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Metabolic consequences of the incorporation of a Roux limb in an omega loop (mini) gastric bypass: evaluation by a glucose tolerance test at mid-term follow-up

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Abstract
Background In the technique used in our department, Roux-en-Y gastric bypass (RYGB) anatomically only differs from the mini- or omega loop gastric bypass (OLGB) by the incorporation of an isolated alimentary limb, called the Roux limb. The metabolic consequences of the incorporation of a Roux limb are unknown.
Objectives To evaluate differences in glucose and insulin dynamics between RYGB and OLGB in normoglycemic patients, by submitting them to a glucose challenge after stabilization of their weight.
Methods Nondiabetic patients who had undergone OLGB 4 years earlier were matched with nondiabetic patients who had undergone RYGB around the same time and with healthy controls. Participants underwent oral (OGTT) and intravenous glucose tolerance test (IVGTT). Endpoints of the study were: progression of plasma glucose and insulin, changes in their concentration [calculated by area under the curve (AUC)] at OGTT and IVGTT, incretin effect and incidence of hypoglycemia.
Results Each of the three groups comprised 14 participants. At OGTT, plasma glucose and insulin incremental values were comparable after OLGB and RYGB, and substantially higher than in controls. Overall glucose concentration, however, did not vary across the three groups. Thirty-minute and overall insulin plasma concentration, indicators of early and total insulin secretion, respectively, was significantly higher in both bypass groups than in controls, and was greatest in OLGB. Severe hypoglycemia occurred in one out of two patients in both bypass groups. At IVGTT, no differences were registered across the three groups and no participant experienced hypoglycemia. The incretin effect was higher after OLGB than after RYGB, but the difference was not statistically significant.
Conclusions The incorporation of a Roux limb in a loop gastric bypass appears to create a statistically nonsignificant tendency toward reducing insulin hypersecretion observed at OGTT after OLGB, and consequently toward tapering the incretin effect.

Keywords Mini-gastric bypass · Omega loop gastric bypass · Roux-en-Y gastric bypass · Hypoglycemia · Glucose tolerance test · Insulin hypersecretion

Laparoscopic Roux-en-Y gastric bypass (RYGB) is one of the most popular weight loss operations [1]. Recently a simpler version of laparoscopic gastric bypass has emerged: the mini-gastric bypass (MGB), also called omega loop (OLGB) [2]. Our department offers the OLGB since 2008 to morbidly obese patients, selected according to our treatment algorithm (Fig. 1).

Because of the anatomical similarity of OLGB with the Billroth II gastrectomy, the safety of this type of bypass in terms of alkaline gastritis and reflux esophagitis is a concern for some [3, 4]. To our knowledge, however, so far there have been no reports on mid- or long-term deleterious effects of OLGB on gastric pouch and/or esophagus [5, 6]. Conversely, safety and efficacy of the OLGB procedure have been claimed by several authors [7, 8].

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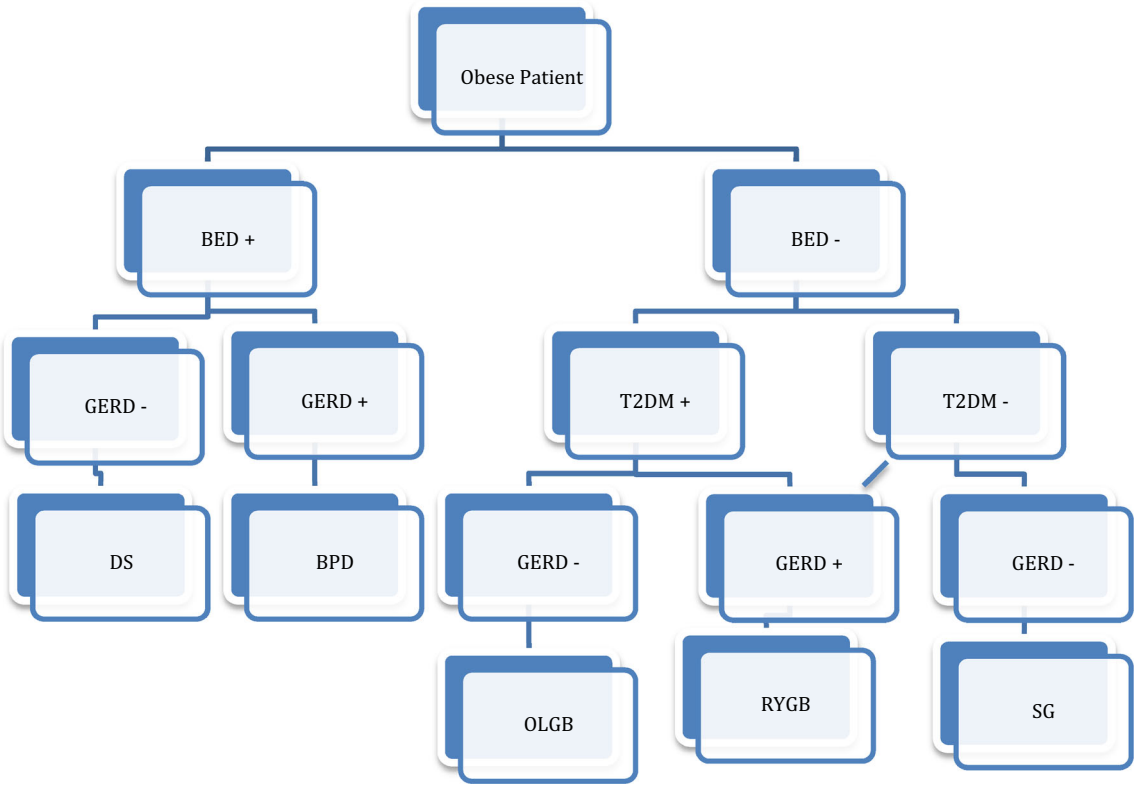


