Received: 9 November 2023 | Accepted: 23 October 2024
DOI: 10.1111/cob.12721

ORIGINAL RESEARCH

Clinical OBESITY WILEY

Changes in gastrointestinal motility and gut hormone secretion after Roux-en-Y gastric bypass and sleeve gastrectomy for individuals with severe obesity

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Funding information
Wetenschappelijk fonds Catharina ziekenhuis

Summary

Background: Bariatric surgery is very effective in long-term weight management. The present study was undertaken to investigate the short-term effects of sleeve gastrectomy (SG) and of Roux-en-Y gastric bypass (RYGB) on (a) gastrointestinal (GI) motility, that is gastric emptying and oro-cecal transit time and (b) secretion of regulatory gut peptides and (c) their interrelationship.

Methods: Prospective single-centre study in which we assessed gastric emptying, oro-cecal transit time and gut peptide release in 28 severely obese individuals before and 2, respectively, 12 months after bariatric surgery (either SG or RYGB). Plasma PYY, GLP-1, ghrelin, insulin and glucose levels were measured fasting and after intake of a solid standard 459 kcal meal at each occasion. Gastric emptying was measured by 13 C octanoic acid breath testing, and oro-cecal transit time was measured by lactulose H_2 breath testing. Satiation was measured using VAS scores.

Results: After both RYGB and SG gastric emptying become significantly accelerated, and postprandial release of the distal gut peptides GLP-1 and PYY becomes significantly increased, pointing to ileal brake activation. Oro-cecal transit time becomes significantly accelerated after SG but not after RYGB. No significant correlations were observed between changes in distal gut peptide release, changes in GI motility and clinical parameters.

Conclusion: Both SG and RYGB resulted in significant weight loss and significantly affected GI motility and PYY and GLP-1 secretion. Subtle differences between both procedures were found in effect on oro-cecal transit time and patterns of peptide secretion.

KEYWORDS
gastric bypass, gastrointestinal motility, gut peptides, sleeve gastrectomy

What is already known about this subject

- Increased release of GLP-1 and PYY after bariatric surgery.
- Accelerated gastric emptying after sleeve gastrectomy and Roux-en-Y gastric bypass.

What does this research article add

- Confirmation of accelerated gastric emptying after both procedures.
- Accelerated intestinal transit time after sleeve gastrectomy.

1 | INTRODUCTION

Bariatric surgery, such as sleeve gastrectomy (SG) or Roux-en-Y gastric bypass (RYGB), is very effective in long-term weight management.[1] The alterations in anatomy resulting from bariatric surgery are known to affect gastrointestinal (GI) physiology and involve signalling along the gut brain axis, GI motility and secretion and neurohormonal control of GI function, especially the release of regulatory gut peptides.

More detailed information on the alterations in GI physiology induced by bariatric surgery will help to unravel the underlying mechanisms resulting in weight loss, thus enabling to maximize the efficacy of bariatric surgery and reduce adverse events and complications related to the procedure. SG and the creation of a gastric pouch as in RYGB are known to restrict food intake by reducing gastric volume, gastric relaxation and accommodation capacity.[2,3] These procedures result in more rapid delivery of nutrients to the duodenum (gastric sleeve) or small intestine (RYGB), presumably resulting from acceleration of gastric emptying. Indeed, in most studies, after sleeve gastrectomy, gastric half emptying time of solid meals measured by scintigraphy was found to be reduced.[4–9] Concerning RYGB, reliable data on gastric emptying from scintigraphic studies are scarce.[10] Some studies have measured gastric emptying after RYGB indirectly via paracetamol absorption or via pouch retention of tracers.[11–13]

More rapid gastric emptying may result in accelerated intestinal transit time. Indeed, in patients with sleeve gastrectomy, the GI content was found to reach the terminal ileum faster.[5,14,15] Data on intestinal transit after RYGB are scarce and show conflicting results of either accelerated oro-cecal transit time,[16,17] delayed OCTT[13] or unaltered OCTT.[18]

The presence of undigested nutrients in the distal part of the small bowel triggers the release of ileal brake gut peptides such as GLP-1 and PYY.[19,20] A more rapid and more pronounced postprandial secretion of these peptides has been observed after both SG and RYGB. The ileal brake is a potent feedback mechanism that brings the process of ingestion of food and the transport, digestion and absorption of nutrients to an end.

The present study was undertaken to investigate the short-term effects of SG and of RYGB on (a) GI motility that is gastric emptying and oro-cecal transit time, (b) the secretion of regulatory gut peptides and (c) their interrelationship.

2 | MATERIALS AND METHODS

This study was set up as a prospective single centre open follow-up study to evaluate GI motility (gastric emptying and intestinal transit time) and gut peptide secretion in severely obese individuals before and at 2 and 12 months after laparoscopic sleeve gastrectomy (LSG) or RYGB.

Patients were considered candidate for bariatric surgery when they fulfilled the IFSO criteria[21] evaluated by a multidisciplinary team. Exclusion criteria for the study were patients with GI or hepatic disorders influencing GI secretion, motility, digestion or absorption. Other study exclusion criteria were alcohol consumption >20 units/week, eating disorders (all candidates for bariatric surgery were screened by a psychologist to exclude eating disorders), pregnancy, lactation or recent use of antibiotics (<4 weeks). Patients were asked to participate in this prospective study when visiting the outpatient department of surgery before the operation was planned. All individuals were informed about the test days with ingestion of a test meal, breath tests for transport/motility recordings (gastric emptying time and oro-cecal transit time) and the collection of blood samples to investigate gut peptide secretion.

Informed consent was obtained from each individual. The study protocol had been approved by Ethics Committee of the Catharina Hospital Medical Centre, and the study was executed according to the revised Declaration of Helsinki (general assembly of the WMA, Fortaleza, Brazil, 2013).

