
Metabolic Surgery. A New Surgical Discipline?

Nicola Scopinaro

Department of Surgery, University of Genoa,
School of Medicine, Italy

Keywords: *Bariatric surgery, metabolic surgery, gastric bypass.*

Abstract

Metabolic surgery can be considered as part of functional surgery, where the function to be corrected is a metabolic one. The first known example of metabolic surgery is probably the partial ileal bypass for the treatment of hypercholesterolemia. Modern metabolic surgery was preceded and inspired by bariatric surgery, basing on the strong metabolic effect of some obesity surgery operations, especially gastric bypass and biliopancreatic diversion (BPD), mainly active on type 2 diabetes mellitus. A true metabolic operation, primarily aimed at obtaining a favourable metabolic change, should on one side not provoke undue weight loss, on the other side act through specific mechanisms independent of weight changes. BPD, in clinical use since the late 70s, has proven to meet these requirements and is successfully used today in clinical trials for the treatment of the metabolic syndrome. New developed metabolic operations are represented by duodenal-jejunal bypass, endointestinal sleeve, and ileal interposition. All the efforts should be aimed at conceiving an operation equally effective as BPD, yet less invasive.

Correspondence

NICOLA SCOPINARO
DICMI – Università di Genova, Azienda
Ospedaliera Universitaria “San Martino”, Largo
Rosanna Benzi, 8, 16132 Genova, Italy
Tel: +39 010 3537301
Mobile Phone: +39 335 6040819
Fax: +39 010 502754
E-mail: nicola.scopinaro@unige.it

Introduction

Any type of surgical activity, to be labelled as “discipline”, needs that that specific surgical activity be used with the only aim of obtaining a specific effect, which, in this case, would be a metabolic change. In other words, metabolic surgery can be considered a discipline if one or more types of operation can be used with the only aim of obtaining, as a result, a metabolic change.

Metabolic surgery can be considered as part of the more generally named “functional surgery”, which in turn may be defined as “a surgically-induced anatomic modification which provokes either the reduction or the annulment of the altered function that causes the disease, or a functional change of opposite direction able to counteract partially or totally the originally altered function”. If that function is a metabolic function, that is metabolic surgery. Good examples of the first type of functional surgery are ablation of endocrine tumors, or splenectomy for idiopathic thrombocytopenic purpura, or antrectomy or vagotomy for peptic disease: in all of these cases the surgically-induced anatomic change simply reduces or annuls the altered function. A nice example of the second type of action is pyloroplasty associated with vagotomy, where the gastric emptying problems caused by vagotomy are counteracted by the facilitated emptying provoked by pyloroplasty.

Obesity surgery is obviously functional surgery, where the excessive food intake can be reduced or annulled with gastric restriction procedures, or counteracted with the operations which reduce intestinal energy absorption. Bariatric surgery has many beneficial metabolic effects, which, being simply due to the weight loss, do not allow obesity surgery to be

considered as metabolic surgery, for at least two good reasons: 1) bariatric surgery is primarily aimed at weight reduction, with metabolic effects being only beneficial side effects secondary to weight loss, which are the better the greater the weight loss and would disappear in case of weight regain, while true metabolic surgery should be primarily aimed at the correction of the metabolic alteration, and it should work independently of weight changes; 2) most important, the metabolic disturbances that accompany obesity, like hypercholesterolemia, hypertriglyceridemia, insulin resistance and type 2 diabetes mellitus, can occur also in the absence of obesity, and, in these case, even the best weight reducing operation would be not only ineffective, but also potentially very harmful. On the contrary, a true metabolic operation should be able to resolve one or more of the above conditions independently of the body weight, that is, also in the lean patient, and without causing any undue weight loss. In a few words, when talking about metabolic surgery, we should simply forget about body weight or BMI.