Fig. 1 Empiric treatment algorithm of our bariatric department. The laparoscopic procedure choice is based on the findings of the multidisciplinary team. *BED* binge eating disorder (diagnosed by psychologist, dietician), *GERD* gastroesophageal reflux disease (diagnosed by endoscopist), *T2DM* type 2 diabetes mellitus (diagnosed by endocrinologist), *DS* duodenal switch, *BPD* biliopancreatic diversion, *OLGB* omega loop gastric bypass, *RYGB* Roux-en-Y gastric bypass, SG sleeve gastrectomy

Moreover, OLGB might offer clinical benefit over other bariatric procedures such as sleeve gastrectomy, especially in terms of activity on type 2 diabetes mellitus (T2DM) [9, 10].

Along the same lines, Lee et al. [11] demonstrated that OLGB has an enhanced activity on metabolic syndrome compared to RYGB.

Interestingly, Carbajo et al. [12] found that OLGB patients do not suffer from the dumping syndrome.

Because with our technique the only anatomical difference between OLGB and RYGB lies in the absence (as in the former) or the presence (as in the latter) of a Roux limb, it was our hypothesis that the reported differences in glucose dynamics might be related to the Roux limb.

To analyze the possible role of the Roux limb in glucose metabolism, we submitted a group of preoperatively nondiabetic patients who had undergone OLGB some 4 years ago and a matching group of patients who had undergone RYGB to a glucose tolerance test and compared both groups to control subjects. The time frame of the fifth postoperative year (for bypass patients) was selected because patients' weight is assumed to have stabilized by that time [13, 14].

Materials and methods

Study design

The study included all consecutive nondiabetic patients—as defined by the American Diabetes Association (ADA) guidelines [15] [no diabetic medication, fasting plasma glucose <126 mg/dl and glycated hemoglobin A1c (HbA1c) <6.0 %]—who had undergone OLGB between December 1, 2009 and November 30, 2010. These participants were compared to the best matching individuals selected among the patients who had undergone a RYGB in our department during the same period. A comparable group of nonobese, nondiabetic volunteers was selected as controls. The participants were recently submitted to an oral and an intravenous glucose tolerance test (OGTT, respectively IVGTT) with serial measurement of plasma glucose and insulin.

Surgical technique

Laparoscopic gastric bypass involved the creation of a long 30-ml gastric pouch, anastomosed end-to-side to the small

bowel with linear stapling technique, at a level situated some 150 cm distally to Treitz' angle. In case of RYGB, the intestine was transected just proximal to the GE and reanastomosed end-to-side to the bowel some 60 cm distal to the GE. Hence, with both techniques the afferent (or biliopancreatic) limb had the same length (Fig. 2).

Baseline data

The preoperative baseline data of the bypass patients were obtained from their electronic charts. The baseline data of the participants from the three groups at the time of the study were registered on the day of OGTT.

Oral glucose tolerance test

OGTT involved oral ingestion of 50 grams of glucose after an overnight fast. We used 50 grams rather than the usual 75 grams to reduce dumping symptoms in the bypass patients, as proposed by Bose et al. [16]. Blood was sampled at 0, 30, 60, 90, 120, 180 and 240 min. Samples were placed in chilled tubes, and plasma was separated within 20 min and stored at −80 °C. Plasma glucose was measured by photometrical measurement with hexokinase Roche Cobas c501 (Roche Belgium). Plasma insulin and C-peptide were measured by electrochemiluminescence immunoassay (ECLIA), sandwich principle on Roche Cobas e601 (Roche Belgium).

Intravenous glucose tolerance test

IVGTT was performed after an overnight fast, by injecting in one arm vein a bolus of glucose (0.33 g per kg of body weight), mixed with a 50 % water solution. Blood samples were obtained from a contralateral arm vein at 0, 10, 20, 30, 40, 50 and 60 min relative to the start of the dextrose injection. The samples were handled and plasma glucose and plasma insulin measured as described above.

Mathematical models and statistics

Insulin resistance was expressed as homeostasis model of assessment for insulin resistance (HOMA-IR) and was calculated by an online formula obtained at https://www.dtu.ox.ac.uk/homacalculator.

Whole-body insulin sensitivity and insulinogenic index were calculated according to the Matsuda formula [17].

Plasma glucose incremental levels (Δ glucose) were evaluated as the maximum glucose level minus the minimum glucose level during OGTT.

Area under the curve (AUC) values for insulin and glucose were obtained by the trapezoidal method. Total AUC was calculated (as opposed to incremental or positive AUC calculations) because it is not dependent upon baseline levels that may significantly vary across groups [18].

Early-phase insulin secretion was calculated as AUC for insulin between time points 0′ and 30′ (insulin $AUC_{0' \rightarrow 30'}$); late-phase insulin secretion was calculated as AUC for insulin between 60′ and 240′ (insulin $AUC_{60' \rightarrow 240'}$), and total insulin secretion as insulin $AUC_{0' \rightarrow 240'}$ [19].

