to Anuzzi *et al.* (2004) insulin resistance is associated with postprandial lipoprotein abnormalities in type 2 diabetes even after correction for hyperglycemia and hyperinsulin-emia [13]. The effect of BPD on postprandial metabolic profile has not been studied so far. In this pilot study, we therefore examined the changes in postprandial glucose, insulin, and triglyceride in women with severe obesity and T2D two and ten years after BPD.

Materials and Methods

Subjects

Our cohort included 7 women with obesity and T2D (mean BMI=45.7±2.9 kg/m²; mean age = 49.3±8.2 years). These patients underwent BPD at the OB Clinic in Prague, between 2009 and 2012 and were examined at baseline, 2, and 10 years after surgery. Subjects treated with incretin mimetics and/or insulin were excluded from the study.

Patients were examined at baseline (before BPD), and then at 1 month, 6 months, 2, and 10 years after BPD. BPD was performed according to Scopinaro's standard procedure, but with a 90 cm common channel instead of the 50 cm one originally suggested [14]. To avoid hypoglycemia the dosage of antidiabetics was appropriately reduced after surgery. Patients were not treated with other drugs that could affect glucose levels.

During the follow-up, dietary and physical activity records were evaluated by obesity specialists and dietitians. Metabolic and nutritional status was regularly monitored in order to prevent vitamin and micronutrient deficiencies and provide appropriate supplementations.

Meal test

Oral antidiabetic drugs were discontinued 3 days before meal tests. For the purpose of this study, all subjects underwent a standardized liquid mixed-meal test (300 ml: 375 kcal; 1, 581 kJ; 30 % (28.2g) protein, 25 % (10.5 g) fat, and 45 % (42 g) carbohydrate) with blood withdrawal 15 and 10 minutes before the test initiation, at baseline and 15, 30, 45, 60, 90, 120, 150 and 180 minutes after the meal ingestion. The meal test protocol was described in detail elsewhere [10].

The study was approved by the Ethics Committee of the Institute of Endocrinology in Prague and subjects signed informed consent in accordance with the Declaration of Helsinki.

Anthropometric Characteristics

Body weight was measured with a TANITA MC 980 MA bioelectrical impedance analyzer. Height was measured by a stadiometer, and the body mass index (BMI) was calculated (weight (kg) / height (m) ²). Dual X-ray densitometry (DEXA) scanning (GE LUNAR iDXA, GE Healthcare Technology, USA) was used to assess body composition before surgery and 2 and 10 years after the operation. Weight and fat mass lost were calculated.

Biochemical Characteristics

Plasma glucose, insulin, and triglyceride (TG) levels were analyzed by standard laboratory procedures using Integra 400+, Modular E170, and Cobas 6000 instrumentation (Roche Diagnostics GmbH, Mannheim, Germany).

Statistical Analysis:

Follow-up differences in the mean postprandial response of glucose, insulin, and triglyceride levels to meal ingestion were evaluated by ANOVA. Values are presented as means with their 95 % confidence intervals. The ANOVA testing was followed by Bonferroni multiple comparisons. Statistical software Statgraphics Centurion 18 from Statgraphics Technologies (The Plains, Maryland, USA) was used.

Results

During the follow-up period (2 and 10 years after BPD) body weight, body mass index, and fat mass (Table 1) in the studied cohort significantly decreased. At 10 years follow-up, the average weight loss was 28.1 % (35.1 kg) while the average weight loss at 2 years follow-up was 27.8 % (34.7 kg).

Mean plasma glucose, insulin, and TG levels were determined during a standardized liquid mixed-meal test. Plasma glucose and insulin levels significantly decreased 2 years after BPD compared to baseline and then moderately increased after 10 years but the measured mean levels of plasma glucose, and insulin remained significantly lower than the pre-treatment levels. Plasma TG levels significantly decreased both 2 and 10 years after BPD (Fig. 1).

Table 1. Anthropometric parameters during follow-up compared to baseline.

