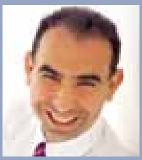
Obesity

Duodenal bypass for the treatment of obesity and T2D



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Several hypotheses have been put forward for the mechanisms mediating the improvement and/or resolution of T2D post bariatric surgery (Taheri, 2009). These include weight loss, changes in body fat distribution, alterations in gut flora and bile acids, increased intestinal glucose metabolism, increased energy expenditure and physical activity, as well as enhanced insulin secretion (Taheri et al, 2000; Kohli et al, 2013; Liou et al, 2013; Saeidi et al, 2013). The upper intestinal hypothesis proposes that the diabetes improvement/resolution after gastric bypass surgery is mediated through nutrients bypassing the upper intestinal tract, thus preventing the release of as yet unidentified factor(s) from the upper intestine that are diabetogenic or may have an inhibitory role in insulin secretion (i.e. a potentially anti-incretin effect). Also, a known hormone that has been implicated in the upper intestine hypothesis is gastric inhibitory peptide (GIP), a minor incretin hormone released by upper intestinal K cells (Taheri et al, 2000). The lower intestinal hypothesis proposes an enhanced release of the incretin hormone, glucagon-like peptide-1 (GLP-1) due to earlier introduction of food to the intestine. GLP-1 is co-secreted from lower intestinal L cells with peptide tyrosine tyrosine (PYY), which has a satiety effect. This, in combination with the removal of ghrelin secretory cells from the stomach that promote hunger, could explain the satiety experienced by people after gastric bypass surgery. The fact that similar levels of diabetes improvement/resolution can be achieved with the sleeve gastrectomy procedure makes these hypotheses, particularly the upper intestinal hypothesis, questionable.

The endoscopically placed duodenal sleeve (duodeno-jejunal bypass liner; DJBL) is believed to rely on the upper intestinal hypothesis. The 60 cm sleeve is introduced such that food bypasses the upper intestine and the sleeve is kept in position through a wire mesh. In the non-randomised study by de Jonge and colleagues (summarised alongside), 17 obese people (average BMI of 37 kg/m^2) with T2D (received a DJBL for 6 months and were assessed before and during DJBL placement, and after endoscopic DJBL removal. Hormonal responses to a standard meal were also assessed. At 6 months, the participants lost on average 12.7 ± 1.3 kg with significant improvement in HbA_{1c} to 53 ± 1.3 mmol/mol (7.0 ± 0.2%). With the DJBL, there was a reduction in fasting and post-prandial glucose. Despite changes in glucose, fasting and post-prandial insulin levels remained unchanged suggesting an improvement in insulin sensitivity. The post-prandial GLP-1 response was enhanced with the DJBL. The improved GLP-1 response was observed as early as 1 week after placement of the liner. There was a reduction in the area under the curve for GIP and glucagon responses to a meal after the DJBL, with the changes in glucagon levels being most concrete. The authors concluded that their findings support both the upper and the lower intestinal hypothesis for the improvement/resolution of diabetes.

While this small study suggests potential hormonal mechanisms for diabetes improvement after bariatric surgery, only a few of the potential mechanisms were explored. Understanding the full mechanisms will hopefully, eventually, result in novel therapies for obesity and T2D. What about the viability of using the DJBL in treatment of patients with obesity and/or T2D? So far, only small studies have been carried out with no large multicentre randomised controlled trials (Escalona et al, 2010; de Moura et al, 2012; Escalona et al, 2012). Also, there are several concerns regarding the use of the liner, including its temporary nature and cost. Furthermore, there is a need to examine the safety of the liner including both potential mechanical and nutritional complications. Larger randomised controlled trials will determine the role of the liner in the management of obesity and T2D.

de Moura EG, Martins BC, Lopes GS et al (2012) Metabolic improvements in obese T2D subjects implanted for 1 year with an endoscopically deployed duodenal-jejunal bypass liner. *Diabetes Technol Ther* **14**:183–9

Escalona A, Yáñez R, Pimentel F et al (2010) Initial human experience with restrictive duodenal-jejunal bypass liner for treatment of morbid obesity. *Surg Obes Relat Dis* **6**:126–31