The difference in β-cell response (total insulin secretion) depending on the administration route of glucose (estimated by insulin total AUC responding to the oral and the IV glucose challenge, insulin AUCO and IV, respectively) represented the incretin effect, expressed as a percentage of the response to oral glucose (insulin AUCO) [16].

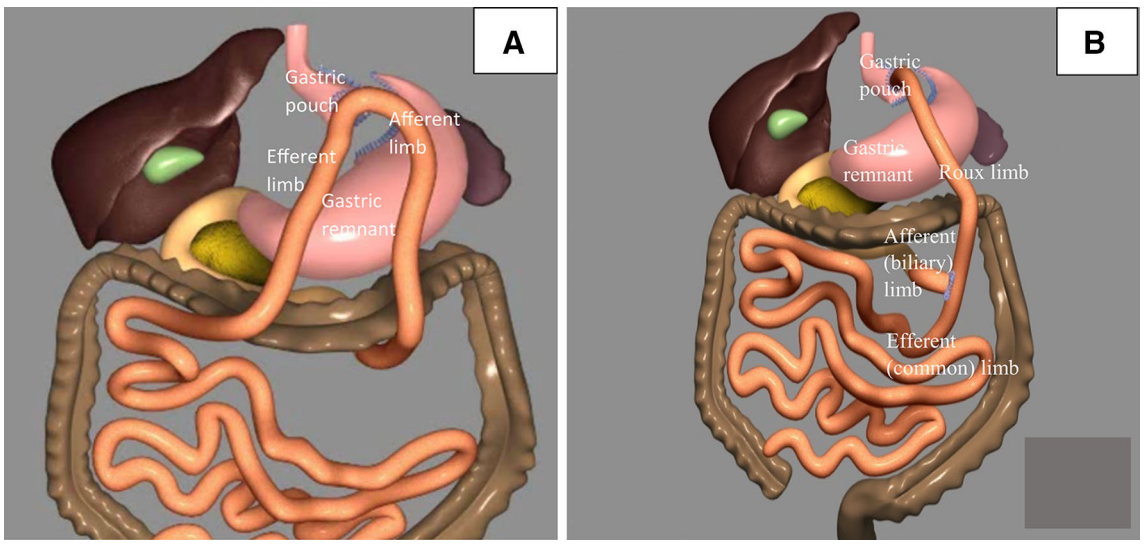


Fig. 2 Schematic representation of the omega loop gastric bypass (OLGB), Fig. 1A and the Roux-en-Y gastric bypass (RYGB), Fig. 1B. The main difference resides in the absence of an alimentary limb in OLGB. The length of bypassed bowel is similar in both techniques

The formula used was:

$$\text{Incretin action}\,(\%) = \frac{\text{Insulin AUCO} - \text{Insulin AUCIV}}{\text{Insulin AUCO}} \times 100\,\%$$

Severe hypoglycemia was defined as plasma glucose <50 mg/dl at any point during OGTT or IVGTT.

All data were expressed as means (SD) when normally distributed as confirmed by the Shapiro–Wilk's test or by median [interquartile range] otherwise. Intra-group comparisons were statistically evaluated by the Student's *T* test when data were normally distributed or by the Wilcoxon rank-sum test otherwise. Intergroup categorical variables were compared with the *Z* test for nonpaired categorical variables. Intergroup comparisons of continuous data were performed by the Student's *T* test for nonpaired variables in case of normal distribution or by the Mann–Whitney test otherwise. When allowed by the Levene test, three-way intergroup comparisons were performed by analysis of variance (ANOVA) for repeated measurements followed by Tukey's "post hoc" test. Three-way intergroup comparisons were performed by the Kruskal–Wallis rank-sum test when the Levene test did not allow ANOVA. Covariance between independent and dependent variables was evaluated by Pearson's correlation checked by Holm's test. Statistical significance was reached when $P < 0.05$. Statistical calculations were performed using Excel 97–2003 worksheets computed by Anastats (www.Anastats.fr/downloads). Figure 3 displays values as means; error bars indicate standard error of the mean (SEM).

Results

Baseline data

The three groups (OLGB, RYGB and controls) comprised 14 patients each. Preoperatively, the two bypass groups were statistically comparable, but the RYGB patients were slightly heavier and older (Table 1). At 4 years, the baseline parameters linked to glucose metabolism had significantly improved in both bypass groups compared to preoperatively (Table 2). The OLGB procedure had induced significantly more weight loss than RYGB, but in intergroup comparison the three groups did not differ in terms of weight, BMI, fasting plasma glucose, HbA1c, C-peptide and HOMA-IR. Fasting plasma insulin was significantly greater in the control group than in either bypass group (Table 3).

Oral glucose tolerance (OGTT)

- For the three groups, the progression of plasma glucose and insulin at OGTT can be found in Fig. 3A, B.
- Plasma glucose incremental values were similar in both bypass groups (Tukey's post hoc) and significantly greater than in controls (ANOVA): OLGB: 132 [118.250–149.250] mg/dl; RYGB: 124 [104.25–133] mg/dl; controls: 59.5 (31.99) mg/dl: $P < 0.01$.
- Area under the curve (AUC) values for plasma glucose and plasma insulin can be found in Tables 4, 5. Insulin $AUC_{0' \rightarrow 30'}$ and total insulin AUC were significantly higher in both gastric bypass groups than in controls. In intergroup comparison, the aforementioned values were higher after OLGB than after RYGB, but the difference did not reach statistical significance (Table 5).
- Insulin sensitivity and insulinogenic index did not differ statistically across the 3 groups. The difference across the two bypass groups did not reach statistical significance (Table 3).