Each severely obese patient referred for bariatric surgery was tested within an interval of 2 months—2 weeks prior to bariatric surgery and at 2 months and at 12 months after bariatric surgery. In the obese patients, a low caloric diet was prescribed for the 2 weeks prior to surgery. All baseline measurements had been performed before this diet was initiated. Weight, BMI and weight loss were assessed at the test days. On these test days, gastric emptying half-time and oro-cecal transit time were assessed and pre- and postprandial blood samples were taken to assess gut peptide secretion.

2.1 | Surgical technique and diet

A SG was performed, preserving the antrum, using a 34 Charriere dilator, as described earlier.[22] RYGB was performed, creating a 50 mL pouch, 80 cm biliary limb and 150 alimentary limb.[23] The choice for the type of operation was based on surgeon and patient preferences. Two weeks before surgery all candidates were advised to follow a strict low calory diet based on Modifast. In the first 2 weeks after surgery, all candidates were advised to eat liquid food only. All patients were seen regularly in the outpatient department of surgery for follow-up (5 year period).

2.2 | Gastric emptying test

Gastric emptying was determined using the ^{13}C stable isotope breath test with octanoic acid. Maes et al. have previously shown that the [^{13}C]-octanoic acid breath test is a reliable and noninvasive tool for the analysis of gastric emptying rates of solids without radiation exposure.[24] For this purpose, 100 microliter [^{13}C]-octanoic acid (Eurisotop, France) added to egg yolk was ingested at $t = 0$ min. A basal breath sample (to determine background enrichment) was taken ($t = 0$ min) before consuming the solid meal containing the [^{13}C]-octanoic acid, subsequent samples were taken at 15 min intervals during the first 2 h and at 30 min intervals thereafter until $t = 240$ min. Breath samples for $^{13}CO_2$ enrichment were collected using reusable plastified aluminium bags.

Samples were collected, stored and analysed afterwards using isotope ratio mass spectometry (Iris Wagner, Bremen, Germany). Half times of gastric emptying time and lag times were calculated after curve fitting using methods described by Maes et al.[24]

On three test days, the patient received a meal consisting of 2 slices of white bread (150 kcal), 1 scrambled egg (110 kcal), 1 slice of Dutch Gouda cheese (111 kcal) and butter (88 kcal), in total 459 kcal (17.3 g of protein, 34.6 g of carbohydrates and 23.4 g of fat). To this meal, 10 g of lactulose was added, to enable measurement of oro-cecal transit time.[25]

2.3 | Oro-cecal transit time

Oro-cecal transit measurement was performed by lactulose hydrogen breath analysis, as described by Ledeboer et al.[25] Ten gram of lactulose was ingested directly before consuming the breakfast meal. Samples of end-expiratory breath were taken under basal conditions and at 15 min intervals during the first hour and at 30 min intervals during the second, third and fourth hour after meal ingestion with lactulose intake. The samples were directly analysed using a portable hydrogen breath test unit. OCTT was defined as the time between oral lactulose ingestion and the onset of a sustained rise in breath hydrogen concentration of at least 10 parts per million (ppm) above basal level.

2.4 | Blood samples

On each test day, 6 blood samples were taken: at time 0 min and at 15, 30, 60, 90 and 120 min after onset of meal ingestion. Blood was collected in ice-chilled tubes (BD Vacutainer) containing EDTA and DDPIV-inhibitor (10 μL DDPIV inhibitor per ml blood) to prevent immediate degradation of GLP-1 and PYY by dipeptidyl peptidases IV. Tubes were centrifuged (3000 rpm, 15 min at 4°C). The supernatant plasma was stored at −80°C until determination. HbA1c, C-peptide, insulin and glucose were directly measured in the general laboratory of the Eindhoven Catharina Hospital.

Total GLP-1 (included both 7–36 and 9–36) was determined with the use of a GLP-1 ELISA kit (EZGLP1T-36 K; Millipore, Linco Research, St. Louis, USA) with a range of 4–1000 pmol/L and an intra-assay CV of <5% (EZGLP1T-36 K; Millipore, Linco Research, St. Louis, USA). Total PYY (included both peptide YY1–36 and peptide YY3–36) was measured with the use of a human PYY (total) ELISA kit (EZHPYYT66K; Millipore) with an intra-assay CV of 3% (EZHPYYT66K; Millipore, Linco Research, St. Louis, USA).

Active ghrelin was measured with a RIA kit (GHRA-88HK Millipore; Linco Research, St. Louis, USA).

Pre-operative levels and levels at regular follow-up (at 2 and 12 months postoperatively) of total cholesterol, HDL cholesterol and triglycerides were determined.

2.5 | Sample size calculation

An acceleration of 25% in gastric half emptying time after bariatric surgery was hypothesised. Power calculation was based on the study of Melissas et al.[26] in which gastric emptying time for solids before and after SG was measured. With a 1-β of 0.9, an α of 0.05 and a previous standard deviation of 23 min, a minimum sample size of at least 8 subjects per group was considered sufficient to reach statistical significant differences.

2.6 | Statistical analysis

Statistical analyses were performed with Prism 6.0 (Graphpad Software, INc. La Jolla, CA USA).

VAS scores and gut peptide levels were expressed as area under the curve (AUC). Curves for VAS scores and hormone responses were analysed with 2-way repeated measures ANOVA. A post hoc Tukey–Kramer test was performed to analyse differences in gut peptides, motility parameters and satiation scores (VAS). Pearson's R correlations were calculated between VAS scores for satiation, gut peptide, gastric emptying, transit time and excessive weight loss. Data are presented as median ± interquartile ranges. A p value of <0.05 was considered as statistically significant.

