Available online at www.sciencedirect.com

Metabolism

www.metabolismjournal.com

Clinical Science

# Biliopancreatic diversion with duodenal switch leads to better postprandial glucose level and beta cell function than sleeve gastrectomy in individuals with type 2 diabetes very early after surgery

*Andréanne Michaud*[a,1], *Thomas Grenier-Larouche*[b,c,1], *Dominique Caron-Dorval*[b], *Simon Marceau*[d], *Laurent Biertho*[d], *Serge Simard*[b], *Denis Richard*[b], *André Tchernof*[b,*], *André C. Carpentier*[c,**]

[a] *Montreal Neurological Institute, Department of Neurology and Neurosurgery, McGill University, 3801 University Street, Montreal, QC H3A 2B4, Canada*

[b] *Centre de recherche de l'Institut universitaire de cardiologie et de pneumologie de Québec, Université Laval, Québec, Canada*

[c] *Department of Medicine, Division of Endocrinology, Centre de recherche du Centre hospitalier universitaire de Sherbrooke, Université de Sherbrooke, Québec, Canada*

[d] *Department of Surgery, Institut Universitaire de Cardiologie et de Pneumologie de Quebec, Université Laval, Québec, Canada*

ARTICLE INFO

*Article history:*
Received 22 March 2017
Accepted 17 June 2017

*Keywords:*
Sleeve gastrectomy
Biliopancreatic diversion with duodenal switch
Insulin sensitivity
β-cell function
Type 2 diabetes remission

ABSTRACT

*Objective.* The aim of this study was to compare the short-term effect of sleeve gastrectomy (SG) and biliopancreatic diversion with duodenal switch (DS) in order to determine if exclusion of the upper gastrointestinal tract confers greater metabolic improvement, independent of weight loss.

*Methods.* Standard meals were administered before and on day 3 and 4 after SG to assess insulin sensitivity, β-cell function and gastrointestinal hormone responses in matched normoglycemic (NG) and type 2 diabetes (T2D) participants. A third group of matched T2D participants who underwent DS with the same meal test administered prior to and 3 days after surgery was also recruited.

*Results.* Despite significant metabolic improvement, T2D participants failed to fully normalize insulin resistance and β-cell dysfunction 3 and 4 days after SG. Our results demonstrate the superiority of DS over SG in terms of short-term improvement in

*Abbreviations:* BMI, body mass index; T2D, type 2 diabetes; DI, disposition index; RYGB, Roux-in-Y gastric bypass; SG, sleeve gastrectomy; DS, biliopancreatic diversion with duodenal switch; GLP-1, glucagon like peptide-1; NG, normoglycemic; BMR, basal metabolic rate; HbA1c, hemoglobin A1c; PP, pancreatic polypeptide; GIP, glucose-dependent insulinotropic peptide; TNF-α, tumor necrosis factor alpha; PYY, polypeptide tyrosine tyrosine; ELISA, enzyme-linked immunosorbent assay; HOMA-IR, homeostatic model assessment-estimated insulin resistance; ISR, insulin secretion rate; ISI, insulin secretion index; AUC, area under the curve; FPG, fasting plasma glucose; SGT1, sodium-glucose cotransporter 1; D3, Day 3 Post-surgery; D4, Day 4 Post-surgery; BWL, body weight loss.

* Correspondence to: A. Tchernof, Endocrinology and Nephrology, CHU de Quebec-Laval University, 2705 Laurier Blvd. (R-4779), Québec, QC G1V 4G2, Canada. Tel.: +1 418 654 2296; fax: +1 418 654 2761.

** Correspondence to: A.C. Carpentier, Department of Medicine, Centre de Recherche du Centre Hospitalier Universitaire de Sherbrooke, Université de Sherbrooke, Sherbrooke, QC J1H 5N4, Canada. Tel.:+1 819 564 5241; fax: +819 564 5292.

E-mail addresses: andre.tchernof@crchudequebec.ulaval.ca (A. Tchernof), andre.carpentier@usherbrooke.ca (A.C. Carpentier).

[1] The first two authors contributed equally to this work.

http://dx.doi.org/10.1016/j.metabol.2017.06.005

postprandial glucose excursion and β-cell function 3 days after the surgery, with similar improvement in hepatic insulin sensitivity.

*Conclusion*. Our findings support the notion that caloric restriction represents an important mechanism to explain the very early anti-diabetic effects observed after bariatric surgery. However, exclusion of the upper gastrointestinal tract also provides further metabolic improvements, possibly mediated by gastrointestinal hormonal responses and altered postprandial glucose absorption.