Eight (57 %) OLGB patients, and 7 (50 %) RYGB patients, versus 1 (7 %) of the controls displayed glucose levels <50 mg/dl during OGTT ($P < 0.05$) (Table 3). In the 15 bypass patients who experienced severe hypoglycemia, total insulin secretion was significantly greater than in the 13 bypass patients who did not [6325 (2168.66) vs. 4305.31 (1887.76) mU l^{-1} min, $P = 0.014005$, Student's *T* test]. No link could be found between any of the preoperative or postoperative baseline variables and Δ glucose during OGTT (Table 6).

Intravenous glucose tolerance test

Progression of plasma glucose and insulin at IVGTT can be found in Fig. 3C, D.

Insulin $AUC_{0' \rightarrow 60'}$ values were similar for the three groups. Values were (in mU l^{-1} min): for OLGB: 1032.50 [704.45–1136.63]; RYGB: 1037.33 (388.34); controls: 1163.38 (585.69), $P = 0.4609$ (ANOVA).

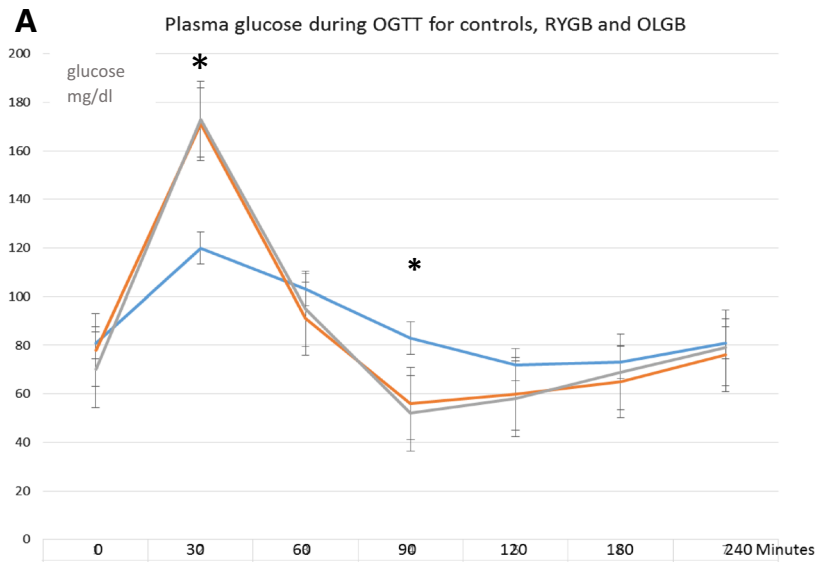
During IVGTT, none of the subjects suffered significant hypoglycemia.

Incretin effect

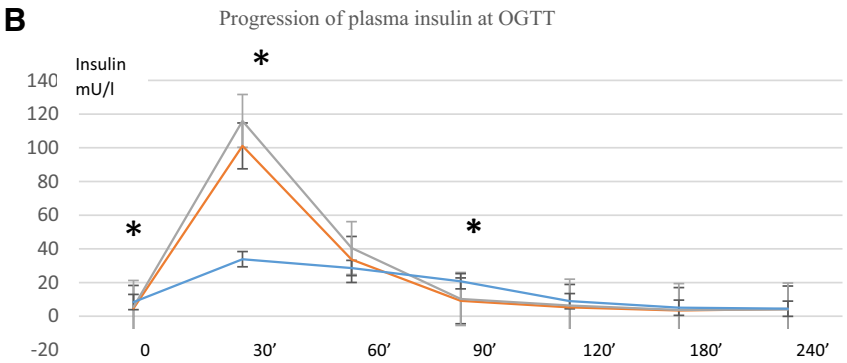
The calculated incretin effect was significantly greater in the bypass groups than in the control group. The incretin values were higher after OLGB than after RYGB, but the difference did not reach statistical significance (Table 3).

Discussion

Our data show that 4 years both after RYGB and OLGB these nondiabetic subjects displayed a significant enhancement of the baseline parameters reflecting β-cell activity (i.e., fasting plasma glucose and C-peptide, fasting



	0′	30′	60′	90′	120′	180′	240′
RYGB	78.0	171.2	91.36	56.0	60.14	65.03	76.0
OLGB	70.08	173.46	94.75	51.50	57.79	69.20	78.5
CONTR	81.29	120.43	103.71	85.86	71.79	73.07	78.57