3 | RESULTS

3.1 | Baseline characteristics

A total of 32 severely obese patients were recruited, agreed to participate and were included in the study and underwent the preoperative, baseline analyses. Of the 32 patients, 16 underwent either SG and 16 underwent RYGB. Postoperatively we had 4 drop outs. Two patients in the sleeve group were not able to eat solid foods, and 1 patient was converted from SG to gastric bypass. One gastric bypass patient only tested once postoperatively resulting in missing data. The choice for the type of operation was based on surgeon's and patient's preferences after consultation. Baseline characteristics such as age, gender, BMI, blood pressure and laboratory parameters did not significantly differ between the two groups (see Table 1).

3.2 | Effects of surgery on BMI, metabolic and vascular parameters

Each patient underwent three tests: one test preoperatively (baseline) and two tests postoperatively, at 2 and at 12 months after surgery, respectively. BMI and total weight loss percentage (TWL%) decreased significantly in both groups (Tables 2 and 3). C-peptide levels and HbA1C levels decreased significantly ($p < 0.05$); however, fasting glucose levels did not significantly change. Lipid profiles improved significantly ($p < 0.05$) as well as blood pressure in both groups (see Tables 2 and 3).

3.3 | Satiation

After meal ingestion scores of fullness increased significantly and scores of hunger decreased significantly, both before and after SG and RYGB (see Figure 1). The AUC score for fullness was significantly higher at 2 and 12 months after SG compared to baseline. For RYGB only, the 12 months but not the 2 months AUC score of fullness was significantly ($p < 0.05$) increased compared to baseline.

Concerning hunger, AUC scores at 2 and 12 months after SG and RYGB were lower compared to baseline but only at 2 months after SG were the scores significantly ($p < 0.05$) reduced compared to baseline.

3.4 | Gastric emptying

Data on gastric emptying tests for all test days were available for 11 RYGB patients and 10 SG patients. Gastric emptying was

TABLE 1 Baseline characteristics of the 28 severely obese subjects that underwent both pre and postoperative testing of gastrointestinal motility and gut peptide secretion before and after bariatric surgery.

Baseline characteristics	Sleeve *n* = 13	RYGB *n* = 15	*p* value
Age (years)	46.4 ± 6.7	45.5 ± 6.4	ns
Gender (F/M)	9 F, 4 M	14 F,1 M	ns ($p = 0.11$)
BMI (kg/m^2)	42.8 [40.6–47.4]	43.6 [38.9–46.2]	ns
HbA1c (%)	6.0 [5.6–7.3]	5.9 [5.8–7.3]	ns
Diabetes mellitus	6	5	ns
Total cholesterol (mmol/L)	4.5 [3.6–5.2]	5.3 [4.1–6.4]	ns
Cholesterol/HDL ratio	4.6 [3.4–5.2]	4.1 [3.3–5.7]	ns
C-peptide (nmol/L)	1.2 [0.8–1.4]	1.4 [0.9–1.6]	ns
Systolic blood pressure (BP) (mmHg)	134 [123–144]	135 [124–146]	ns
Diastolic blood pressure (BP) (mmHg)	83 [75–90]	80 [72–90]	ns

Note: Data are presented as means (±SD) or as medians with interquartile ranges.

TABLE 2 Changes in BMI, total weight loss % (TWL%), metabolic and vascular parameters in the 13 severely obese patients that underwent SG.

Sleeve *n* = 13	T = 0 baseline	T = 2 months	T = 12 months	*p*-value
BMI (kg/m^2)	42.8 [40.6–47.4]	37.4 [36.1–41.0]	31.7 [28.0–33.7]	$p < 0.0001$
TWL%	0	13.1 [12.0–14.9]	19.1 [14.0–22.8]	$p < 0.0001$
Hba1c (%)	6.0 [5.6–7.3]	6.0 [5.3–6.4]	5.5 [5.2–6.3]	$p < 0.0001$*
Total cholesterol (mmol/L)	4.5 [3.6–5.2]	3.7 [3.1–4.5]	3.9 [3.8–4.7]	$p < 0.01$
Cholesterol/HDL	4.6 [3.4–5.2]	4.0 [3.4–4.8]	3.5 [3.1–3.8]	$p < 0.01$*
C-peptide (nmol/L)	1.2 [0.8–1.4]	0.82 [0.7–0.97]	0.68 [0.54–0.98]	$p < 0.05$
Systolic BP (mmHg)	134 [123–144]	122[110–132]	122 [114–135]	$p = 0.06$
Diastolic BP (mmHg)	83 [75–90]	70 [66–80]	75 [70–79]	$p < 0.05$

Note: Data are presented as medians with interquartile ranges. *p*-values indicate significant differences between T = 2 months and baseline (T = 0) and T = 12 months and baseline (T-0). *p* indicate only differences between T = 2 months and T = 0.
*Significant differences between T = 12 months and T = 0.

TABLE 3 Changes in BMI, total weight loss % (TWL%), metabolic and vascular parameters in the 15 severely obese patients that underwent RYGB, at baseline and 2 and 12 months after RYGB.

