Digestive Adaptation with Intestinal Reserve: A New Surgical Proposal for Morbid Obesity

Adaptação Digestiva com Reserva Intestinal: Nova Proposta Cirúrgica para Obesidade Mórbida

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ABSTRACT BACKGROUND: Most bariatric surgery techniques include narrow anastomoses, bands or exclusion of digestive segments, especially duodenum, which is a potential cause of symptoms or complications. This is a preliminary report on a new surgical technique for obesity: Digestive Adaptation with Intestinal Reserve. METHOD: The technique includes a sleeve gastrectomy, omentectomy and enterectomy that leaves the first 40 cm of jejunum and the last 260 cm of ileum (totaling three meters of remnant small bowel). This is within the lower limit of normal range. The digestive reconstruction creates a bipartition in digestive tract nutrient transit, avoiding the exclusion of segments and prostheses, with the intention of causing minimal to no malabsorption. Three initial cases are presented. RESULTS: Three patients, two at the age of 16 and one, 39, were operated. With a follow-up of 9, 7 and 5 months, respectively, initial rate of weight loss is satisfactory. Patients are free of symptoms, without diarrhea, referring early satiety and all of them have metabolic profile improvement. CONCLUSIONS: Early results show that this procedure is capable of provoking a significant weight loss. However, it does not create obstacles to ingestion of food nor uses prostheses. There are no nutrient excluded segments, pylorus and duodenum are in transit and there are no blind endoscopic areas. It aims to cause a modest gastric restriction with early satiety and the procedure intends to modify neuroendocrine response to food ingestion towards a positive change in metabolic profile.

Key words: OBESITY, GHRELIN, RESISTIN, PAI-1, GLP-1, PYY, VISCERAL FAT, CHOLECYSTOKININ, OMENTECTOMY, ENTERECTOMY.

INTRODUÇÃO: A maioria das técnicas cirúrgicas bariátricas inclui anastomoses estreitas, bandas ou exclusão de RESUMO segmentos digestivos, especialmente do intestino delgado proximal, o que pode causar sintomas e complicações. Este é um relato inicial de uma nova técnica cirúrgica para tratar obesidade: Adaptação Digestiva com Reserva Intestinal. MÉTODO: A técnica inclui uma gastrectomia vertical, omentectomia e enterectomia que preserva os primeiros 40 cm de jejuno e os últimos 260 cm de íleo (totalizando 3 m de intestino delgado remanescente). Esta dimensão está no limite inferior da normalidade. A reconstrução digestiva cria uma bipartição no trânsito de nutrientes no trato digestivo, evitando a exclusão de segmentos e próteses, sem a intenção de causar má-absorção. Três casos iniciais são apresentados. RESULTADOS: Três pacientes, 2 com 16 anos de idade e 1 com 39 anos foram operados. Com um seguimento de 9, 7 e 5 meses, respectivamente, o ritmo inicial de perda de peso é satisfatório. Os pacientes estão sem sintomas, sem diarréia, referindo saciedade precoce e todos com melhora do perfil metabólico. CONCLUSÕES: Os resultados preliminares mostram que este procedimento é capaz de provocar uma perda de peso significante. Entretanto, não se cria obstáculo à ingestão de alimentos, nem se usa prótese. Não há segmentos exclusos da passagem de nutrientes, o piloro e o duodeno estão no trânsito e não há áreas fora do alcance endoscópico no trato digestivo alto. O procedimento visa causar uma adaptação do volume gástrico e modificar a resposta neuro-endócrina à ingestão de alimentos para gerar saciedade precoce e melhorar o perfil metabólico.

Palavras-chave: OBESIDADE, GRELINA, RESISTINA, PAI-1, GLP-1, PYY, GORDURA VISCERAL, COLECISTOQUININA, OMENTECTOMIA, ENTERECTOMIA.

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besity has become a major public health problem for modern civilization and many surgical techniques are available, since conservative treatment alone is not sufficient in a significant proportion of patients. However, all current techniques present some features that would be better avoided from a strictly physiological point of view, such as the creation of obstacles to food ingestion (for examples prostheses or narrow anastomoses), exclusion of digestive tract segments from nutrient transit and unspecific malabsorption. Exclusion of digestive segments impedes endoscopic evaluation of the excluded area and may cause structural damage to the mucosa, bacterial

proliferation and, maybe, bacterial translocation. Some procedures that involve digestive tract nutrient exclusion have been related to hepatic fibrosis^{1,2,} worsening the hepatic condition of patients that may present with some degree of nonalcoholic fat liver disease³.