Baseline			2 years follow-up			10 years follow-up		
Weight (kg)	BMI (kg/m²)	Fat mass (kg)	Weight (kg)	BMI (kg/m²)	Fat mass (kg)	Weight (kg)	BMI (kg/m²)	Fat mass (kg)
124.9±11.1	45.7±4.7	64.7±12.9	90.1±14.7*	35.2±3.5*	44.3±7.1*	89.8±12.5*	35.4±3.5*	45.2±6.2*

Values are presented as means ±SD. * p< 0.05 was considered significant – after 2 or 10 years compared to baseline.

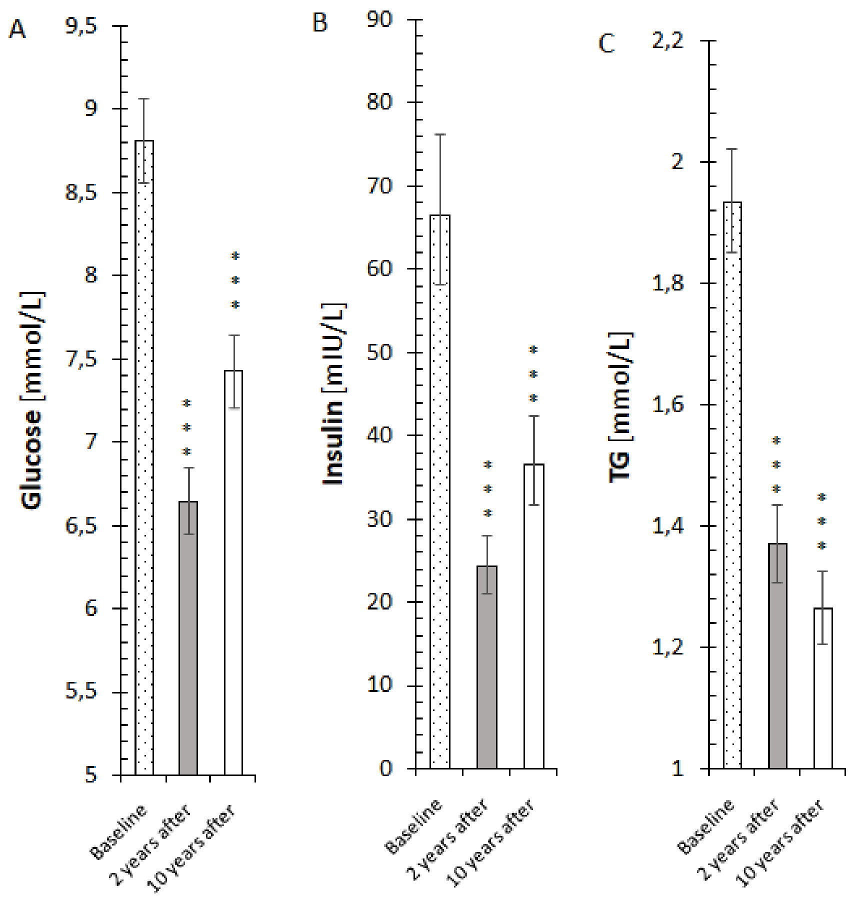

Fig. 1. Mean postprandial levels of glucose, insulin, and triglyceride during a standardized liquid mixed-meal test before surgery, and then 2 and 10 years after BPD. **A**) Change in mean plasma glucose levels: F=155.3, p<0.001. **B**) Change in mean plasma insulin levels: F=69.8, p<0.001. **C**) Change in mean plasma triglyceride levels: F=139.9, p<0.001. Values are presented as means with 95% confidence intervals shown. Levels of significance compared to baseline: *** p<0.001.

Discussion

Previous studies have demonstrated that bariatric/metabolic surgery is an effective treatment for patients with obesity and T2D [2, 7]. In our cohort, we assessed changes in anthropometric parameters, metabolic characteristics, and postprandial profiles of glucose, insulin, and TG in women with obesity and T2D 2, and 10 years after BPD. Vrbikova *et al.* (2016) compared the same cohort 1 and 6 months after BPD and found significant improvements in insulin sensitivity in women with T2D after both BPD and LGCP [11].

