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Original article

Remission of type 2 diabetes in patients undergoing biliointestinal bypass for morbid obesity: a new surgical treatment

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Abstract

Background: Nutrient interaction with the mid-gut may play a role in improving type 2 diabetes mellitus (T2D) after bariatric surgery. However, Roux-en-Y gastric bypass, biliopancreatic diversion, and sleeve gastrectomy include diversion of food from the duodenum and/or partial gastrectomy. Biliointestinal bypass (BIBP) was introduced to eliminate the major side effects of jejunoileal bypass. It does not involve any change to the anatomy of the stomach or the duodenum. A prospective evaluation of the role of BIBP in glycemic control has not been reported.

Objectives: Longitudinal evaluation of T2D after BIBP.

Setting: University hospitals in Europe and Canada.

Method: The effects of BIBP on metabolism and glycemia in 28 consecutive patients with T2D were evaluated over 2 years.

Results: Decreases ($P < .001$) in fasting glycemia, insulinemia, and homeostasis model assessment were observed 3 months after surgery, were improved after 1 year, and remained stable after 2 years. Glycosylated hemoglobin levels decreased at 3, 12, and 24 months after surgery (from 9.2 ± 2.1 to 6.3 ± 1.1 ($P < .0001$), 4.9 ± 1.7 ($P < .0001$), and 4.8 ± 1.1 ($P < .0001$), after 3, 12, and 24 months, respectively). Medical therapy was discontinued in 83% (20 of 24) of the patients; for the remaining 17% (4 of 24), therapy was reduced to oral hypoglycemic agents.

Conclusion: BIBP had a favorable risk–benefit relationship and positive metabolic effects in the short term. How BIBP achieves optimal glycemic control and whether it improves β-cell function and/or insulin sensitivity require further study. (Surg Obes Relat Dis 2016;▮:00–00.)

Keywords: Type 2 diabetes; Bariatric surgery; Biliointestinal bypass; T2D; Metabolic surgery

A surgical approach for type 2 diabetes (T2D) may be deemed a major challenge because of the large number of patients needing treatment and the uncertainties around the underlying physiologic mechanisms contributing to its

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potential benefits despite its tremendous potential to reveal new targets for therapeutic intervention [1]. Mechanistic studies of surgery for T2D have focused on incretin levels and their effects on glycemic control. Diversion of food from the duodenum [2], elimination of the gastric fundus [3], and food contact with the mid-gut or interposing a distal segment of the intestine [4] may all potentially play a role in improving T2D. Specifically, Roux-en-Y gastric bypass (RYGB) [5], Scopinaro's biliopancreatic diversion (BPD), BPD/duodenal switch (DS) [6], sleeve gastrectomy (SG) [7], SG–duodenojejunal bypass [8], and ileal interposition [9] all include a gastric resection, duodenal exclusion, or both.

Biliointestinal bypass (BIBP) was introduced several years ago to overcome the side effects of jejunoileal bypass [10]. Specifically, compared with jejunoileal bypass, by eliminating the blind bowel loop, BIBP either avoids intestinal bacterial overgrowth or increases reabsorption of bile acid, with subsequent less postoperative diarrhea and malabsorption syndrome [11].

Compared with other bariatric procedures, BIBP provides a different framework. That is, it does not include any duodenal diversion, gastric exclusion or resection, or ileal interposition. Reported data obtained by postoperative Tc99 hepatobiliary iminodiacetic acid scan showed an effective cholecystojejunostomy diverting bile from the common bile duct in 90% of patients [10].

To the best of our knowledge, no data on the effects of BIBP on T2D have been reported so far. We undertook this longitudinal prospective study to evaluate the impact of BIBP on remission of T2D.

Materials and methods

This study was conducted according to the Declaration of Helsinki and approved by the local institutional review board. All patients provided written informed consent.

Inclusion criteria were age 18–60 years, body mass index (BMI) >35 kg/m^2 for at least 5 years, and T2D with suboptimal response to nonsurgical treatment. All participants were offered dietary support, psychiatric support, physical activity, medical treatment for T2D and nonsurgical treatments (i.e., endoscopic intragastric balloon). All cases were discussed in the multidisciplinary meeting.

Exclusion criteria were history of acute cholecystitis, previous cholecystectomy, hepatobiliary stones, and bariatric surgery. For patients who were excluded, a different bariatric procedure, such as SG or BPD, was offered, as previously reported [12–16]. All tests were performed after an overnight fast by the patients; antidiabetic medications were withdrawn 3 days before testing. In patients requiring regular insulin, insulin was used up to 8 hours before the metabolic studies. Clinical history and symptoms were assessed, at the time of prehospitalization and postoperatively, through a standardized questionnaire specifically designed to investigate T2D [17]. Blood samples and patient information were obtained during routine follow-up outpatients visits. Each patient was studied at baseline, at 3 months, and 1 year and 2 years after surgery. Initial assessment included anthropometric measurements: The participants fasted overnight and then were weighed barefoot and in light clothing to the nearest .1 kg. Height was measured by using a fixed wall stadiometer; height and weight were recorded and BMI (kg/m^2) was calculated. Body composition was assessed by bioimpedance analysis (BIA). BIA was carried out by the same operator using a leg-to-leg tetrapolar bioelectrical impedance analysis (Tanita TBF-300 MA Body Composition Analyzer, Tanita Corporation, Tokyo, Japan). Measurements were taken at an ambient temperature of 22°C to 24°C after the patients voided and had been in the supine position for 20 minutes. BIA measurements were done according to the manufacturer's guidelines at a frequency of 50 kHz. Height, gender, and age were entered manually; weight was recorded automatically, with .5 kg as an adjustment for the weight of clothes. The Tanita software uses in-built prediction equations to estimate fat mass (FM) and fat-free mass (FFM).

A standard regimen of vitamin and mineral supplementation was prescribed after surgery, including vitamins A, E, and D; iron; and calcium. Patients who reported using a supplement ≥ 5 days a week were considered users of that supplement. Vitamin deficiencies were defined as concentrations less than the standard laboratory reference values, and patients with deficiencies received a tailored and relevant top-up supplementation if concentrations were below these cutoffs levels (vitamin A, .9 μmol/L; 25-hydroxyvitamin D, 37 nmol/L; and vitamin E, 2.2 μmol/mmol, adjusted for serum total cholesterol and triacylglycerols). The following cutoffs for total protein (6.6 g/dL) albumin (3.5 g/dL), ionized calcium (1.10 mmol/L), plasma iron (59 μg/dL) and ferritin (191 ng/dL) were considered.

Hypercholesterolemia, hypertriglyceridemia, and low high-density lipoprotein cholesterolemia were diagnosed when values were >200 in men and >150 mg/dL in women and <40 mg/dL in men and <50 mg/dL in women, respectively. The cutoff points were chosen according to the American Heart Association criteria to identify metabolic syndrome, as previously described [15].

T2D remission was defined as withdrawal of all diabetes medications, in conjunction with fasting plasma glucose concentration (<126 mg/dL) associated with glycosylated hemoglobin (HbA1C) $<6.5\%$ (<44 mmol/mol). Homeostasis model assessment, based on fasting plasma insulin (μU/L) multiplied by fasting plasma glucose (mg/dL), and multiplied by a correction factor of 405^{-1}, was also used as an index of insulin resistance [17].

Surgical technique

The patient was placed in the supine position, and a mild left rotation was applied. The surgeon stood on the side of the patient's right flank, the first assistant on the right side, and the camera operator on the opposite side. Four trocars