The first known example of metabolic surgery is probably the partial ileal bypass (PIB) for the treatment of hypercholesterolemia.^{1,2} The operation consists of the exclusion from the intestinal flow of the last portion of the ileum, where the bile salts are absorbed. What results is a near total interruption of the entero-hepatic bile salt circulation, with huge loss of bile salt into the colon and consequent greatly increased bile acid neosynthesis by the liver, which occurs at the expense of the cholesterol pool.³ The same effect on serum cholesterol is obtained by jejunoileal bypass (JIB),^{4,5} where only a few centimeters of the distal ileum are left in-continuity. The difference between the two operations is that the primary aim of JIB is weight loss, and serum cholesterol reduction is a beneficial side effect, while the PIB is a procedure specifically designed for the treatment of hypercholesterolemia, which can be used in any case of high serum cholesterol, independently of the body weight and the body

weight changes, that is true metabolic surgery.

Although both JIB and PIB, because of the many side effects, were abandoned, the concept of bariatric surgery was accepted, with gastric banding,^{6,7} gastroplasty,⁸ gastric bypass (GBP)^{9,10} and biliopancreatic diversion (BPD)^{11,12} being developed for this purpose. The latter, due to its specific actions on serum cholesterol, which is exactly the same as in PIB, and on type 2 diabetes mellitus,¹³ actions totally independent of weight changes, is to be considered the best example both of functional surgery for obesity and of metabolic surgery for the metabolic syndrome.

BPD, by diverting bile and pancreatic juice into the distal ileum, causes a delayed mixing between food and biliopancreatic secretions resulting in a limited digestion, and thus a limited absorption which is selective for fat and starch, responsible for weight loss and indefinite weight maintenance.¹⁴

In 1984 the powerful specific metabolic actions of BPD¹⁵ were well known, but at that time bariatric surgery in general and BPD in particular were far from being widely accepted, therefore BPD was continued to be used only for morbid obesity therapy. About ten years later, in the mid nineties, Walter Pories,^{16,17} followed by many others,¹⁸⁻²⁰ described the powerful action of gastric bypass on the resolution of type 2 diabetes. In GBP a very small proximal gastric pouch (15-30 ml) causes rapid gastric emptying which, on the one hand, provokes an intense and long lasting postprandial syndrome, and on the other, allows food to reach the ileum, where the production of anorexigenic gut hormones like GLP-1 and PYY is stimulated.²¹⁻²³ Both these actions, provoking reduced food intake, act in tandem to cause weight loss.

As in the case of BPD, GBP action appeared to be a specific one, which was independent of weight loss, since the effect became apparent a few days after the operation. At that moment, bariatric surgery became a discipline

that was accepted worldwide. BPD and GBP had been in clinical use for more than 20 years, and they both showed very important antidiabetic activities. It had become possible to consider surgery for the treatment of diabetes and metabolic syndrome, even if that was not yet true "metabolic surgery" - that is operations that could be considered specifically or primarily aimed at obtaining beneficial metabolic effect- independently of the presence of obesity. Surgical treatment of obesity is indicated for patients with a minimum BMI of 35 kg/m², but since more than 90% of type 2 diabetic patients have a BMI in the range of 25-35, treatment of diabetes then becomes the real target of metabolic surgery.

A first meeting on "true" diabetes surgery was held almost secretly (we were not more than 15 people) in Strasbourg, June 2006, thanks to the initiative of Francesco Rubino, a young researcher, author of wonderful experimental studies in rats,^{24,25} and a second one, more official and with larger participation, though disguised as a meeting on animal model surgery, was held in Boston, in October of the same year. But the main event was the large international consensus conference called Diabetes Surgery Summit, held in Rome in March 2007,²⁶ the first endorsing body being the American Diabetes Association. The goal of the meeting was to reach a consensus on the essential guidelines for the use of surgery to treat type 2 diabetes. After two days of presentations on the subject, the about 50 more prominent world researchers in the field of endocrinology, diabetology and gut hormones reached some important agreements, the most important, approved unanimously, being that "in patients with BMI lower than 35, determining the appropriate use of gastrointestinal surgery for the treatment of type 2 diabetes is an important research priority". The statement had been carefully constructed, because, while opening the door to the use of surgery for the treatment of diabetes in patients not morbidly obese, a totally new population, the word "research" clearly indicated that this surgery would be allowed only within

carefully designed clinical trials, after the approval of an Ethics Committee.