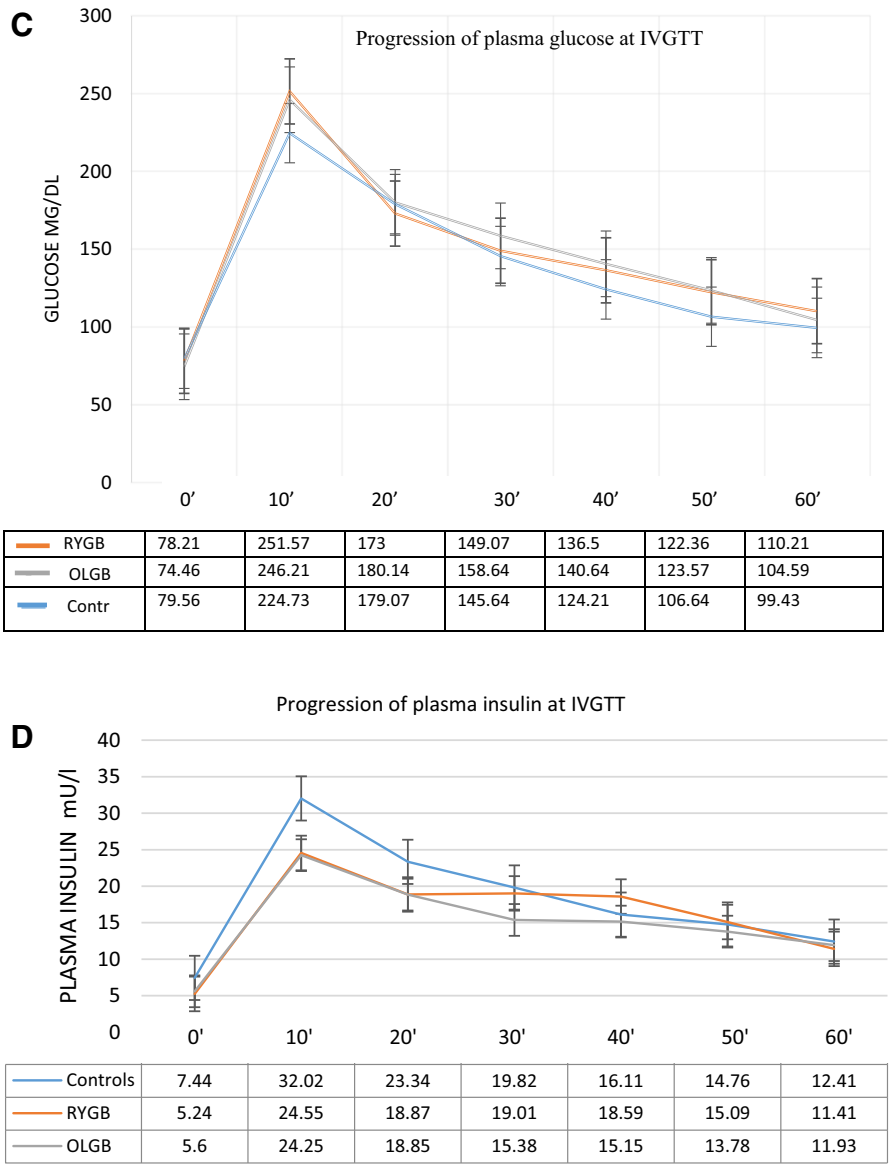
RYGB	4.67	101.13	33.7	9.13	5.23	3.4	4.36
OLGB	5.53	115.94	40.48	10.25	6.32	3.73	4.02
Controls	8.42	33.86	28.62	20.75	8.95	5.06	4.5

Fig. 3 Progression of plasma glucose and plasma insulin (**A**, **B**) at different time points (min) during oral glucose tolerance test (OGTT) and during intravenous glucose tolerance test (IVGTT) (**C**, **D**). *OLGB* omega loop gastric bypass, *RYGB* Roux-en-Y gastric bypass, *Contr* controls. The figures display mean values ± standard error of the mean (*error bars*). Plasma glucose levels are expressed in mg/dl; insulin levels are expressed in mU/l. * Statistical significance (ANOVA)

plasma insulin and HOMA-IR) [20] compared to preoperatively. This finding is most likely explained by the significant weight loss the participants experienced in both groups [21]. Interestingly, weight loss appeared more effective after OLGB, as previously reported [2].

When analyzing glucose progression at OGTT, the subjects in both bypass groups responded to an oral glucose challenge in a similar way, which was quite different from controls. The marked plasma glucose fluctuations, reflected by the glucose incremental values, were almost identical in both bypass groups and included a rapid peak value, followed by a significant trough, corresponding to the rapid absorption followed by the swift disappearance of ingested glucose in the blood stream. The absorption pattern of glucose resulted in early concentration values (glucose $AUC_{0' \rightarrow 30'}$) that were very similar in both bypass groups, and significantly higher than in controls. In both bypass groups, the subsequent fast clearance of glucose from the plasma diminished the plasma glucose content to such a degree that total AUC glucose numbers (i.e., the overall glucose content) became comparable across the three cohorts. Our findings corroborate earlier findings on RYGB

Fig. 3 continued



of Campos et al. [22] and of Promintzer-Schifferl et al. [23].

In terms of insulin dynamics at OGTT, plasma insulin levels paralleled glucose fluctuations in all groups, but insulin $AUC_{0' \rightarrow 30'}$, reflecting early insulin secretion, was significantly greater in both bypass groups than in controls. Between the two bypass groups, early insulin secretion appeared greater after OLGB than after RYGB; the difference, however, did not reach statistical significance.

The insulinogenic index—an indicator of β cell activity [16]—was higher (but again not statistically) and the insulin sensitivity lower (but not statistically so) after OLGB than after RYGB.

