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Original article

Long-term clinical and functional impact of biliopancreatic diversion on type 2 diabetes in morbidly and non–morbidly obese patients

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Abstract

Setting: Obesity surgery has been proposed as a treatment option for diabetic patients with body mass index (BMI) < 35 kg/m^2, but the efficacy of metabolic surgery has not been conclusively determined.

Objective: To evaluate the long-term metabolic outcome of non–morbidly obese (NMO) patients with type 2 diabetes (T2D) after biliopancreatic diversion (BPD).

Material and methods: Two groups of T2D patients with different degree of obesity (NMO, 17 cases, BMI 25–35 kg/m^2; and morbidly obese [MO], 13 cases, BMI > 35 kg/m^2) were studied before and at 1 and 5 years after BPD in a university hospital setting. Insulin secretion was assessed by acute insulin response (AIR) to intravenous glucose and by insulinogenic index (IGI).

Results: In all MO patients, T2D was remitted or controlled (1 case) at 1 year and results were maintained at 5 years; AIR (μU/mL) and IGI (μU/mg) improved ($P < .001$) at 1 year (from .1± 3.1 to 18.52 ± 21.9, and from 6.0 ± 8.5 to 9.1 ± 22.8, respectively) with a further increase (to 24.8 ± 25.5 and to 14.3 ± 13.8, respectively) at 5 years. Within the NMO group, T2D was remitted in 1/17 and controlled in 14/17 patients at 1 year, and in 2/17 and in 4/17 patients at 5 years, respectively; AIR (μU/mL) and IGI (μU/mg) remained unchanged throughout the postoperative period (from .31 ± 9.26 to 1.5 ± 2.8 at 1 yr and to .4 ± 3.29 at 5 yr for AIR, and from 2.2 ± 4.9 to 1.3 ± 9.0 at 1 yr and to 2.3 ± 3.3 at 5 yr for IGI).

Conclusions: After BPD, restoration of β-cell secretion/production plays a pivotal role in determining postoperative T2D remission. (Surg Obes Relat Dis 2016;▮:00–00.)

Keywords: Acute insulin response; Insulinogenic index; Bariatric surgery; Biliopancreatic diversion; Obesity degree; Type 2 diabetes

The effect of biliopancreatic diversion (BPD) on type 2 diabetes (T2D) is well established. In 1986 we first reported the stable normalization of fasting plasma glucose levels in the vast majority of the morbidly obese (MO) patients with overt type 2 diabetes submitted to BPD [1]. These results were confirmed in subsequent series [2,3] as well as in recent meta-analyses [4–6]. Resolution of diabetes and other components of the metabolic syndrome was found to be sustained for up to 10 years [7,8]. Shortly after the operation, when weight was still in the obese range, functional studies have found both the restoration of insulin sensitivity [9,10] and a marked increases in the acute insulin response to intravenous glucose load (AIR), reflecting an

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amelioration of insulin secretion [11,12]; therefore, a specific antidiabetic effect of BPD independent on the weight loss was suggested, which could be accounted for by changes in the incretin pattern [13,14], by fall of insulin resistance due to the postoperative intramyocellular fat depletion [15], and by still undetermined factors [16,17].

In clinical practice, the majority of T2D patients are not MO, their body mass index (BMI, kg/m^2) typically ranging between 25 and 35 kg/m^2. We have previously published a prospective controlled study of the BPD effects in a population of T2D patients with BMI from 25 to 35 kg/m^2 [18,19]. Other similar patients were subsequently enrolled in 3 more protocol studies. The short-term (1–2 yr) clinical, biochemical, and functional results in that population was encouraging. However, they progressively deteriorated with time, being unsatisfactory in those patients which reached the 5-year follow-up. This prompted us to investigate the AIR and insulinogenic index (IGI) in the patients from that BMI range compared with the MO patients (BMI $>$ 35 kg/m^2).