Escalona A, Pimentel F, Sharp A et al (2012) Weight loss and metabolic improvement in morbidly obese subjects implanted for 1 year with an endoscopic duodenal-jejunal bypass liner. *Ann Surg* **255**: 1080–5

Kohli R, Setchell KD, Kirby M et al (2013) A surgical model in male obese rats uncovers protective effects of bile acids post-bariatric surgery. *Endocrinology* **154**: 2341–51

Liou AP, Paziuk M, Luevano J-M et al (2013) Conserved shifts in the gut microbiota due to gastric bypass reduce host weight and adiposity. *Sci Transl Med* **178**: 178ra41

Saeidi N, Meoli L, Nestoridi E et al (2013) Reprogramming of intestinal glucose metabolism and glycemic control in rats after gastric bypass. *Science* **341**: 406–410

Taheri S, Ghatei MA, Bloom SR (2000) Gastrointestinal hormones and tumor syndromes. In: Endocrinology (6th edition) Pearson: 152

Taheri S (2009) Bariatric surgery: a cure for diabetes? *Practical Diabetes* **26**: 356–8

OBES SURG

DJBL: Promising results in obese people with T2D

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 Improvements in glycaemic control have been observed as early as a few days after the completion of bariatric procedures which exclude the proximal small intestine.

2 The authors examined glucose homeostasis in a group of obese participants with T2D, who had undergone endoscopic duodenal-jejunal bypass liner (DJBL) surgery.

3 Seventeen obese individuals with a BMI between 30–50 kg/m^2 and T2D were included in the study. Participants received the DJBL for 24 weeks in total.

4 After 24 weeks with the DJBL, participants displayed a significant reduction in body weight (12.7 ± 1.3 kg; P<0.01) and HbA_{1c} (68 ± 2.1 mmol/mol [8.4 ± 0.2 to 7.0 ± 0.2%]; P<0.01).

5 Fasting and postprandial glucose levels were reduced after week 1 and week 24 with DJBL (baseline versus week 1 versus week 24: 11.6 ± 0.5 versus 9.0 ± 0.5 versus 8.6 ± 0.5 mmol/L and 1999 ± 85 versus 1536 ± 51 versus 1538 ± 72 mmol/L/min; P<0.01).

6 Glucagon-like peptide-1 (GLP-1) levels had decreased after week 24 (baseline: 115 272 ± 10 971 versus week 24: 88 499 ± 10 971 pg/mL/min, P<0.05), as had glucagon response (23 762 ± 4 732 versus 15 989 ± 3 193 versus 13 1207 ± 1946 pg/mL/min; P<0.05).

7 The authors concluded that the DJBL was associated with changes in gut hormones and a marked improvement in glycaemic control.

de Jonge C, Rensen SS, Verdam FJ et al (2013) Endoscopic duodenal-jejunal bypass liner rapidly improves type 2 diabetes. *Obes Surg* **23**: 1354–60

DIABETES CARE

Roux-en-Y gastric bypass versus a low caloric diet

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 Previous research suggests that glycaemic control can rapidly improve during the early post-operative period after Roux-en-Y gastric bypass (RYGB), although the mechanism for this improvement is unclear. A restrictive post-operative diet and surgically induced changes in hormone levels have been implicated as potential mechanisms.

2 The authors aimed to investigate the effects of caloric restriction compared to surgically induced changes on glucose homeostasis in a cohort of 10 people undergoing RYGB.

3 Participants had a mean BMI of 51.2 kg/m^2 (range 46.1–56.4 kg/m^2) and a mean HbA_{1c} of 70 mmol/mol (8.5%) (range 54 mmol/mol [7.0%]–85 mmol/mol [9.9%]). Participants lost more weight during the pre-surgery period when receiving a reduced caloric diet (7.3 kg, range 8.1–6.5 kg) compared with the post-operative period (4.0 kg, range 6.2–1.7 kg).

4 Daily capillary blood glucose level was lower before surgery than after surgery. Fasting glucose, maximum post-stimulation glucose, and glucose area under the curve during the mixed-meal challenge test improved during the pre-surgery period only.

