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Original article

Mucosal glucagon-like peptide-1 and gastric inhibitory polypeptide cell numbers in the super-obese human foregut after gastric bypass

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Abstract

Background: Super-obesity, a body mass index $> 50 \text{ kg/m}^2$, is difficult to treat. Many studies have focused on the anatomic changes of the intestines; the physiologic background is not clearly identified. It is established that Roux-en-Y gastric bypass (RYGB) augments secretion of glucagon-like peptide-1 (GLP-1), peptide tyrosine tyrosine (PYY), and insulin, but other aspects of gut hormone cell function in the alimentary limb are unknown.

Objective: To study the effects of laparoscopic RYGB on enteroendocrine cells.

Setting: University-affiliated, high-volume bariatric surgery center.

Methods: Eighteen nondiabetic patients were drawn from the present study (NCT 01514799), randomizing between biliopancreatic (BP) limbs of either 60 cm (BP60) or 200 cm (BP200). Demographic characteristics did not differ at baseline or 12 months. Pouch and jejunal biopsies were obtained intraoperatively and using endoscopy at 12 months. Mucosal height and density of hormone-producing cell populations were assessed and mRNA expression measured with real-time polymerase chain reaction.

Results: In perianastomotic jejunum, a 4.9-fold increase in GLP-1 cell density was evident 12 months after RYGB, most pronounced in the BP200-group. The densities of glucose-dependent insulinotropic polypeptide (GIP) cells and PYY immunoreactive cells were doubled after 12 months. GIP mRNA was unaffected, but GLP-1 and PYY mRNA were lower 12 months after RYGB. RYGB had no impact on villi length or density of ghrelin-, cholecystokinin-, neurotensin-, secretin-, or serotonin-producing cells after 12 months. Pouch mucosal height and cell densities of ghrelin-, histamine-, serotonin-, and somatostatin-producing cells remained unaffected by RYGB in both groups.

Conclusions: RYGB selectively increased the density of incretin-producing cell populations in the jejunum. This may provide anatomic explanation for the observed increased plasma levels of incretins. (*Surg Obes Relat Dis* 2015;■:00–00.) © 2015 American Society for Metabolic and Bariatric Surgery. All rights reserved.

Keywords:

Enterohormones; Gastric bypass; GIP; GLP-1; Incretins; Superobesity

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The increasing prevalence of obesity has led to the widespread use of Roux-en-Y gastric bypass (RYGB), currently the most common surgical treatment for morbid obesity. Worldwide, hundreds of thousands of patients undergo RYGB every year. Beneficial effects on overall mortality [1], cancer incidence [2], and quality of life [3] have been established. More advanced obesity, super-obesity (body mass index >50), is difficult to treat successfully, because a standard RYGB normally causes loss of only about 14–16 body mass index units [4,5]. Therefore, attention has been given to the effect of lengthening the alimentary limb [6] or the biliopancreatic limb (BP-limb) [5]. However, the mechanisms at play for weight loss remain to be elucidated. The incretin hormones are, however, central to our understanding, because they are known to participate in both satiety regulation and glucose homeostasis. The secretion of incretin hormones is thought to be stimulated by constituents of food. Glucagon-like

peptide-1 (GLP-1) is produced by L-cells in the distal parts of the intestine. These cells also co-express the hormone peptide tyrosine tyrosine (PYY) [7]. It is established that

Table 1
Patient anthropometric characteristics (median, [range]; Mann-Whitney U-test)

Characteristic	BP60 (n = 10)	BP200 (n = 8)	P value
Age (yr)	40 (20–62)	37 (24–45)	.9645
Male/female	4/6	5/3	.3186
Weight at surgery (kg)	156 (127–225)	179 (151–232)	.1309
Weight at 12-mo FU (kg)	99 (83–139)	117 (98–169)	.0620
BMI at surgery (kg/m ²)	53.9 (50.2–64.1)	56.7 (52.9–66.3)	.2480
BMI at 12-mo FU (kg/m ²)	35.7 (30.5–41.9)	36.4 (28.3–48.3)	.6569
A-limb length (cm)	150 (150–400)	400 (290–520)	.0008
BP-limb length (cm)	60 (60–200)	200 (200–200)	.0009

Abbreviations: BP = biliopancreatic limb; FU = follow-up; BMI = body mass index.