RYGB $n = 15$	T = 0 baseline	T = 2 months	T = 12 months	p value
BMI (kg/m^2)	43.6 [38.9–46.2]	36.0 [34.4–38.8]	27.2 [26.4–29.6]	$p < 0.0001$
TWL%	0	14.7 [11.6–18.1]	23.0 [20.2–25.8]	$p < 0.0001$
Hba1c (%)	5.9 [5.8–7.3]	5.5 [5.2–5.8]	5.4 [5.4–5.6]	$p < 0.001$
Total cholesterol (mmol/L)	5.3 [4.1–6.4]	3.7 [3.2–4.9]	4.3 [3.6–4.7]	$p < 0.0001$
Cholesterol/HDL	4.1 [3.3–5.7]	3.7 [3.1–5.8]	2.9 [2.3–4.0]	$p < 0.0001$*
C-peptide (nmol/L)	1.4 [0.88–1.6]	0.99 [0.87–1.1]	0.72 [0.58–0.88]	$p < 0.05$
Systolic BP (mmHg)	135 [124–146]	124 [118–128]	117 [106–126]	$p < 0.001$
Diastolic BP (mmHg)	80 [72–90]	80 [70–84]	73 [68–80]	$p = 0.052$

Note: Data are presented as medians with interquartile ranges. p-values indicate differences between T = 2 months and baseline (T = 0) and T = 12 months and baseline (T = 0).
*Significant differences between T = 12 and T = 0 months.

significantly accelerated ($p < 0.05$) at 2 and 12 months after RYGB compared to baseline (see Table 4). Gastric emptying T1/2 decreased from 263 [250–486] min to 128 [86–152] and 125 [113–144] min, respectively, at 2 and 12 months post RYGB. Lag time became significantly shorter post RYGB. After SG gastric emptying also accelerated significantly. Gastric emptying T1/2 decreased significantly ($p < 0.05$) from 245 min to 130 and 125 min, respectively, at 2 and 12 months post sleeve gastrectomy. Lag time became significantly shorter post sleeve gastrectomy.

3.5 | Oro-cecal transit time

After sleeve gastrectomy, OCTT decreased significantly from 150 min [53–210] at baseline to 60 [38–90] min at 12 months (see Table 5). Although OCTT was shorter at 2 and 12 months after RYGB, the differences compared to baseline were not statistically significant.

3.6 | Gastrointestinal peptides

3.6.1 | GLP-1 and PYY

Data on GLP-1, PYY and ghrelin secretion before and at 2 and 12 months after RYGB and SG are shown in Figure 2 as baseline and postprandial plasma concentrations over time and as AUC values. *GLP-1* and *PYY*.

After RYGB, the AUCs of PYY secretion were significantly higher after 2 months and 12 months compared to the preoperative measurement ($p < 0.05$). At 2 months, the AUC of GLP-1 secretion was significantly increased compared to the preoperative measurement ($p < 0.05$). At 12 months, AUC of GLP-1 secretion decreased and was no longer significantly different from the preoperative measurement.

After sleeve gastrectomy, the AUCs of GLP-1 and PYY were significantly higher after 2 months compared to preoperative measurement ($p < 0.05$). At 12 months only AUC of PYY secretion but not of GLP-1 secretion remained significantly ($p < 0.05$) increased compared to preoperative measurement.

When comparing the patterns of postprandial GLP-1 and PYY secretion at 12 months versus 2 months change between post-RYGB and post-SG: after SG, the AUC PYY further increases while it decreases after RYGB and the AUC GLP-1 slightly decreases after SG and markedly decreases after RYGB. Thus, at 12 months after surgery, the secretion pattern of ileal brake peptides remains more pronounced after SG compared to RYGB.

3.6.2 | Ghrelin

The pattern of plasma ghrelin secretion was not affected by RYGB. After sleeve gastrectomy, however, the pattern of ghrelin secretion had significantly changed. The fasting and postprandial ghrelin levels at 2 and 12 months after SG had decreased significantly ($p < 0.05$) compared to the preoperative condition.

3.7 | Correlations between study parameters

We analysed our data for correlations between changes in weight loss and peptide responses, weight loss and motility parameters (e.g. gastric emptying time and OCTT). We also analysed correlations between peptide responses and motility parameters. No significant or relevant correlations were observed between changes in clinical parameters, gastric emptying parameters, oro-cecal transit time and peptide secretion.

4 | DISCUSSION

We measured gastric emptying, oro-cecal transit time and gut peptide release before and 2 and 12 months after SG and after RYGB. Both procedures resulted in significant weight loss with increased satiation