Material and methods

Thirty T2D patients with different degree of obesity were studied in a prospective setting, 13 of whom had BMI $>$35 kg/m^2 (MO group, 8 male and 5 female) and 17 with BMI values between 25 and 35 kg/m^2 (non–morbidly obese [NMO] group, 11 male and 6 female). Inclusion criteria were T2D as per American Diabetes Association criteria [20], age between 35 and 70 years, minimum diabetes duration 3 years, and HbA1C $\geq$7.5% on standard medical therapy. Exclusion criteria were positivity for anti-islet and/or anti–lutamic acid decarboxylase (GAD) antibodies; fasting C-peptide levels $<$.5 ng/mL; severe current inflammatory, neurologic, or cardiovascular illness; malignancy; and contraindications to obesity surgery or specifically to BPD. Preoperative demographic and anthropometric findings are referred to in Tables 1 and 2. The study was approved by the Ethics Committee of IRCCS San Martino Hospital, and all patients gave written informed consent.

All patients underwent the standard type of BPD. The operation was described in detail elsewhere [1,2]. Peri- and postoperative treatment was the usual for BPD at our institution.

The preoperative data and data at 1 and at 5 years after BPD were available for all patients. For this study, only the preoperative findings and those obtained at 1 and at 5 years were considered. Furthermore, only data directly regarding glucose metabolism and β-cells function are illustrated and discussed.

Weight was determined to the nearest .1 kg and height at the nearest .5 cm. Fasting blood glucose (FBG, mg/dL) and glycated hemoglobin (HbA1C %) concentrations were measured with routine analyzer and insulin concentration by commercial enzymatic method (Randox, Crumlin, UK) and sandwich immunoradiometric assay (Immunotech, Prague, Czech Republic). Homeostasis model assessment of insulin sensitivity (HOMA-IR) was calculated [21].

Table 1
Type 2 diabetes (T2D) patients undergoing biliopancreatic (BPD) diversion with initial BMI values between 25 and 35 kg/m^2 (group non–morbidly obese [NMO]) and $>$35 kg/m^2 (group morbidly obese [MO]): demographic and anthropometric data before and after BPD

	Before BPD	At 1 yr after BPD	At 5 yr after BPD
Cases (#)			
NMO	17	17	17
MO	13	13	13
Age (yr)			
NMO	57.7 ± 6.4		
MO	51.6 ± 9.8		
Insulin therapy			
NMO	6 (35%)	1 (6%)	4 (23%)
MO	4 (30%)	0	0
T2D duration (yr)			
NMO	12.3 ± 8.3		
MO	7.4 ± 5.7		
BW (kg)			
NMO	82.7 ± 9.6	70.4 ± 12.0*	72.7 ± 12*
MO	120.6 ± 14.6‡	82.0 ± 9.7*,§	84.2 ± 12.3*,§
BMI (kg/M^2)			
NMO	29.9 ± 2.5	25.3 ± 2.4*,§	26.2 ± 2.8†,§
MO	44.6 ± 5.3‡	30.7 ± 3.3*	31.3 ± 4.4*
% EWL (%)			
NMO		64.0 ± 28.7	58.0 ± 37.1
MO		61.5 ±14.6	60.3 ±17.4

BMI = body mass index; BW = weight; % EWL = percent of excess weight loss.
*P $<$ .001 versus before BPD.
†P $<$ .01 versus before BPD.
‡P $<$ .001 versus NMO group.
§P $<$ .01 versus NMO group.

Insulin secretion was assessed as the AIR to an intravenous glucose bolus (glucose 35 g over 2 min) before surgery and at 1 and 5 years after BPD. All patients completed the 5-year functional study. The intravenous glucose tolerance test was performed at 8:30–9:00 AM after a 12-hour overnight fast; blood samples were collected 10 minutes before and immediately before the glucose injection and 2, 3, 5, and 10 minutes afterward. Quantitative data were obtained as the difference of the mean insulin concentration at 2, 3, 5, and 10 minutes after glucose injection minus the mean insulin concentration at –10 and at 0 minute of the intravenous glucose tolerance test. Furthermore, the IGI was calculated by the ratio between the increase in insulin concentration to the increase in glucose concentration at 10 minutes after the glucose load [22,23].

Diabetes remission was defined as an HbA1C $\leq$ 6% and FBG $<$ 126 mg/dL on a free diet and with no antidiabetic therapy. Diabetes control was defined as an HbA1C $<$ 7% on a free diet and without any antidiabetic medical treatment.

Data are given as mean ± SD. Because of the small sample size of the specimen, statistics were performed by