In accordance with the existing literature, our study demonstrated that bariatric/metabolic surgery favorably affected body weight loss and glucose profile in women with obesity and T2D both 2, and 10 years after surgery [15]. The average weight loss in this study was 27.8 %, (34.7 kg at 2 years follow-up) and 28.1 % (35.1 kg at 10 years follow-up). In our study, a significant decline in mean postprandial glucose, insulin, and triglyceride levels compared to baseline values was observed at both 2 and 10 years after BPD. Moderate increases in postprandial glucose and insulin levels observed 10 years after BPD in comparison with those at 2 years after surgery may be partly influenced by aging [16]. Previous studies on postprandial glucose and triglyceride profile after bariatric surgery were conducted after sleeve gastrectomy or gastric bypass and have not been extended over 2 year period. Griffo *et al.* (2016) observed improved postprandial response of blood glucose, insulin, and triglyceride 2 years after sleeve gastrectomy or gastric bypass in patients with obesity and T2D [17]. On the other hand, Liaskos *et al.* (2018) demonstrated that gastric bypass is superior to sleeve gastrectomy in improving the postprandial profile of glucose and triglyceride 6 months after surgery carried out in non-diabetic patients with severe obesity [18]. Mechanisms of improved insulin sensitivity after bariatric/metabolic surgery have been broadly investigated. These surgeries affect gastrointestinal incretins secretion and bile acids metabolism, and in this way improve mitochondrial health, beta cell function, and insulin sensitivity [19]. In our previous study, BPD produced the best metabolic outcomes among the evaluated procedures (BPD>LGCP>LAGB) and highlighted mitochondria in adipose tissue as a potential target of fibroblast growth factor-19 during diabetes remission [19]. A recent study carried out in our patients with severe obesity demonstrated that an improvement in cardiometabolic health after bariatric surgery is associated with a reduction of metabolic endotoxemia and an increased browning process in human adipocytes [20]. The role of gut hormones in bariatric surgery-induced weight loss and improvement in glucose profile was recently reviewed [21]. Several studies compared Roux-en-Y gastric bypass (RYGP), BPD, and laparoscopic sleeve gastrectomy (LSG) with LAGB. RYGP, BPD, and LSG were superior to LAGB in terms of weight loss and improvement in metabolic risks [22-24]. Based on previous studies, bariatric procedures influence food intake and weight loss, and this way contributes to favorable metabolic changes [25]. This is in agreement with a recent study that described a significant weight reduction and normalization of both glucose and TG profiles [26]. Schauer *et al.* (2017) reported a 3-fold greater reduction in TG levels and a 4-fold increase in HDL levels in patients 5 years after sleeve gastrectomy compared to those receiving a conservative treatment [5]. Bariatric surgery improves insulin resistance and increases adiponectin levels in serum [27]. Postprandial dyslipidemia and insulin resistance are inversely related to GLP-1. It could therefore be suggested that a blunted GLP-1 response to a meal may contribute to postprandial hypertriglyceridemia and insulin resistance in obesity. On the other hand, improvements in GLP-1 secretion observed after bariatric surgery, particularly after BPD, may favorably affect postprandial glucose, insulin, and TG levels [18,28]. Our results demonstrated that women with severe obesity who underwent BPD retained both significant weight loss and improved postprandial metabolic profile 2 and 10 years after surgery.

Limitations and strengths

Limitations of our study include a small sample size and a missing control group treated with lifestyle modification and antidiabetic drugs. On the other hand, a particular strength of our study is the evaluation of postprandial glucose and triglyceride levels as well as body composition during the long-term follow-up after BPD.

Conclusions

Overall, our results demonstrate a strong and long-term effect of BPD on weight loss and improvement in postprandial glucose and triglyceride levels.

Conflict of Interest

There is no conflict of interest.

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Abbreviations

BMI, Body Mass Index; BPD, Biliopancreatic diversion; GLP-1, Glucagon-like peptide-1; T2D, Type 2; diabetes mellitus; TG, Triglyceride

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