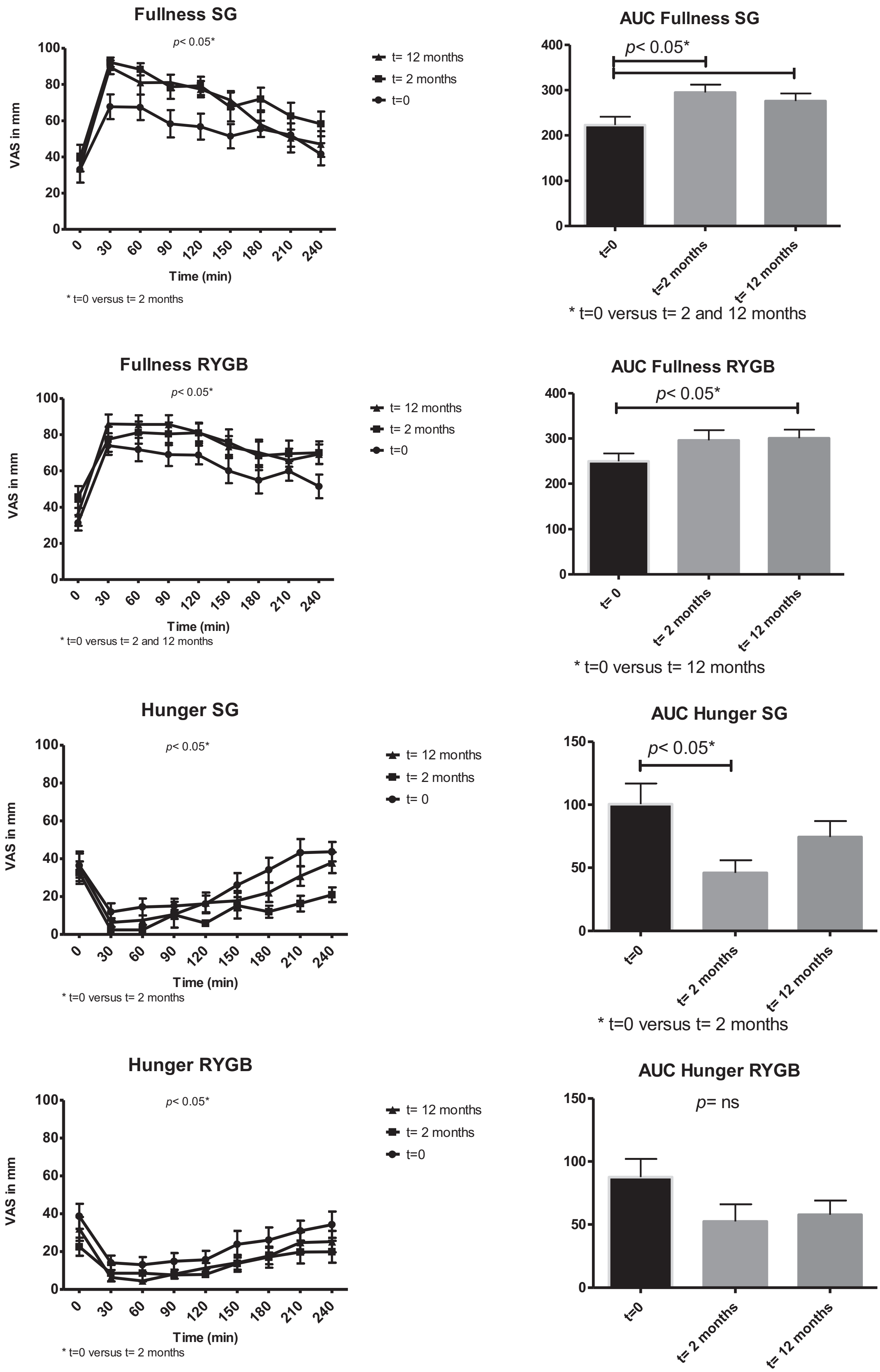

FIGURE 1 Legend on next page.

TABLE 4 Data of gastric emptying measured with 13C octanoic breath test in severely obese patients measured at baseline and 2 and 12 months after sleeve gastrectomy (SG) or Roux-en-Y gastric bypass (RYGB).

Gastric emptying	T = 0 baseline	T = 2 months	T = 12 months	*p*-value
SG (*n* = 10)				
T1/2 (min)	245 [193–402]	130 [125–154]	125 [97–146]	$p < 0.05$
Tlag (min)	157 [121–169]	101 [86–106]	102 [77–121]	$p < 0.05$
RYGB (*n* = 11)				
T1/2 (min)	263 [250–486]	128 [86–152]	125 [113–144]	$p < 0.0001$
Tlag (min)	221 [164–267]	81 [75–108]	80 [58–100]	$p < 0.0001$

Note: Data are presented as medians with interquartile ranges. *p* values indicate differences between T = 2 months and baseline (T = 0) and T = 12 months and baseline (T = 0).

TABLE 5 Oro-cecal transit time measured with lactulose H_2 breath testing at baseline and at 2 and 12 months in severely obese patients before and 2 and 12 months after sleeve gastrectomy (SG) or Roux-en-Y gastric bypass (RYGB).

OCTT (min)	T = 0 baseline	T = 2 months	T = 12 months	*p*-value
SG (*n* = 12)	150 [52.5–210]	105 [75.0–163]	60 [37.5–90,0]	$p < 0.05$
RYGB (*n* = 13)	120 [82.5–225]	105 [52.5–105]	90 [52.5–150]	$p = 0.33$

Note: Data are presented as medians with interquartile ranges. *p* values indicate significant changes between T = 12 months and baseline (T = 0).

parameters. Gastric emptying became significantly accelerated after both procedures. OCTT became significantly shorter only after sleeve gastrectomy, not after RYGB. Release of the distal gut peptides GLP-1 and PYY was significantly increased after both bariatric procedures.

4.1 | Satiation

After both RYGB and SG satiation was more pronounced at 2 and 12 months postoperatively compared to the preoperative condition. These data are in line with those of previous reports. At 12 months after sleeve gastrectomy, hunger scores had returned to levels not different from the preoperative condition.

4.2 | Gastric emptying

We found a significant acceleration of gastric emptying at 2 and 12 months after SG and RYGB with significant reductions in lag times and in half emptying times. Our data are in line with the majority of published studies on gastric emptying after SG and point to an acceleration of gastric emptying, both of liquid and solid meals.[5,6,8,9,26–33] The accelerated gastric emptying after SG is probably explained by higher intragastric pressure due to resection of (part of) the fundus, thus impairing relaxation and accommodation. Accelerated gastric emptying after SG may also be related to the remaining antrum size. Garay et al.[34] found that after SG with antrum preservation (antrum preserved from 0 to 5 cm distance of the pylorus), gastric emptying was accelerated, whereas after SG with near complete antrum resection (antrum preserved from 0-2 cm distance of pylorus) gastric emptying was not accelerated.

After RYGB, we observed a significant acceleration of gastric emptying in the range of that observed in patients after sleeve gastrectomy. Concerning RYGB, reliable data on gastric or pouch emptying from scintigraphic studies or breath test studies with stable isotopes including pre- and postsurgical comparisons are scarce.[34] Studies using indirect methods for gastric or pouch emptying point to a rapid emptying of the pouch both for solid and liquid meals.[13,17,35–38] Deden et al.[35] observed that in patients with poor weight loss after RYGB, the pouch emptying was significantly faster compared to patients with successful long-term weight loss. Up to now, data on pre- and postoperative RYGB comparisons for gastric/pouch emptying were lacking.