Here, we report three patients submitted to this new surgical procedure, designed to spare pylorus, duodenum and jejunum from nutrient exclusion. Indeed, our objective was to avoid any nutrient exclusion, blind endoscopic areas, narrow anastomoses and bands.

MATERIAL AND METHODS

This proposed surgical procedure combines many aspects of preexisting procedures, although it creates a new concept that is the Intestinal Transit Bipartition. The procedure begins through a laparoscopic access. Five trocars are positioned: two 12mm (one in the midline 8 cm above the umbilicus and the other in the upper left quadrant); three 5mm trocars (one in the upper right quadrant, one in the epigastrium for the liver retractor and one lateral in the upper left quadrant).

First, the omental bursa is opened and section of greater omentum is done with the help of

Figure 1 - *Diagram showing the proportions of the sleeve gastrectomy.*

a harmonic scalpel. Dissection starts just beside the gastric greater curvature at a point located 6 cm from the pylorus up to the angle of His. A sleeve gastrectomy is performed with a laparoscopic linear cutting stapler (Figure 1). A Fouchet's tube is passed to the stomach to guarantee that the gastric tube, left in the lesser curvature, is approximately 3 cm wide. The stapling line is covered with 4-0 polypropylene running suture, interrupted every 4 cm. After that, a 10 to 15 cm midline laparotomy is made to remove the gastric specimen and the greater omentum (after detaching it from the colon) and to perform an enterectomy, leaving the first 40 cm of jejunum and the last 260 cm of ileum.

Ileum is anastomosed to the lower limit of the stapling line in the stomach, through the mesocolon (Figures 2 and 3). Jejunum is laterally anastomosed to the ileum, at 80 cm from ileocecal valve (Figure 2). The mesenteric borders are closed to avoid internal hernias. Abdominal wall and laparoscopic incisions are closed. Antibiotic and



Figure 2 - General aspect of the Digestive Tract after the procedure.



Figure 3 - Two endoscopic views: Left - proportions of the sleeve gastrectomy; Right - pylorus (right lower corner) and ileo-gastrostomy at the end of the stapled suture (left upper quadrant).

deep vein thrombosis prophylaxes were used in all patients (cephalothin 1g q6 hours for one day; enoxiparin 60 mg once daily, preoperatively and for two weeks after the procedure).

The Ethical Committee of the Hospital da Policia Militar do Estado de São Paulo approved the protocol. The procedure was reviewed and also accepted at the Instituto da Criança do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo. A detailed informed consent was signed by patients or by responsible relatives.

PATIENTS

CASE 1 - Female, 16y; weight 137 Kg (height 158 cm; Body Mass Index 54.9 Kg/m2). Although very young, she presented with systemic arterial hypertension and insulin resistance (glucose/insulin ratio = 2.0). She was operated on October 2003. Presently, she refers early and intense satiety. Hunger became an infrequent sensation and, in some periods, she ate even less than that expected by the medical team. She no longer presents systemic hypertension and is symptom free.

She has lost weight efficiently. She weighed 88 kg in April 2004. Her fasting glucose is normal (78 mg/dl) and fasting insulin is 21.8 mIU/ml (glucose/Insulin ratio = 3.8 indicative of improvement in insulin resistance). At the end of July, 2004 she weights 75 Kg (62 kg lost in 10 months)

CASE 2 - Male, 16y; weight was 219 Kg (height 175cm; Body Mass Index 71.5 Kg/m2). Although very heavy, he did not present comorbidities. He was operated on December 2003. He presented an intraabdominal infection that required surgical drainage, but no dehiscence or fistula was detected. Now he is also symptom free and presents early and prolonged satiety. His bowel movements became more frequent (twice, sometimes three times a day), but liquid feces have not been observed. Now he weights 140 Kg (79 Kg lost in 9 months). Blood tests, as before, continue normal. He is still loosing weight.

CASE 3 - Female, 39y, weight was 146 Kg (height 161 cm; Body Mass Index 56.3 Kg/m2). She presented arterial systemic hypertension, hypertriglyceridemia (267 mg/dl) and hypercholesterolemia (299 mg/dl). She was operated in February, 2004. Due to a very large fatty liver, the laparotomy was done with a transverse incision. After five months, she is symptom free. Her bowel movements are a little less frequent (once every two days) and

she lost 41 kg in 5 months. Total cholesterol fell to 168 mg/dl and triglycerides fell to 136 mg/dl. She does not take antihypertensive drugs anymore.

The surgical procedures took from 200 to 290 min. All patients resumed taking oral liquids in the second post-operative day and they were advised to maintain only a liquid diet for seven days and then resume solid foods. Omeprazol, 20 mg per day and polyvitamin pills are initially recommended, since the amount eaten may be low enough to generate deficiencies.