Therefore, even though only as part of an investigation in this phase, surgery could be used to treat type 2 diabetes in the BMI range for which the use of bariatric surgery is not indicated, that is, independently of BMI. What is immediately evident is that the operations performed in patients with BMIs in the lower range, especially simple overweight (BMI 25-30), should be able to achieve two aims: 1) to cause little or no weight loss in case there is little or no excess weight to lose; 2) to act on type 2 diabetes through specific actions, independent of weight loss. Once we have surgical procedures that meet these two requirements and can be used solely to obtain metabolic changes, only then will we be able to talk about a "new discipline".

Specific metabolic surgery can be found among those currently used for the surgical therapy of obesity, or new operations can be developed which possess the above two requirements. The two well established bariatric procedures which have proved to possess specific mechanisms of action independent of weight reduction are BPD and GBP. However, only BPD can be considered true "metabolic surgery", as it can be used with the unique aim of diabetes treatment also in lean people. In fact, in GBP the effect of diabetes resolution cannot be separated from that of weight loss, so that the operation, obligatorily causing weight loss, cannot be used in normal weight people. This does not apply to BPD because BPD does not make one lose weight, it simply leads the operated subject to the weight commensurate with the amount of calories that is able to be absorbed after the operation, so that if the patient's weight is equal to or lower than that weight, there is no reason for weight loss. Therefore, BPD, as it causes weight loss only if there is an excess weight to lose, can be used with the only aim of diabetes treatment at any body weight, and thus can be considered a true "metabolic operation". Actually, while GBP for type 2 diabetes

was used only in patients in the BMI 30-35 range,²⁷ BPD was successfully employed in both the mild obesity and simple overweight patient ranges.^{28,29} We have recently completed the first year follow-up of a prospective study of 30 type 2 diabetes patients equally distributed between BMI 25 and 35 submitted to BPD, obtaining 83% of control (HbA_{1c} ≤7% on free diet and with no antidiabetic therapy), and 17% of improvement (unpublished data).

How do BPD and GBP work? Let us mention first a peculiar mechanism of action of BPD, which is based on the minimal fat absorption,³⁰ causing intramyocellular fat depletion^{31,32} with consequent return to glucose utilization as a source of energy and disappearance of insulin resistance.^{33,34} The two other specific (i.e. independent of weight loss) mechanisms of action which have been hypothesized to explain the effects of GBP and BPD are based on two anatomic-functional features shared by the two operations, that is the bypass of the duodenum and the food stimulation of the ileum. These mechanisms are related to a family of gut hormones, called "incretins", characterized by the property of stimulating insulin production by the beta-cell,^{35,36} and mainly represented by the gastric inhibitory polypeptide (GIP)³⁷ and the glucagon-like peptide-1 (GLP-1),³⁸ respectively released by the duodenum and the ileum. The first mechanism, which is known as the "foregut hypothesis" is based on the bypass of the duodenum, which is considered responsible for the type 2 diabetes causation. Particularly, Pories³⁹ hypothesized that an excessive response of the duodenum to food stimulation causes excessive incretin secretion, and thus insulin release, the insulin resistance representing a mechanism of defense. Rubino⁴⁰ speculated the existence of "anti-incretins", produced by an ill duodenum on food stimulation, which would interfere with normal incretin action. In both cases, the bypass of the duodenum would solve the problem.

On the contrary, according to the "hindgut hypothesis", the beneficial effect of GBP and

BPD would be based on the food-stimulated release by the ileal mucosa of a powerful incretin, the GLP-1, which has proven to be able not only to improve beta-cell function,³⁸ but also to stimulate beta-cell proliferation⁴¹ and decrease beta-cell apoptosis⁴². An increased production of GLP-1 was demonstrated both after GBP²¹ and after BPD^{43,44}.