For gastric emptying, we used a validated stable isotope breath test with octanoic acid and a solid meal. This indirect test differs from direct scintigraphic tests in that the [^{13}C]-octanoic acid substrate is being processed (digested, absorbed and metabolized) after gastric emptying before it is excreted into breath. Therefore, lag times in stable isotope breath tests are longer than lag times in scintigraphic studies. We assume that metabolic processing time of the [^{13}C]-octanoic acid is not affected by bariatric surgery so that reductions in lag time after SG and RYGB result from shorter retention times in the stomach remnant.

Scintigraphy is the most commonly used technique to quantify gastric emptying but is costly and lacks standardization. Recent

FIGURE 1 Satiation scores before and 0–240 min after meal ingestion in severely obese patients at baseline (preoperative state) and 2 and 12 months after sleeve gastrectomy or 2 and 12 months after RYGB. Left figures: Satiation scores over time. $p < 0.05$ values indicate significant differences between postprandial absolute values at baseline compared to postoperative values. Right figures: Integrated postprandial satiation scores (0–240 min). Data are given as means (±SD). *p* values indicate significant differences between T = 0 and T = 240 min.

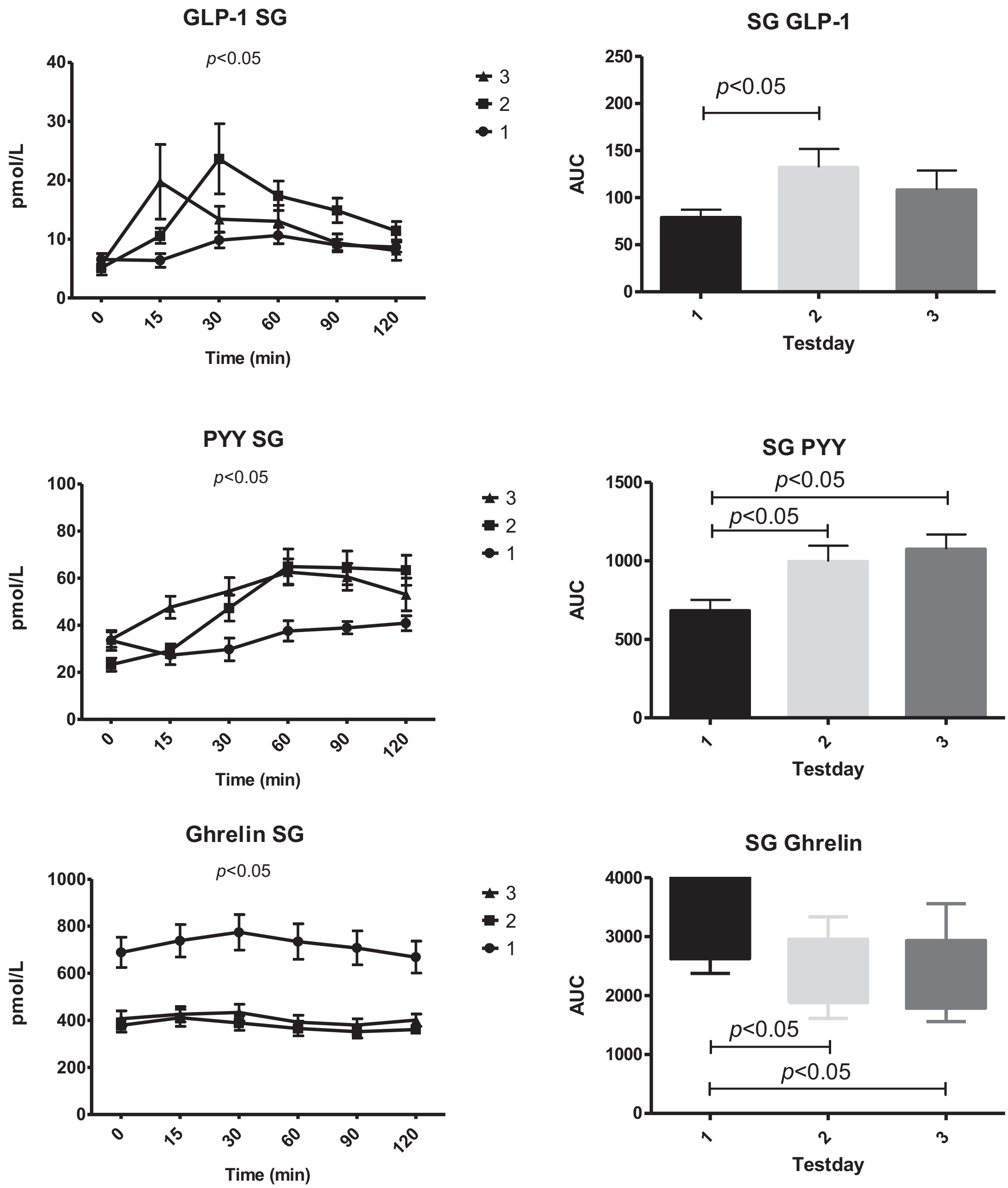

FIGURE 2 Plasma levels of the gut peptides GLP-1, PYY and ghrelin from 0 to 120 min after meal ingestion in patients before operation and 2 and 12 months after sleeve gastrectomy and RYGB. Right figures: Integrated scores of 0–120 min postprandial peptide secretion. Data are presented as means (±SD). *p* values for SG indicate differences between T = 2 months and baseline (T = 0) and between T = 12 months and baseline for ghrelin (GLP-1 and PYY only significant after 2 months). *p* values for RYGB indicate significant differences between T = 2 months and T = 12 months versus baseline.

guidelines advise to measure gastric emptying of solids for at least 240 min after meal ingestion. Most studies that evaluated gastric emptying after bariatric surgery have measured gastric emptying only up to 90–120 min after meal ingestion and caloric content and nutrient composition of the meals differed substantially between studies. Summarising the published data so far, gastric emptying time after SG and RYGB is found to be accelerated. However, the published studies vary in methodology using different techniques, variable meal tests and limited assessment time. The strength of our study is that we used a solid test meal and measured gastric emptying for up to 4 h after meal ingestion. Our test meal consisted of 2 slices of white bread (150 kcal), 1 scrambled egg (110 kcal), 1 slice of Dutch Gouda cheese (111 kcal) and butter (88 kcal), in total 459 kcal per meal. Some patients after bariatric surgery in our study were not able to consume all of the bread so that intake was around 400 kcal instead of 459 kcal.