In contrast with total glucose AUC, total insulin secretion values (insulin $AUC_{0' \rightarrow 240'}$) were significantly higher in both bypass groups relative to controls, and again substantially, but not statistically significantly, higher in OLGB than in RYGB. Notwithstanding the slight (i.e., statistically nonsignificant) difference in age and weight between the two bypass groups and the greater weight loss experienced by the OLGB participants which may have skewed the outcomes to a certain extent [24], our findings may indicate that the well-documented enhanced β-cell response to an oral glucose challenge described after RYGB [25] tends to actually be augmented after OLGB. Because the only anatomical difference between the two types of bypass consisted of the presence/absence of a Roux limb, the trend toward enhanced insulin secretion after OLGB may have to do with the Roux limb. The explanation for the possible role of the Roux limb in insulin dynamics at OGTT is not clear. Fact is that with the Roux construction, the jejunal mucosa at the GE is exposed to

Table 1 Preoperative baseline data

	OLGB	RYGB	*P* value
Weight (kg)	105.5 [100.5–117.3]	113.21 (11.71)	0.107 (Mann–Whitney)
BMI (kg/m^2)	39.7 (2.5)	40.8 [39.85–41.48]	0.857 (Mann–Whitney)
Gender (male/female)	3/11	5/9	0.4 (*Z* test)
Age (years)	32.4 (11.2)	36.3 (10.5)	0.383 (*T* test)
Fasting glucose (mg/dl)	91.5 [82.0–96.5]	89.5 (10.16)	0.646 (Mann–Whitney)
HbA1c (%)	5.40 (0.40)	5.35 (0.25)	0.447 (*T* test)
Fasting insulin (μU/ml)	16.82 (6.90)	16.69 (7.47)	0.713 (*T* test)
Fasting C-peptide (ng/ml)	3.18 [2.99–3.55]	2.99 [2.42–4.07]	0.3739 (Mann–Whitney)
HOMA-IR (%)	2.04 (0.88)	2.0 (1.1)	0.744 (*T* test)

Data registered at the time of the bypass surgery: OLGB (omega loop gastric bypass) or RYGB (Roux-en-Y gastric bypass). Data are expressed as mean (standard deviation) when normally distributed or median [interquartile range] otherwise. *P* values are provided with the statistical test used. *T* test is the Student's *T* test

BMI body mass index, *HOMA-IR* homeostasis model of assessment for insulin resistance

Table 2 Pre- and postoperative baseline data

	Pre-OLGB ($n = 14$)	Post-OLGB	*P* value	Pre-RYGB ($n = 14$)	Post-RYGB	*P* value
Weight (kg)	105.5 [100.5–117.3]	65.0 [56.25–76.75]	0.0005* (Wilcoxon)	113.21 (11.71)	74.02 (10.44)	<0.0001* (*T* test)
BMI (kg/m^2)	39.7 (2.5)	23.80 [21.80–26.95]	0.0005* (Wilcoxon)	40.8 [39.85–41.48]	26.48 (2.57)	0.0005* (Wilcoxon)
EBMIL (%)	NA	103.9 (20.3)	NA	NA	87.21 (15.74)	NA
Fasting glucose (mg/dl)	91.5 [82.0–96.5]	80.07 (3.64)	0.0014* (Wilcoxon)	89.5 (10.16)	78.5 [76–80]	0.0038* (Wilcoxon)
HbA1c (%)	5.40 (0.40)	5.29 (0.23)	0.33 (*T* test)	5.35 (0.25)	5.42 (0.28)	0.783 (*T* test)
Fasting insulin (mU/l)	16.82 (6.90)	5.69 [4.81–6.89]	0.0005* (Wilcoxon)	16.69 (7.47)	4.32 [3.15–6.05]	0.0006* (Wilcoxon)
Fasting C-peptide (ng/ml)	3.18 [2.99–3.55]	1.86 [1.66–1.99]	0.0006* (Wilcoxon)	2.99 [2.415–4.07]	1.68 (0.341)	0.0005* (Wilcoxon)
HOMA-IR (%)	2.04 (0.88)	0.70 (0.39)	0.006* (*T* test)	2.0 (1.1)	0.65 (0.34)	0.00015* (*T* test)

Changes in outcome variables before (pre) and after (post) OLGB (omega loop gastric bypass) or RYGB (Roux-en-Y gastric bypass). Data are expressed as mean (standard deviation) when normally distributed or median [interquartile range] otherwise. *P* values are provided with the statistical test used. *T* test is the Student's *T* test

BMI body mass index, *EBMIL%* percentage of excess BMI lost, *HOMA-IR* homeostasis model of assessment for insulin resistance

* Statistical significance

undiluted nutrients, the mix with gastric (from the remnant stomach) and biliopancreatic fluids occurring some 60 cm more distally. In contrast, in OLGB the mix of nutrients occurs immediately after the exit from the gastric pouch. In an animal model, the delay of mixing food stuffs with digestive juices (as in RYGB) appeared to have an impact on (i.e., to taper) the production of GLP1 by the jejuno-ileal L cells and consequently on the GLP1 induced insulin secretion [26, 27]. Consequently, the immediate interaction between ingested glucose and bile and other intestinal juices in OLGB might be responsible for the possibly (not statistically significant) enhanced insulin dynamics compared to RYGB.