With the exception of omentectomy, which has proven to be totally ineffective,⁴⁵ the newly developed operations specifically designed for type 2 diabetes treatment were inspired by the two above hypothesis. The foregut hypothesis generated the duodenal-jejunal bypass (DJB) surgery, consisting of transecting the duodenum 1-2 cm distal to the pylorus, and then fashioning a short (30 + 50 cm) Roux-en-Y reconstruction with pyloro-jejunal anastomosis. The experiences reported so far by Cohen⁴⁶ and Ferzli⁴⁷ are rather disappointing. It seems (personal communication by Dr. Ricardo Cohen) that better results can be obtained by adding to this operation a sleeve gastrectomy (SG, a subtotal longitudinal gastrectomy leaving a gastric tube along the lesser curve of no more than 100 ml capacity, which results in much more rapid gastric emptying), but this evidently represents a mix of foregut and hindgut mechanisms. Moreover, sleeve gastrectomy is a weight loss operation, with the consequent risk of excessive weight reduction if used in simply overweight diabetic patients.

Another procedure suggested by the foregut hypothesis is the so called "endobarrier" surgery, consisting of a tubular prosthesis 60 to 100 cm in length which is inserted endoscopically in the duodenum and anchored to the muscular layer distal to the pylorus.⁴⁸ What results is a lack of contact between food and duodenal mucosa, but also a shortening of food pathway to the ileum, thus again mixing the two mechanisms. The results, reported by Galvao-Neto⁴⁹ after a 12-week implant, are good both in terms of weight loss and of diabetes improvement.

Finally, the procedure exploiting the hindgut mechanism, that is ileal interposition, has been extensively studied in animals in the past for the effect on food intake,^{50,51} and recently for the beneficial influence on type 2 diabetes,⁵²⁻⁵⁴ and pioneered in man by De Paula^{55,56}. After a disappointing experience with ileal interposition alone (personal communication by Dr. Aureo Ludovico De Paula), De Paula had much better results by adding a sleeve gastrectomy to the procedure, with or without the bypass of the duodenum, the former procedure being more effective. Again, the presence of a weight loss component entails the unpleasant side-effect of undue weight loss. Moreover, it is a formidable major surgery operation, entailing the presence of 4 to 7 staple lines at risk of dehiscence, with no demonstrated advantages compared to the much safer and more effective BPD.

In summary, metabolic surgery can be considered today a true new discipline, which includes all the operations that can be used with the only aim of treating type 2 diabetes, and/or severe hypercholesterolemia, and/or the other components of the metabolic syndrome, independent of BMI. All of these operations belong today to major abdominal surgery, so all future efforts must be aimed at designing new operations equally effective but less invasive.