5 Pre-operative caloric restriction was associated with a greater improvement in glycaemia compared to after surgery. This suggests that decreased caloric intake after RYGB could be responsible for the rapid improvement in glycaemia which is associated with the procedure.

Lingvay I, Guth E, Islam A et al (2013) Rapid improvement in diabetes after gastric bypass surgery: Is it the diet or surgery? *Diabetes Care* 25 Mar [Epub ahead of print]

> "Participants lost more weight during the pre-surgery period when receiving a reduced caloric diet (7.3 kg, range 8.1–6.5) compared with the post-operative period (4.0 kg, range 6.2–1.7)."

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BPD: Resolution of T2D in non-obese people?

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 Bariatric surgeries such as biliopancreatic diversion (BPD) are associated with T2D remission in morbidly obese individuals. Little is known, however, about the relationship between BPD and T2D remission in people who are not obese.

2 Insulin sensitivity and beta-cell function were measured 2 months and 1 year after BPD in a total of 15 non-obese people with T2D (age 55 ± 1 years, T2D duration 16 ± 2 years, HbA_{1c} 70 mmol/mol [8.6%] ± 14.2 mmol/mol [1.3%] BMI 28.3 ± 0.6 kg/m^2) compared to 15 age and sex matched controls without T2D.

3 T2D remission (HbA_{1c}<48 mmol/mol [6.5%] and normal oral glucose tolerance test [OGTT]) was achieved in 6/15 non-obese participants with T2D after BPD.

4 Two months post BPD, insulin resistance had resolved (19.8 ± 0.8 µmol.min^{-1} kg$_{ffm}^{-1}$, P<0.001 versus 40.9 ± 5.3 controls) and was maintained at the 1-year follow-up.

5 After 1 year, beta-cell glucose sensitivity (19[12] pmol.min^{-1} m^{-2}.mM^{-1} versus 96 [73] of controls, P<0.0001) improved (P=0.02) to 31[26] and was worse in non-remitters 16[18]) compared to those who achieved remission (46[33]).

6 The authors concluded that BPD resulted in improved metabolic control of T2D in non-obese people, but remission occurred in only 40% of the cohort.

Astiarraga B, Gastaldelli A, Muscelli E et al (2013) Biliopancreatic diversion in nonobese patients with type 2 diabetes: impact and mechanisms. *J Clin Endocrinol Metab* 10 May [Epub ahead of print]

DIABETES CARE

Non-eligible people could benefit from bariatric surgery

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

1 Current guidelines dictate that people with a of BMI <35 kg/m^2 or a BMI between 35–40 kg/m^2 without comorbidities are not eligible for bariatric surgery.

2 The long-term outcomes from participants of the Swedish obese subjects (SOS) study were examined to establish the incidence of adverse events in people eligible (n=3814) and non-eligible (n=233) for bariatric surgery. Participants were followed-up for a median of 10 years.

3 A total of 2010 obese people were included in the study. Of these, 68% underwent vertical-banded gastroplasty, 19% had a banding procedure and 13% had gastric bypass surgery.

4 Bariatric surgery was associated with a decrease in the incidence of diabetes in the non-eligible group (adjusted hazard ratio [HR] 0.33; 95% CI, 0.13–0.82; P=0.017) and the eligible group (HR 0.27; 95% CI, 0.22–0.33; P<0.001), although there was no difference in the effect of surgery between the two groups (adjusted P=0.713).

5 At the 10-year follow-up, cardiovascular risk factors had improved in people from both the eligible and non-eligible groups.

6 The authors concluded that cardiovascular risk factors and diabetes incidence were significantly reduced in both eligible and non-eligible people, suggesting that BMI cut-offs may be detrimental to the reduction of diabetes and cardiovascular risk factors via bariatric surgery.

Sjöholm K, Anveden A, Peltonen M et al (2013) Evaluation of current eligibility criteria for bariatric surgery: diabetes prevention and risk factor changes in the Swedish obese subjects (SOS) study. *Diabetes Care* **36**: 1335–40