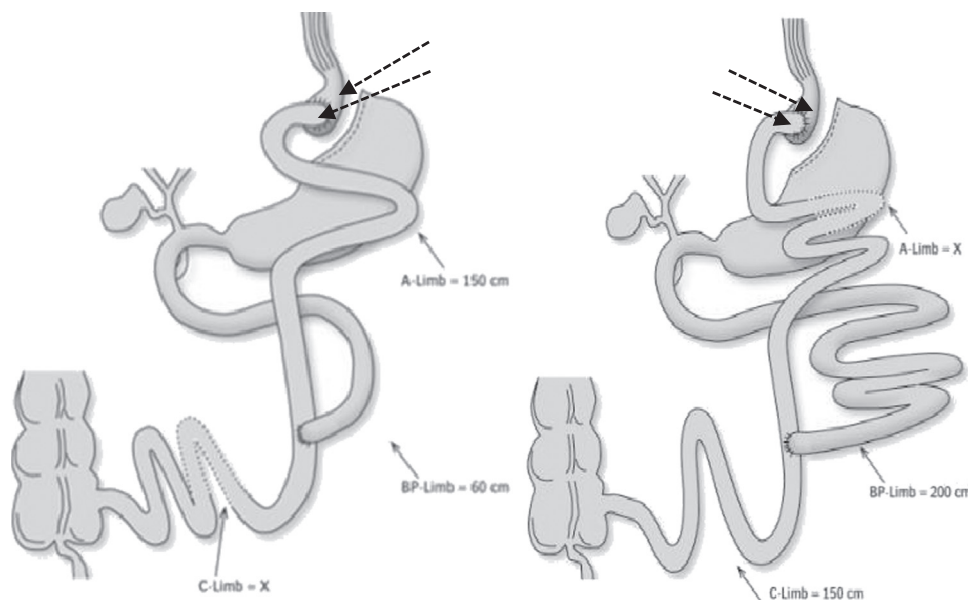


Fig. 1. Schematic drawing of the 2 Roux-en-Y gastric bypass (RYGB) techniques. The left drawing represents the procedure yielding a BP-limb of 60 cm and the right the procedure yielding a 200-cm BP-limb. Biopsy sites are marked with dashed arrows. X = remaining bowel, the length of which was not predefined in protocol. Abbreviations: A-limb = alimentary limb; BP-limb = biliopancreatic limb; C-limb = common limb.

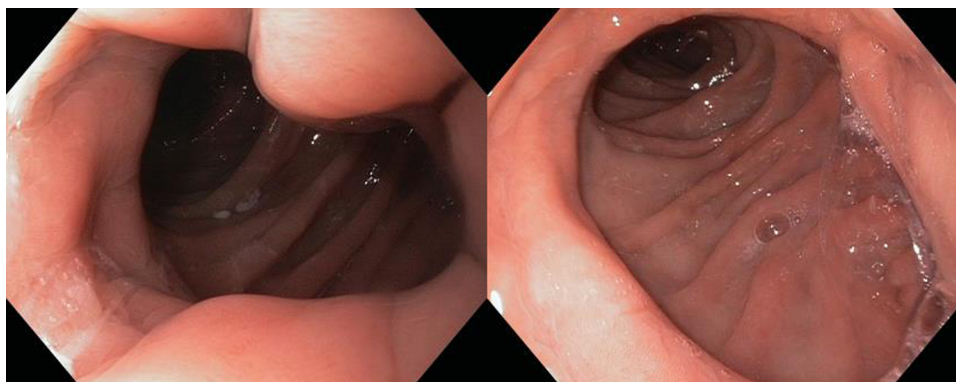


Fig. 2. Representative endoscopic appearances 12 months after Roux-en-Y gastric bypass (RYGB). The left panel shows the appearance in a patient in the BP60 group, and the right panel shows the appearance in a patient in the BP200 group.

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