## 1. Introduction

Patients with class II and III obesity (body mass index (BMI) ≥35 kg/m$^2$) display twice the risk of developing type 2 diabetes (T2D) compared to individuals with lower BMI [1]. The increased risk of T2D conferred by obesity may be explained by adipose tissue dysfunction [2], peripheral insulin resistance [3] and excess hepatic glucose production [4]. However, β-cell dysfunction is essential for the development of impaired glucose tolerance and fully-installed T2D [5]. β-cell dysfunction is better captured by the insulin disposition index (DI) [6]. This index is based on the hyperbolic relationship between insulin secretion and sensitivity; a decline in DI reflects a reduction in insulin secretion for any given degree of insulin resistance and characterizes patients with pre-diabetes or T2D.

Substantial improvement in glucose metabolism has been observed after bariatric surgery, but the degree of glycemic improvement varies depending on the type of procedure. Procedures combining restriction of food intake and exclusion of the proximal intestinal track such as the Roux-in-Y gastric bypass (RYGB) and biliopancreatic diversion with duodenal switch (DS), achieve greater weight loss and higher T2D remission rates compared to restrictive procedures without intestinal exclusion, such as the sleeve gastrectomy (SG) [7,8]. It has been proposed that one of the mechanisms explaining the anti-diabetic effect of bariatric surgeries is the exclusion of the proximal gut and/or the rapid delivery of food to the distal jejunum with ensuing increase in intestinal incretin hormones [9]. One of the most consistent observations across studies remains the exaggerated postprandial secretion of glucagon like peptide-1 (GLP-1) after RYGB [10–12] and DS [13,14]. Some studies also reported modified gastric emptying half-time [15], glucose absorption dynamics [16] and secretion of gastrointestinal hormones [13,17] after SG. However, a few studies reported higher postprandial secretion of GLP-1 after RYGB compared to SG 3 days to 1 week post-surgery [18,19].

Interestingly, RYGB, SG [16] and gastric banding [20] have similar effects on muscle insulin sensitivity and β-cell function after 20% excess weight loss, suggesting that the reduction in body weight itself is the main mechanism for long-term T2D remission [21]. However, fasting and postprandial plasma glucose levels and hepatic insulin resistance are quickly reduced after SG, RYGB and DS [22–24], suggesting that weight loss-independent mechanisms take place after these surgeries. Our group [14] and others [25] have previously shown that caloric restriction recapitulated the short-term effects of bariatric surgery on insulin sensitivity and β-cell function, independently of modifications in fasting or postprandial secretion of gastrointestinal hormones.

We designed the present study to compare the short-term effect of SG and DS in order to test the hypothesis that exclusion of the upper gastrointestinal tract would confer greater metabolic improvement in patients with T2D undergoing bariatric surgery, independent of weight loss. We thus administered standardized test meals prior to and on the third and the fourth postoperative days after SG or DS in participants with T2D. This timeline has been selected because we showed significant improvement in insulin resistance and β-cell function as early as 3 days after the DS procedure in participants with T2D [14].

## 2. Material and Methods

### 2.1. Participants Recruitment

Participants were recruited through the elective surgery schedule of the *Centre de recherche de l'Institut universitaire de cardiologie et de pneumologie de Québec* (CRIUCPQ). The study sample included nine T2D and nine NG participants with severe obesity who underwent SG as well as nine T2D participants with severe obesity who underwent DS. The three groups of patients were matched for age (42.7 ± 7.1 yr), sex and BMI (46.5 ± 5.3 kg/m$^2$). The indications for surgery followed the National Institutes of Health guidelines [26]. Exclusion criteria were the following: 1) participants with kidney, hepatocellular, thyroid, or cardiovascular disorders or poorly controlled lipid disorders; 2) treatment with insulin, thiazolidinedione, GLP-1 agonist or dipeptidyl peptidase-IV inhibitor, beta-blocker, anti-psychotic medications or glucocorticoids; and 3) participants having any uncontrolled medical, surgical or psychiatric condition. The duration of T2D was validated from medical records. The Research Ethics Committee of the CRIUCPQ approved the study. All participants provided written informed consent to participate in the study.

### 2.2. Surgical Procedures

All participants received intravenous antibiotics (antibioprophylaxis) and subcutaneous heparin (thrombo-prophylaxis) 2 h before surgery. A 250 cm$^3$ SG starting 7–8 cm proximal to the pylorus was performed in all participants using a 34-44 Fr Bougie for calibration, as previously described [27]. A