In accordance with Roslin's findings [28], 50 % of the RYGB patients experienced hypoglycemia to a level under 50 mg/dl at OGTT. The incidence of severe hypoglycemia appeared to be similar (57 %) after OLGB. Hence, the presence or absence of a Roux limb in gastric bypass does not seem to influence the incidence of reactive hypoglycemia. The patients who developed hypoglycemia in both bypass groups secreted significantly more insulin overall than the patients who did not, confirming that hypoglycemia is caused

Table 3 Overview of the parameters measured in the three study groups

Variable	OLGB ($n = 14$)	RYGB ($n = 14$)	CONTROL ($n = 14$)	P value
Age (years)	35.36 (7.92)	39.21 (10.52)	31.86 (7.92)	0.1704 (ANOVA)
Gender (male/female)	5/9	3/11	3/11	0.4009 (Z test)
Weight (kg)	65 [56.25–76.75]	74.02 (10.44)	65.18 (9.49)	0.0644 (ANOVA)
BMI (kg/m^2)	23.80 [21.80–26.95]	26.48 (2.57)	22.40 (3.01)	0.1258 (ANOVA)
EBMIL (%)	103.9 (20.3)	87.21 (15.74)	N.A.	0.022* (T test)
Fasting glucose (mg/dl)	80.07 (3.64)	78.5 [76–80]	81 [79–85]	0.2059 (Kruskal–Wallis)
Fasting HbA1c (%)	5.29 (0.23)	5.42 (0.28)	5.24 (0.23)	0.0733 (ANOVA)
Fasting insulin (mU/l)	5.69 [4.81–6.89]	4.32 [3.15–6.05]	6.70 [5.14–9.48]*	0.0180 (ANOVA, Tukey's post hoc)
Fasting C-peptide (ng/ml)	1.86 [1.66–1.99]	1.68 (0.341)	1.74 [1.55–2.29]	0.5335 (Kruskal–Wallis)
HOMA-IR (%)	0.70 (0.39)	0.65 (0.34)	0.80 [0.7–1.15]	0.1199 (Kruskal–Wallis)
Insulin sensitivity (%)	8.855 [7.678–14.443]	15.85 (7.847)	13.316 (7.087)	0.4415 (ANOVA)
Insulinogenic index	24.69 (16.26)	15.84 [11.73–29.25]	11.03 [5.88–20.62]	0.923 (ANOVA)
Hypoglycemia (n, %)	8 (57 %)	7 (50 %)	1 (7 %)*	<0.05 (Z test)
Incretin effect (%)	81.15 [73.93–82.55]	70.5 [66.58–76.05]	29.6 [26.48–38.88]*	0.0001* (ANOVA).

Data measured at the time of the oral glucose tolerance test (OGTT) and the intravenous glucose tolerance test (IVGTT). Data are expressed as mean (standard deviation) when normally distributed or median [interquartile range] otherwise. P values are provided with the statistical test used

BMI body mass index, *EBMIL%* for percentage Excess BMI lost, *HOMA-IR* homeostasis model of assessment for insulin resistance, hypoglycemia for the patients experiencing a plasma glucose of <50 mg/dl at any point during OGTT, *OLGB* omega loop gastric bypass, *RYGB* Roux-en-Y gastric bypass, *Control* control group consisting of 14 healthy nonsurgical individuals

* Statistical significance. Tukey's post hoc test failed to show a significant difference for fasting insulin and the incretin effect between the two bypass groups

Table 4 AUC glucose at OGTT

AUC glucose	$0' \rightarrow 30'$	$30' \rightarrow 60'$	$0' \rightarrow 60'$	$60' \rightarrow 240'$	Total
OLGB	3897 (578.26)	4113.21 (1114.64)	8011.67 (1639.63)	16,337.57 (2255.77)	24,348.64 (3679.70)
RYGB	3753.21 (542.53)	3938.71 (997.28)	7691.93 (1471.60)	16,006.79 (2646.33)	23,698.71 (3906.78)
Controls	3060 (481.44)	3372.86 (815.34)	6432.86 (1261.85)	16,687.5 [15,502.5–17,808.75]	22,912.5 [21,491.3–25,485]
P value (ANOVA)	0.0014* + Tukey's post hoc test	0.1280	0.0169* + Tukey's post hoc test	0.5229	0.7694

Area under the curve (AUC) values for plasma glucose during oral glucose tolerance test (OGTT) for the time span 0–30, 30–60, 0–60, 60–240 and 0–240 min (total) after omega loop gastric bypass (OLGB), Roux-en-Y gastric bypass (RYGB) and in controls. Values are expressed in mg dl^{-1} min. Mean values (standard deviation) are given when the data distribution is normal or median values [interquartile range] otherwise

* Statistical significance according to the ANOVA test complemented by Tukey's post hoc test, which did not reveal a difference across the two bypass groups

by an exaggerated insulin response to an oral glucose challenge [29, 30], a concept that was recently challenged in a small series of patients [31].

Why some patients experience more severe hypoglycemia than others is not known. We were not able to link the glucose incremental values to any of the baseline preoperative or postoperative baseline variables related to glucose metabolism (Table 6).