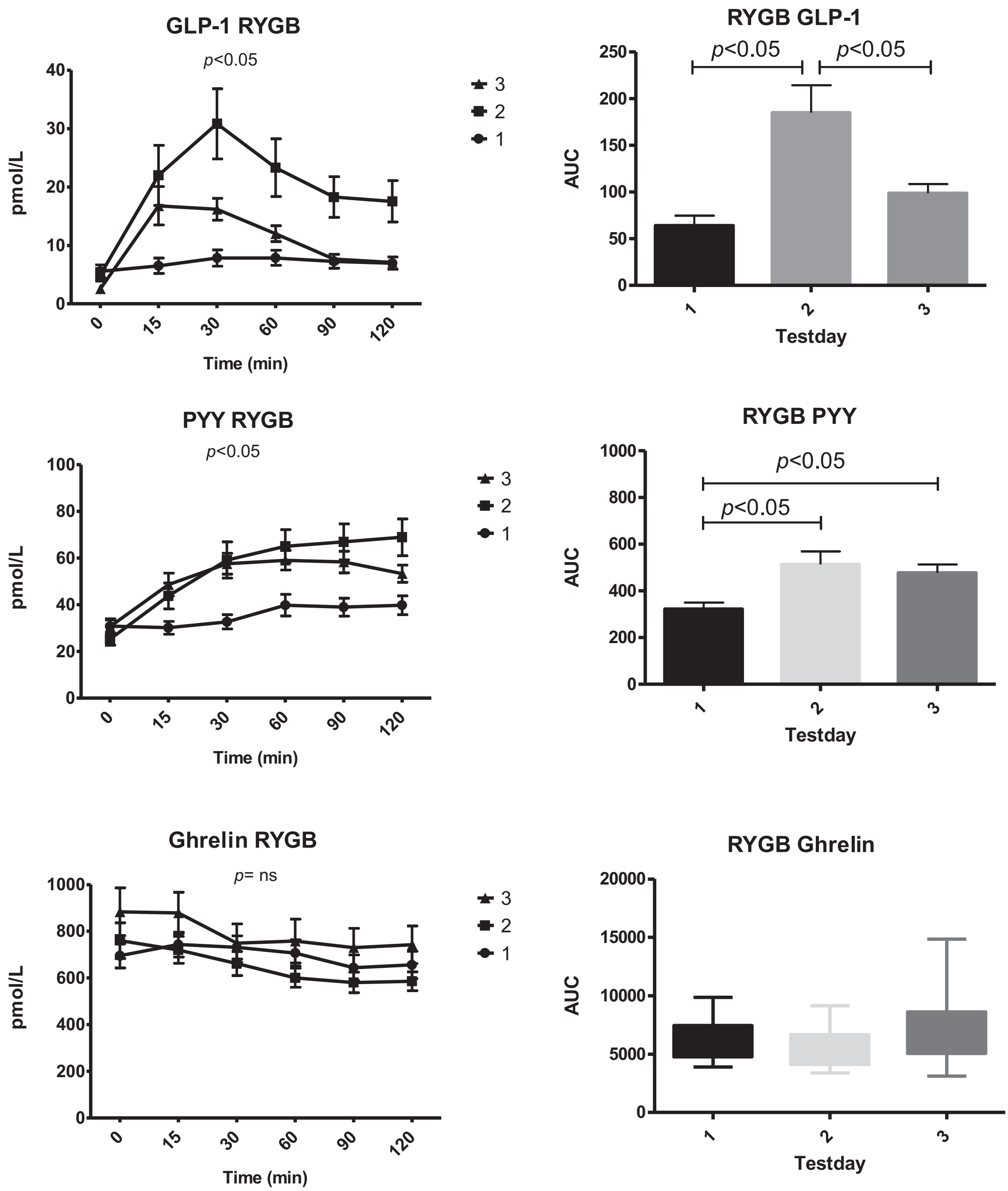

FIGURE 2 (Continued)

4.3 | Oro-cecal transit time

We found significantly shorter OCTT 12 months after SG but not after RYGB compared to the preoperative state. Our findings of a shorter OCTT confirm those of two published studies on OCTT after sleeve gastrectomy, stating that the GI content reaches the terminal ileum faster.[5,15]

We did not find a significant reduction in OCTT after RYGB. Theoretically, bypassing of the pylorus and of the proximal small intestine might accelerate OCTT. Morinigo et al.,[16] Nguyen et al.[36] and Ladebo et al.[39] (using a wireless motility capsule) also found an acceleration of OCTT after RYGB. Carswell et al.[18] and Steenackers et al.[40] found no differences in OCTT between patients after RYGB and controls. Dirksen et al.[13] found a much slower OCTT after RYGB when compared to controls. Up to now data on OCTT after RYGB are scarce and when data are available, these are not consistent. One should take into consideration that after an initial rapid transit of the head/front of the meal to the distal small bowel, the ileal brake is activated as shown by a more pronounced GLP-1 and PYY secretion, resulting in slowing down the transport of the mid to tail portion of the meal. This would imply a prolongation of intestinal transit after surgery, especially after RYGB. OCTT is composed of gastric emptying time and small intestinal transit time. At 2 and 12 months after RYGB, the overall OCTT did not significantly change despite a significant acceleration of gastric emptying. Thus, we assume that intestinal transit time after RYGB was not affected or was prolonged. The more pronounced pattern of PYY and GLP-1 secretion at 12 months after SG may point to a more ongoing ileal brake activation due to significantly accelerated OCTT after sleeve gastrectomy. Differences in outcome of OCTT after bariatric surgery may be related not only to the magnitude of ileal brake activation but also to vagal nerve damage by the surgical procedure, to the methodology to measure OCTT and to meal composition as liquid meals are transported more rapidly than solid meals. Lactulose breath test can be influenced by the presence of bacterial overgrowth which can be seen after RYGB. Bacterial overgrowth is usually reflected in higher fasting levels of breath hydrogen (H_2). However, in our study, fasting H_2 breath samples were low, and therefore, it was unlikely that the presence of bacterial overgrowth will have affected our results.