After two months, radiological studies show that the main part of the ingested contrast follows the gastroenterostomy route, but also a significant part passes through the pylorus. Patients do not report any worsening neither in flatulence nor in the feces odor. All three patients expressed satisfaction with the procedure.

DISCUSSION

We have recently hypothesized that the long length of human small bowel, especially jejunum, is an evolutionary remnant and is not adapted to a modern diet⁴. Primitive diet was hypocaloric and full of poorly digestible fiber. A primitive human would have to ingest large food volumes to obtain just a small amount of calories. Also, it is hard to extract nutrients from the bulky non-nutritive particles and to absorb them. A large stomach and a long bowel are important as containers, but they also provide the opportunity for absorption of all nutrients among the fiber and indigestible particles. On this diet, nutrients would reach distal parts more easily.

Modern diet has concentrated, highly absorbable nutrients (including unnatural elements such as refined sugar and white flour) and with progressively less fiber and residues. It is possible to efficiently absorb these in the very first portions of the intestine, thereby creating peaks of nutrient absorption and an "empty distal gut". Nutrientinduced secretion of enterohormones produced by the distal bowel would be attenuated in this scenario.

Glucagon-like peptide 1 (GLP-1) is a polypeptide hormone that is secreted from the enteroendocrine L-cells of the distal gut in response

to nutrient ingestion⁵. It has five fundamental actions. First, it causes potent stimulation of insulin biosynthesis and release from pancreatic beta-cells (potent enough to potentially cure type II diabetes)⁶. Second, it reduces gastric acid output⁷. Third, it causes major reduction in gastric emptying⁸. Fourth, it causes relaxation of the gastric fundus, allowing the stomach to contain a larger volume without increase in distension sensation⁹. Finally, GLP-1 goes beyond the blood brain barrier and causes satiety¹⁰. The evolutionary aspects of the GLP-1 functions are fascinating. Because of sporadic access to food in Nature, primitive man instinctively ate as much as possible to create reserves for periods of hunger. While he is hungry during a meal, the digestive transit must be fast to create space for further eating, but, when nutrients reach the distal gut, intestinal transit must be slowed, otherwise nutrients could be lost in stools. The secretion of GLP-1 by the distal gut controls the entire process slowing gastric emptying, provoking intense insulin secretion to help the organism stock absorbed nutrients inside the cells, relaxing the gastric fundus to let it contain the food that cannot be processed straight away, causing central satiety to stop eating and diminishing gastric acid output, since the meal is about to finish. Polypeptide YY (PYY) is also a gut hormone involved in the response to food ingestion. It belongs to the pancreatic polypeptide (PP) family along with PP and neuropeptide Y, and it is found in two forms $\text{PYY}_{1\text{-}36} \text{ and } \text{PYY}_{3\text{-}36}.$ $\text{PYY}_{3\text{-}36}$ is more specific to Y2 receptors in hypothalamus¹¹. It is released, also, by L cells in the gut in response to food ingestion and it causes saciety¹².

Oxyntomodulin is another polypeptide hormone that is generated by processing proglucagon molecule and is secreted after nutrients reach the small bowel; it reduces food intake and appetite¹³ and is also involved in the gut-to-brain signaling.

If the presented theory is correct, two facts would have to be proven: first, that obese people do have attenuated secretion of distal bowel hormones; second that obese people are able to produce them adequately, if enough nutrients reach distal gut.

Both facts have already been demonstrated. Obese¹⁴ as well as type II diabetic¹⁵ individuals have attenuated postprandial GLP-1 secretion. Also, immediately and many years after a jejuno-ileal bypass is performed (which throws nutrients to distal gut through a shortcut), normal GLP-1 secretion is reestablished 16 . A bowel resection can do the same.

In summary, to have 3 or 8 meters of small bowel (lengths eventually found in normal and never-operated-on persons) makes little difference in terms of absorption, since in neither case malabsorption will occur. However, it seems clear that to have nutrients reaching and being absorbed by the distal gut is an important physiological issue, especially in limiting food intake, through the production of intestinal hormones that work as signs to the pancreas and to the brain.

Following this line of reasoning, we could go still further. Obesity has been related to increased incidence of colon cancer¹⁷. Nutrients reaching distal gut provoke secretion of GLP-2 and generation of short-chain fatty acids (SCFA) in the colon. Both, GLP-2 and SCFA are thought to be protective against colon cancer^{18,19}. So, scarcity of nutrients in distal gut could link colon cancer and obesity. Both conditions have parallel increasing incidences.