References

1. Buchwald H. Lowering of cholesterol absorption and blood levels by ileal exclusion: Experimental basis and preliminary clinical report. *Circulation* 1964; 29: 713-20.
2. Buchwald H, Moore RB, Lee GB, Baltaxe H, Ampaltz F, Frantz ID, *et al.* Five years experience with the use of partial ileal bypass in the treatment of hypercholesterolemia and atherosclerosis. *Isr J Med Sci* 1969; 5: 760-5.
3. Moore RB, Frantz ID, Buchwald H. Changes in cholesterol pool size, turnover rate, and fecal bile acid and sterol excretion after partial ileal bypass in hypercholesterolemic patients. *Surgery* 1969; 65: 98-108.
4. Payne JH, De Wind LT. Surgical treatment of obesity. *Am J Surg* 1969; 118: 141-7.
5. Dean RH, Orcutt TW, Younger RK, Butts WH, Scott HW Jr. Changes in hyperlipidemia and hyperlipoproteinemia in morbidly obese patients treated by jejunoileal bypass. *Surg Forum* 1973; 24: 241-3.
6. Kuzmak LI. A preliminary report on silicone gastric banding for obesity. *Clin Nutr* 1986; 5: 73-77.
7. Belachew M, Legrand MJ, Deferecheux TH, Burtheret MP, Jacquet N. Laparoscopic adjustable silicone gastric banding in the treatment of morbid obesity. A preliminary report. *Surgical Endosc* 1994; 8: 1354-6.
8. Mason EE. Vertical banded gastroplasty for obesity. *Arch Surg* 1982; 117: 701-6.
9. Mason EE, Ito C. Gastric bypass in obesity. *Surg Clin N Amer* 1967; 47: 1345-51.
10. Wittgrove AC, Clark GW, Tremblay LJ. Laparoscopic gastric bypass Roux-en-Y: preliminary report of five cases. *Obes Surg* 1994; 4: 353-7.
11. Scopinaro N, Gianetta E, Civalleri D, Bonalumi U, Bachi V. Biliopancreatic bypass for obesity: II. Initial experience in man. *Br J Surg* 1979; 66: 618-20.
12. Scopinaro N, Gianetta E, Civalleri D, Bonalumi U, Friedman D, Bachi V. Partial and total biliopancreatic bypass in the surgical treatment of obesity. *Int J Obes* 1981; 5: 421-429.
13. Scopinaro N, Marinari GM, Camerini GB, Papadia FS, Adami GF. Specific effects of biliopancreatic diversion on the major components of metabolic syndrome: A long-term follow-up study. *Diabetes Care* 2005; 28: 2406-11.
14. Scopinaro N, Adami GF, Marinari UM, Gianetta E, Traverso E, Friedman D, *et al.* Biliopancreatic diversion. *World J Surg* 1998; 22: 936-46.
15. Scopinaro N, Gianetta E, Friedman D, Adami GF, Traverso E, Bachi V. Evolution of biliopancreatic bypass. *Clin Nutr* 1986; 5(suppl): 137-46.
16. Pories W, Swanson MS, MacDonald KG Jr, Long SB, Morris PG, Brown BM, *et al.* Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus. *Ann Surg* 1995; 222: 339-52.
17. MacDonald KG Jr., Long SD, Swanson MS, Brown BM, Morris P, Dohm GL, *et al.* The gastric bypass operation reduces the progression and mortality of non-insulin dependent diabetes mellitus. *J Gastrointest Surg* 1997; 1: 213-20.
18. Schauer PR, Burguera B, Ikuamuddin S, Cottam D, Gourash W, Harnad G, *et al.* Effect of laparoscopic Roux-en-Y gastric bypass on type 2 diabetes mellitus. *Ann Surg* 2003; 238: 467-84.
19. Torquati A, Luffi R, Abumrad N, Richards WO. Is Roux-en-Y gastric bypass surgery the most effective treatment for type 2 diabetes mellitus in morbidly obese patients? *J Gastrointest Surg* 2005; 9: 1112-8.
20. Buchwald H, Estok R, Fahrbach K, Banel D, Jensen MD, Pories WJ, *et al.* Weight and type 2 diabetes