4.4 | Gastrointestinal peptides

At 2 months after RYGB and SG, postprandial secretion of both PYY and GLP-1 was significantly increased compared to the preoperative condition. These findings point to an activation of the ileal brake. At 12 months after SG, both GLP-1 and PYY secretion remained increased but after RYGB the pattern of PYY and GLP-1 secretion showed a decrease towards the preoperative range.

Several groups have reported on the secretion of gut peptides after bariatric surgery. In the early (0–3 months) postoperative phase, postprandial secretion of PYY and GLP-1 was found to be significantly increased, after both RYGB and SG.[8,41,42] Some studies report that on the longer postoperative term (>12 months) postprandial PYY and GLP-1 secretion remain increased.[11,12,43–45] Others, however, found that on the longer-term after bariatric surgery, peptide secretion, especially of GLP-1 had decreased to preoperative values.[11,46] This was seen after sleeve gastrectomy, less frequent after RYGB.[41–43,47] When looking into detail in the methodology of the published studies, marked differences in meal size, composition and caloric content can be observed.[11,12,41,46,47] Dirksen et al. found lower GLP-1 levels in bad responders compared to good responders after gastric bypass surgery.[48]

The secretion of ghrelin was significantly lower after sleeve gastrectomy. During SG large part of the fundus is removed, which may lead to reduced levels of ghrelin after SG.[49] After RYGB, we did not find a significant change in ghrelin secretion, in line with previous observations of Peterli et al.[12]

We did not measure secretion of proximal gut peptides such as cholecystokinin (CCK). CCK is known to induce satiety, to inhibit gastric emptying and to accelerate intestinal transit. After SG but also after RYGB, postprandial CCK secretion was found to be significantly increased, resulting from accelerated gastric emptying.[12,48,50]

We analysed our data for correlations between peptide secretion and motility parameters, but no significant correlations between PYY, GLP-1 and ghrelin release and gastric emptying or OCTT were observed. The sample size may have been too small to detect relevant correlations. One should realize that in addition to hormonal also neural mechanism are involved in the regulation of motility and interact as 'neurohormonal control'. Neural aspects have not been investigated in our study.

Strength and limitations of our study should be mentioned. A strength of our study lies in consecutive measurements over time: both before and at two time points after the RYGB and SG. With respect to limitations: First, the study was not randomized, thus introducing potential confounding. On the other hand, baseline characteristics of the two groups were comparable. Second, we used a test meal that is different in caloric content from the standard meal we use to determine [^{13}C]-octanoic acid solid meal gastric emptying.[51] The additional amount of fat and total calories may have influenced gastric emptying time. Third, lactulose employed to measure OCTT, may by itself accelerate intestinal transit time. However, the lactulose was administered during all three test days, allowing comparison of data between test days.

In conclusion, after both RYGB and SG (a) gastric emptying becomes significantly accelerated and (b) postprandial release of the distal gut peptides GLP-1 and PYY becomes significantly increased, pointing to ileal brake activation. OCTT becomes accelerated after SG but not after RYGB. No significant correlations were found between clinical parameters, changes in distal gut peptide release and changes in GI motility. Subtle differences between both procedures were found in effect on oro-cecal transit time and patterns of peptide secretion. Further research into the mechanisms by which the various types of bariatric surgery contribute to long-term weight loss is essential.

AUTHOR CONTRIBUTIONS

Conceptualisation, Jennifer Wilbrink, Arnold Stronkhorst, Ad Masclee; Data curation, Jennifer Wilbrink, Mark van Avesaat; Formal analysis, Jennifer Wilbrink, Mark van Avesaat; Investigation, Jennifer Wilbrink; Methodology, Jennifer Wilbrink, Mark van Avesaat, Ad Masclee; Project administration, Jennifer Wilbrink; Resources, Simon Nienhuijs, Arnold Stronkhorst; Supervision, Simon Nienhuijs, Arnold Stronkhorst, Ad Masclee; Validation and visualization, Jennifer Wilbrink, Mark van Avesaat; Writing – original draft, Jennifer Wilbrink, Ad Masclee; Writing – review & editing, Jennifer Wilbrink, Ad Masclee and Simon Nienhuijs.

ACKNOWLEDGEMENTS

The authors would like to thank Anton van der Stokker, Laboratory Catharina Hospital Eindhoven, the Netherlands, and the Department of Human Biology Maastricht University, the Netherlands, and Prof. C. Leroux, Diabetes Complications Research Centre, Ireland, for their assistance.

FUNDING INFORMATION

This research received funding from the Catharina Hospital Scienticific Fund.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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How to cite this article: Wilbrink JA, van Avesaat M, Nienhuijs SW, Stronkhorst A, Masclee AAM. Changes in gastrointestinal motility and gut hormone secretion after Roux-en-Y gastric bypass and sleeve gastrectomy for individuals with severe obesity. *Clinical Obesity*. 2024;e12721. doi:10.1111/cob.12721