These data suggest that, especially if modern, hypercaloric, easily digestible diet is being used, it might be better to be "normal with 3 meters" than to be "normal with 8 meters" of small bowel. Could the length of small bowel be involved in obesity? Do the obese have longer small bowel? There have been few studies into this matter, but the article by HOUNNOU G et al.²⁰, proposes that this is the case.

Evolutionary forces have been at work in this matter. Early hominid species were herbivores. During the process of becoming omnivorous, the higher concentration of calories in the meat and the better foraging strategies allowed these Homo groups to eat less volume of more digestible food. It is known that in these transitions the amount of bowel was reduced^{21,22} (as expected, since exclusively herbivores have longer bowel extensions).

During the last century, another great change occurred in human diet, which became more concentrated in calories and even freer of nondigestible particles, which has led us to consider that a further bowel reduction is now necessary. Evolution continues to perform its timeless job: natural selection. People are becoming obese and dying. Obese people, as HOUNNOU G et al.²⁰ pointed out, have a longer bowel, and thus shorter bowel is being selected. The "contemporary human being" is insufficiently adapted to the abundance of easily absorbable food, which is causing a lack of nutrients in distal bowel with serious endocrine and metabolic consequences.

Faced with this modern diet, our small bowel has become inappropriately long and excessively permeable, and likewise, the stomach, as a storage chamber, is too large. In parallel, our eating instincts are upregulated while daily physical effort has diminished. Obesity, hypertension, dyslipidemia, atherothrombosis, diabetes are some of the consequences.

Based in this rationale, we recently described a new surgical strategy to treat obesity: Digestive Adaptation²³ (Figure 4). It is composed of a vertical (sleeve) gastrectomy, omentectomy and a simple enterectomy that leaves 3 meters of small bowel (1.5 m of jejunum and 1.5 m of ileum). The gastrectomy aims to adapt the size of gastric chamber to the high caloric-dense modern diet²⁴, reducing its volume. Satiety signs caused by distension will be emitted earlier and the main source of ghrelin^{25,26,27}, a gastric orexigenic hormone, is removed. The enterectomy does not aim to create malabsorption (this remnant length is in the lower limit of normal range and sufficient to complete absorption and still with functional reserve). It is performed to adapt the small bowel to modern diet and to adequate intestinal hormonal responses to food ingestion.

It is a physiological approach and twentymonth results with Digestive Adaptation²³, including more than 50 patients, operated in several centers by many other surgeons utilizing the same technique, are very good (in press). However, in patients with BMI greater than 45 Kg/m2, with severe comorbidities, an even shorter bowel (40 cm of jejunum and 80 cm of ileum) would probably be more appropriate. Nonetheless, it would not be wise to perform such an extensive enterectomy because the patient would be left without a functional reserve. This motivated the development of the technical alternative, presented here.

It seems that, as a procedure to treat morbid obesity, it might be superior to other alternatives because it does not involve obstacles to food ingestion, the pylorus remain intact, and duodenum is in transit, so able to develop its special absorptive and neuroendocrine functions. There are no segments excluded from nutrients transit, nor from the access of an endoscope. Furthermore, it is easier to perform, with fewer risky steps. There is neither manipulation of gastric lesser curvature nor the need to adapt prosthesis. The anastomoses involved are easier since they do not involve the duodenum or high pouches in the stomach.

An amount of food goes through the pylorus. This route resembles the jejuno-ileal bypass used in the past²⁸. However, the route is longer (120 cm post Treitz) to reduce malabsorption (or avoid it in the long term) and this is compensated by a smaller gastric capacity. Also, the absence of an excluded segment may avoid complications such as hepatic fibrosis and cirrhosis^{29,30}.

Some food passes through the gastroenterostomy. This will meet a 1.8 meter-long segment of ileum, without (or little) biliopancreatic juice and after that, receive the digestive juices through the enteroenterostomy, and then follow through the terminal ileum. This route is similar to that found in a biliopancreatic bypass.

Radiological studies have shown that after two months, the preferential path is through the gastroenterostomy. However the duodenum is not excluded; its nutrient stimulation may generate its unique hormonal and absorptive response (at least with a part of the meal). Besides the functional gain, it probably will prevent bacterial proliferation and translocation to portal blood, preventing hepatic fibrosis as a consequence; also having all segments in transit might be the reason why none of these patients observed diarrhea, worsening in the odor of feces or in flatulence. This is an important issue when we aim to afford these patients a better social life and improved self-esteem. In summary, it was avoided a non-physiological feature such as nutrient exclusion.