- after bariatric surgery: systematic review and meta-analysis. *Am J Med* 2009; 122: 248-56.
21. Morinigo R, Moizé V, Musri M, Lacy AM, Navarro S, Marin JL, *et al*. Glucagon-like-peptide-1, peptide YY, hunger, and satiety after gastric bypass surgery in morbidly obese subjects. *J Clin Endocrinol Metab* 2006; 91: 1735-40.
 22. Hayes MR, Bradley L, Grill HJ. Endogenous hindbrain glucagon-like peptide-1 receptor activation contributes to the control of food intake by mediating gastric satiation signaling. *Endocrinology* 2009; 150: 2654-9.
 23. Pironi L, Stanghellini V, Miglioli M, Corinaldesi R, De Giorgio R, Ruggeri E, *et al*. Fat-induced ileal brake in humans: a dose-dependent phenomenon correlated to the plasma levels of peptide YY. *Gastroenterology* 1993; 105: 733-9.
 24. Rubino F, Marescaux J. Effect of duodenal-jejunal exclusion in a non-obese animal model of type 2 diabetes: a new perspective for an old disease. *Ann Surg* 2004; 239: 1-11.
 25. Rubino F, Zixari P, Tomasetto C, Blue-Pajot MT, Forgione A, Vix M, *et al*. The role of small bowel in the regulation of circulating ghrelin levels and food intake in the obese Zucker rat. *Endocrinology* 2005; 146: 1745-52.
 26. Rubino F, Kaplan LF, Schauer PR, Cummings DE. On behalf of the Diabetes Surgery Summit Delegates. The diabetes surgery summit consensus conference: recommendations for the evaluation and use of gastrointestinal surgery to treat type 2 diabetes mellitus. *Ann Surg* 2009 Nov 19 [Epub ahead of print].
 27. Cohen R, Pinheiro JS, Corres JL, Schiavon CA. Laparoscopic Roux-en-Y gastric bypass for BMI <35 kg/m²: a tailored approach. *Surg Obes Relat Dis* 2006; 2: 401-4.
 28. Scopinaro N, Papadia F, Marinari G, Camerini G, Adami GF. Long-term control of type 2 diabetes mellitus and the other major components of the metabolic syndrome after biliopancreatic diversion in patients with BMI <35 kg/m². *Obes Surg* 2007; 17: 185-92.
 29. Chiellini C, Rubino F, Castagneto M, Nanni G, Mingrone G. The effect of biliopancreatic diversion on type 2 diabetes in patients with BMI <35 kg/m². *Diabetologia* 2009; 52: 1027-30.
 30. Scopinaro N, Marinari GM, Camerini G, Pretolesi F, Papadia F, Murelli F, *et al*. Energy and nitrogen absorption after biliopancreatic diversion. *Obes Surg* 2000; 10: 436-41.
 31. Greco AV, Mingrone G, Giancaterini A, Manco M, Morroni M, Cinti S, *et al*. Insulin resistance in morbid obesity: reversal with intramyocellular fat depletion. *Diabetes* 2002; 5: 144-51.
 32. Adami G, Parodi RC, Papadia F, Marinari, Camerini G, Corvisieri R, *et al*. Magnetic resonance spectroscopy facilitates assessment of intramyocellular lipid changes: a preliminary short-term study following biliopancreatic diversion. *Obes Surg* 2005; 15: 1233-7.
 33. Adami GF, Cordera R, Camerini G, Marinari GM, Scopinaro N. Recovery of insulin sensitivity in obese patients at short term after biliopancreatic diversion. *J Surg Res* 2003; 113: 217-21.
 34. Adami GF, Cordera R, Camerini G, Marinari GM, Scopinaro N. Long-term normalization of insulin sensitivity following biliopancreatic diversion for obesity. *Int J Obes Relat Metab Disord* 2004; 28: 671-3.
 35. Unger RH, Eisentraut AM. Entero-insular axis. *Arch Intern Med* 1969; 123: 261-6.
 36. Creutzfeld W. The incretin concept today. *Diabetologia* 1979; 16: 75-85.
 37. Creutzfeld W, Ebert R, Willms B, Frerichs H, Brown JC. Gastric inhibitory polypeptide (GIP) and insulin in obesity: increased response to stimulation and defective feedback control of serum levels. *Diabetologia* 1978; 14: 15-24.
 38. Doyle ME, Egan JM. Mechanisms of action of glucagon-like peptide 1 in the pancreas. *Pharmacol Ther* 2007; 113: 546-93.
 39. Hickey MS, Pories WJ, MacDonald KG Jr., Kory KA, Dohm GL, Swanson MS, *et al*. A new paradigm for type 2 diabetes mellitus: could it be a disease of the foregut? *Ann Surg* 1998; 227: 637-43.
 40. Rubino F, Forgione A, Cummings DE, Vix M, Gnulli D, Mingrone G, *et al*. The mechanism of diabetes control after gastrointestinal bypass surgery reveals a role of the proximal small intestine in the pathophysiology of type 2 diabetes. *Ann Surg* 2006; 244: 741-9.
 41. Xu G, Stoffers DA, Habener JF, Bonner-Weir S. Exendin-4 stimulates both beta-cell replication and neogenesis, resulting in increased beta-cell mass. *Diabetes* 1999; 48: 2270-6.
 42. Farilla L, Bulotta A, Hirshberg B, Li CS, Khouri N, Noshmehr H, *et al*. Glucagon-like peptide 1 inhibits cell apoptosis and improve glucose responsiveness of freshly isolated human islets. *Endocrinology* 2003; 144: 5149-58.
 43. Borg CM, le Roux CW, Ghatei MA, Bloom SR, Patel AG. Biliopancreatic diversion in rats is associated with intestinal hypertrophy and with increased GLP-1, GLP-2 and PYY levels. *Obes Surg* 2007; 17: 1193-8.
 44. Valverde I, Puente J, Martín-Duce A, Molina L, Lozano O, Sancho V, *et al*. Changes in glucagon-like peptide-1 (GLP-1) secretion after biliopancreatic diversion or vertical banded gastroplasty in obese subjects. *Obes Surg* 2005; 15: 387-97.