As previously demonstrated [16], the significant differences at OGTT between bypass patients and controls in terms of glucose and insulin dynamics were abolished at IVGTT. The discrepancy in insulin dynamics after oral versus intravenous glucose administration can be measured by the incretin effect. Because unlike in controls total insulin secretion (insulin $AUC_{0' \rightarrow 240'}$) was substantially lower after the intravenous than after the oral challenge in

Table 5 AUC insulin at OGTT

AUC insulin	0′ → 30′	30′ → 60′	0′ → 60′	60′ → 240′	Total
OLGB	1934.33 (893.87)	2367.98 (1002.72)	4302 (1851.65)	1475.56 (828.77)	6246.03 [4276.1–7226.5]
RYGB	1597.38 (743.60)	1852.50 [1422.41–2476.5]	3623.47 (1616.85)	1172.18 [687.86–1829.59]	4588.65 [3452.38–5995]
Controls	603.98 [370.39–746.13]	903.625 (501.38)	1504.31 (796.11)	1852.32 (1114.18)	3356.64 (1834.12)
P value	0.0001* Kruskal–Wallis	0.0001* ANOVA + Tukey's post hoc test	0.0001* ANOVA + Tukey's post hoc test	0.3983 ANOVA	0.0145* ANOVA + Tukey's post hoc test

Area under the curve (AUC) values for plasma insulin during oral glucose tolerance test (OGTT) for the time span 0–30, 30–60, 0–60, 60–240 and 0–240 min (total). Values are expressed in mU l^{-1} min. Mean values (standard deviation) are given when the data distribution is normal or median values [interquartile range] otherwise

OLGB omega loop gastric bypass, *RYGB* Roux-en-Y gastric bypass

* Statistical significance; in the cases where ANOVA test was followed by Tukey's post hoc test, there was no significant difference across the two bypass groups

Table 6 Correlation between glucose incremental values and the evaluated variables

Variables	OLGB		RYGB	
	Correlation coefficient *R*	*P* value	Correlation coefficient R	*P* value
Insulin sensitivity	−0.0762	0.7956	−0.2654	0.3590
HOMA-IR	−0.1884	0.5189	0.3146	0.2734
Fasting glucose	−0.3902	0.1678	0.3825	0.1771
Fasting HbA1c	0.2698	0.3508	0.1572	0.5914
Fasting insulin	0.0802	0.7853	0.5466	0.0431*
Fasting C-peptide	0.0601	0.8383	0.2353	0.4181
BMI	−0.3464	0.2251	0.2497	0.3892
Age	0.0329	0.9111	0.3101	0.2805
EBMIL%	0.2710	0.3486	0.1431	0.0978
Δ fasting insulin pre-op versus post-op	0.1408	0.6310	0.4448	0.1110
			0.4448	0.6254
Pre-op HOMA-IR	0.4037	0.1523	0.5004	0.0684
Pre-op fasting glucose	−0.0655	0.8241	0.1765	0.5461
Pre-op fasting HbA1c	0.3469	0.2243	0.2034	0.4855
Pre-op fasting insulin	0.0758	0.7967	0.5302	0.0511
Pre-op fasting C-peptide	−0.1987	0.4959	0.5535	0.0400**
Pre-op BMI	−0.0773	0.7928	−0.4557	0.1015

Correlation (Pearson) during oral glucose tolerance test (OGTT) between Δ glucose and the various variables recorded in the patients treated by OLGB (omega loop gastric bypass) or RYGB (Roux-en-Y gastric bypass). The two significant correlation coefficients (*, **) lost significance after *P* correction according to Holm. The preoperative insulin sensitivity and insulinogenic index could not be estimated because of the absence of preoperative OGTT data

HOMA-IR homeostasis model of assessment for insulin resistance, *BMI* body mass index, *EBMIL%* percentage of excess BMI lost, Δ difference, *pre-op* preoperative

both bypass groups, the incretin effect was significantly higher. Interestingly, OLGB created a greater incretin effect than RYGB (even though the difference again did not reach statistical significance). This finding may constitute yet another indication of the possible tapering role of a Roux limb on insulin dynamics after an oral glucose challenge.

Shortcomings to our study are many and include:

1. the use of a pure glucose oral challenge model rather than a standardized test meal, the latter constituting a more physiological challenge [32].
2. the absence of documentation of the progression of C-peptide values during the glucose challenge. Consequently, β-cell activity can only be assessed indirectly [33].
3. the use of established formulas to evaluate total insulin resistance and insulin sensitivity, rather than measuring these parameters by euglycemic hyperinsulinemic clamp techniques. [34]. In addition, due to technical limitations we were not able to measure incretin hormones such as GLP1 and PYY.
4. the small number of participants obviously reduces the power of inter- and intra-group comparisons.
5. the patients in the RYGB group were slightly older and heavier and had experienced less weight loss than the OLGB patients, which may have influenced glucose dynamics [25].
6. our patients were evaluated some 4 years after the bypass procedures, i.e., at mid-term follow-up, while long-term data would be preferable

Conclusions

From this small case–control study, it appears that when RYGB and OLGB are constructed with an afferent (or biliopancreatic) limb of 150 cm, the incorporation of a 60-cm Roux limb to complete RYGB does not seem to influence glucose dynamics at OGTT. Nevertheless, the addition of a Roux limb appears to create a tendency toward impairment of the enhanced early and total insulin secretion observed after OLGB in response to the plasma glucose fluctuations caused by an OGTT.

More research involving larger number of participants and a more physiological challenge such as a mixed meal tolerance test is needed to determine the true impact of the Roux limb on glucose metabolism after gastric bypass.

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Compliance with ethical standards

Disclosures Jacques Himpens is a consultant for Ethicon Endosurgery and for Covidien; Guy-Bernard Cadière is a consultant for Ethicon Endosurgery and for Storz. Ramon Vilallonga and Guido Leman have no conflicts of interest.

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