Regarding the improvement in the metabolic profile, the proposed technique may help. Indeed, whatever path the food takes, nutrients will reach distal bowel in larger amounts than they naturally would. Nutrients in distal gut provoke the secretion of GLP-1³¹. Early and effective elevation of secretion of GLP-1 can cause a delay in gastric emptying, central satiety, intense stimulus to trophism of beta pancreatic cells and a strong insulin secretion that can result in the cure of type II

diabetes⁵. Secretion of PYY and Oxyntomodulin, also provoked by luminal nutrients, enhance satiety^{12,13}.

The procedure intends to enhance postprandial secretion of Cholecystokinin (CCK). CCK, besides its other actions, it induces satiety through its hypothalamic receptors. A postprandial elevation of CCK is expected for two reasons. First, since duodenum is in transit (its main site of secretion), it is able to be stimulated by nutrients. Second, because small bowel segments that are not exposed to biliopancreatic juice produce higher amounts of CCK^{32,33}. Here we also have a gut segment with nutrients but without biliopancreatic juice. So, it is reasonable to expect better CCK secretion. Also, nutrient stimulus in the duodenum is thought to generate GIP production and a vagus nerve modulated response that results in an early stimulus to GLP-1 production in the distal gut³⁴.

The technique also includes the resection of greater omentum and an enterectomy that takes out its mesenteric fat. This entails removal of significant amounts of visceral fat, which is clearly linked to metabolic syndrome. Visceral fat is an important source of Plasminogen Activator Inhibitor 1 (PAI-1)³⁵⁻³⁷ and Resistin³⁸⁻⁴⁰. Procedures that cause reduction in PAI-1 levels have already been pointed to for improving metabolic profile and reducing the cardiovascular risk^{41,42}. Resistin is an inductor of insulin resistance⁴⁰.

As visceral fat is insulin resistant, continuous lipolysis generates free fatty acids to the portal vein, and this is related to hepatic insulin resistance, diminution in hepatic insulin clearance and hyperinsulinism⁴³. This provides additional arguments favoring the removal of visceral fat. Besides, systemic free fatty acids are related to a peripheral impairment of insulin action⁴⁴; blood lipids and insulin resistance are related to an inhibition of nitric oxide production (a natural vasodilator)⁴⁵ by vascular endothelium, that also links visceral fat to type II diabetes and hypertension.

As a result of the gastrectomy, enterectomy and omentectomy, the abdominal pressure is reduced. This may result in comfort, and probably less gastroesophageal reflux, a better venous return and decreased rate of postoperative hernias.

As a significant additional gain, enterectomies cause lowering in blood lipids. Patients presented here and those submitted to Digestive Adaptation²³ presented lowered blood lipids. This lowering is enhanced by a restriction in gastric capacity and early satiety.

The proposed procedure, at least initially, provokes weight loss as efficiently as the current bariatric procedures. Weight loss ameliorates the diabetic status, which can be further improved by visceral fat removal and less production of Resistin. Better secretion of GLP-1 also helps improving diabetes. Less food ingestion, less weight, less cholesterol, less triglycerides, less PAI-1, normal blood glucose, all together help protect arteries and the risk of atherothrombotic diseases fall.

There is a possibility that bringing more nutrients to the hindgut may also diminish the increasing incidence of colon cancer among the obese population of industrialized countries. Therefore, the adaptation of the Digestive Tract to modern diet may be a good strategy to help us face the most incident diseases of modern world.

We think that if we had more physiological procedures to treat obesity, without prostheses, without obstacles to ingestion of food, without excluded segments neither unspecific malabsorption and with a positive neuroendocrine influence to regulate hunger, satiety and metabolic profile, we could use this strategy sooner. Adaptive isolated sleeve gastrectomy or gastro-omentectomy²⁴, Digestive Adaptation²³ (gastro-omentectomy with enterectomy - Figure 4) and finally Digestive Adaptation with in-transit Intestinal Reserve (Figure 2), here proposed, may be a logical line of procedures to treat obesity, sooner than done nowadays until established severe obesity, creating a logical progression of procedures to face the problem in its different stages.

The many expected advantages in the field of neuroendocrine response to food ingestion must be proven also in humans. A significant part of the evidence for these responses was obtained in animal models and may not be fully reproduced in humans. The early results of this new approach are promising and justify this communication. Longer follow-up, studies of neuroendocrine peptides production and a greater number of patients are needed.

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Figure 4 - General aspect of the Digestive Tract after Digestive Adaptation (reference 23).

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Digestive Adaptation with Intestinal Reserve: A New Surgical Proposal for Morbid Obesity

Adaptação Digestiva com Reserva Intestinal: Nova Proposta Cirúrgica para Obesidade Mórbida

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