45. Csendes A, Maluenda F, Burgos AM. A prospective randomized study comparing patients with morbid obesity submitted to laparotomic gastric bypass with or without omentectomy. *Obes Surg* 2009 ; 19 : 490-4.
46. Cohen RV, Schiavon CA, Pinheiro JS, Correa JL, Rubino F. Duodenal-jejunal bypass for the treatment of type 2 diabetes in patients with body mass index of 22-34 kg/m²: a report of 2 cases. *Surg Obes Relat Dis* 2007; 3: 195-7.
47. Ferzli GS, Dominique E, Ciaglia M, Bluth MH, GonzalezA, Fingerhut A. Clinical improvement after duodenal jejunal bypass for non obese type 2 diabetes despite minimal improvement in glycemic homeostasis. *World J Surg* 2009; 33: 972-9.
48. Gersin KS, Keller JE, Stefanidis D, Simms CS, Abraham DD, Deal SE. Duodenal-jejunal bypass sleeve: a totally endoscopic device for the treatment of morbid obesity. *Surg Innov* 2007; 14: 275-8.
49. Rodriguez-Grunert L, Galvao-Neto MP, Alamo M, Ramos AC, Baez PB, Tarnoff M. First human experience with endoscopically delivered and retrieved duodenal-jejunal bypass sleeve. *Surg Obes Relat Dis* 2008; 4: 55-9.
50. Koopmans HS, Sclafani A, Fichtner C, Aravich PF. The effect of ileal transposition on food intake and body weight loss in VMH-obese rats. *Am J Clin Nutr* 1982; 35: 284-93.
51. Atkinson RL, Whipple JH, Atkinson SH, Stewart CC. Role of the small bowel in regulating food intake in rats. *Am J Physiol* 1982; 242: 429-33.
52. Strader AD, Vahl TP, Jandacek RJ, Woods SC, D'Alessio DA, Seeley RJ. Weight loss through ileal transposition is accompanied by increased ileal hormone secretion and synthesis in rat. *Am J Physiol Endocrinol Metab* 2005; 288: 447-53.
53. Patriti A, Aisa MC, Annetti C, Siconi A, Galli F, Ferri I, *et al.* How the hindgut can cure type 2 diabetes. Ileal transposition improved glucose metabolism and beta-cell function in Goto-Kakizaki rats through an enhanced Proglucagon gene expression and L-cell number. *Surgery* 2007; 142: 74-85.
54. Wang TT, Hu SY, Gao HD, Zhang GY, Liu CZ, Feng JB, *et al.* Ileal transposition controls diabetes as well as modified duodenal jejunal bypass with better lipid lowering in a non obese rat model of type II diabetes by increasing GLP-1. *Ann Surg* 2008; 247: 968-75.
55. De Paula AL, Macedo ALV, Prudente AS, Oyeroz L, Schraibman V, Pinus J. Laparoscopic sleeve gastrectomy with ileal interposition ("neuroendocrine brake") – pilot study of a new operation. *Surg Obes Relat Dis* 2006; 2: 464-7.
56. De Paula AL, Macedo AL, Mota BR, Schraibman V. Laparoscopic ileal interposition associated to a diverted sleeve gastrectomy is an effective operation for the treatment of type 2 diabetes mellitus patients with BMI 21-29. *Surg Endosc* 2009; 23: 1313-20.

© NICOLA SCOPINARO; Licensee *Bentham Open*.

This is an open access article licensed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>), which permits unrestricted, non-commercial use, distribution and reproduction in any medium, provided the work is properly cited.