Solutions in weight control: lessons from gastric surgery

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ABSTRACT
Surgical therapy is currently the only proven way to achieve significant long-term weight loss, improve obesity-related comorbidities, reduce the risk of premature death, and improve quality of life in a large proportion of treated individuals. Roux-en-Y gastric bypass, the most widely performed procedure in the United States, is known to achieve permanent (>14 y of follow-up) and significant (>50% of excess body weight) weight loss in >90% of patients who undergo the operation. Gastric bypass procedures induce physiologic and neuroendocrine changes that appear to affect the weight regulatory centers in the brain. Researchers have begun to explore the molecular pathways responsible for these outcomes. Identifying the differences between surgical and nonsurgical treatments will eventually lead to new therapeutic options. Am J Clin Nutr 2005; 82(suppl):248S–52S.

KEY WORDS Weight loss surgery, WLS, bariatric surgery, gastric bypass, gastroplasty, laparoscopic adjustable gastric banding

INTRODUCTION
Available weight loss treatments for obesity range from diet, exercise, behavioral modification, and pharmacotherapy to surgery, with varying risks and efficacies. Nonsurgical modalities, although less invasive, typically achieve only relatively short-term and limited weight loss in most patients. However, these therapies are very useful in the preoperative period to reduce risks related to surgical treatment of severe (class III) obesity (1).

Weight loss surgery is an appropriate treatment for patients with class III obesity or class II obesity and major comorbidities (2). Data indicate that weight loss surgery is safe and effective, with well-defined risks (1, 3–10), that it is the most effective modality in terms of extent and duration of weight reduction in selected patients with acceptable operative risks (11). A recent study of >1000 gastric bypass surgery (GBP) patients showed that, after 5 y, there was an 89% reduction in mortality in severely obese patients who had weight loss surgery compared with those who did not (3). A new meta-analysis indicates that weight loss surgery is one of the most effective treatments for diabetes, hypertension, obstructive sleep apnea, and high cholesterol in severely obese patients (12).

The rapid spread of severe obesity, combined with lack of adequately effective dietary and pharmacologic treatments, has led to growing demand for weight loss surgery. Between the early 1990s and 2003, the number of procedures performed nationwide rose from around 16 000 to more than 100 000 per year. Continued growth is expected, with >140 000 procedures anticipated for 2004 (Figure 1) (5). However, fast growth in an unregulated environment has raised concerns that obesity surgery is being performed by those who have inadequate training and experience or are practicing in hospitals and clinics with inadequate facilities and personnel. Those concerns are being addressed (13).

MAJOR MECHANISMS
Surgical treatment produces weight loss via two major mechanisms: gastric restriction and intestinal malabsorption (Table 1). Restrictive operations involve creation of a small neogastric pouch and gastric outlet to decrease food intake. Examples include vertical banded gastroplasty (VBG) (Figure 2A) and laparoscopic adjustable gastric banding (LAGB) (Figure 2B).

Malabsorptive procedures involve rearrangement of the small intestine to decrease the functional length or efficiency of the intestinal mucosa for nutrient absorption. Examples include jejunoileal bypass (Figure 3A), biliopancreatic diversion (Figure 3B), and duodenal switch (Figure 3C). Malabsorptive surgeries produce more rapid and profound weight loss than restrictive procedures but put patients at risk for such metabolic complications as vitamin deficiencies and protein energy malnutrition. Restrictive procedures are considered simpler and safer than their malabsorptive counterparts but tend to result in inferior long-term weight loss.

TYPES OF SURGERIES
Accrued clinical experience and advances in technology have shaped and changed the field of weight loss surgery. Some procedures have evolved, whereas others have become obsolete. Over the past decade, VBG has been displaced by Roux-en-Y gastric bypass (RYGB) and newer laparoscopic approaches. The LAGB, introduced to the US market in 2001, has become increasingly popular.

Surgeries currently being performed include gastric bypass, malabsorptive procedures (eg, biliopancreatic diversions), and restrictive operations (gastroplasties with the use of adjustable

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gastric bands). RYGB and LAGB are the most common weight loss surgeries in the United States. Each can be performed either laparoscopically or in an open manner. Biliopancreatic diversion with duodenal switch, although effective in producing weight loss, is still considered investigational by many surgeons because of limited data on long-term safety and metabolic side effects. Others, who have developed particular expertise with the procedure, consider it an important approach to management of extreme obesity.

**ROUX-EN-Y GASTRIC BYPASS**

RYGB is the gold standard procedure for weight loss surgery in the United States today and the most frequently performed operation. It produces greater long-term weight loss than gastric partitioning alone or VBG. It is also substantially safer than jejunoileal bypass. The most important feature of RYGB (Figure 2C) is a small neogastric pouch and a tight stoma that limits oral intake, making restriction the primary mechanism for weight loss.

The procedure involves creating the small stomach pouch and rerouting a portion of the alimentary tract to bypass the distal stomach and proximal small bowel. This process leads to significant long-term weight loss and improvement or resolution of obesity-related comorbidities (12). Long limb (>150 cm) RYGB may produce superior short-term weight loss in patients who are >200 lb/91 kg overweight or have body mass index ≥50. Optimal limb length is unknown, but long-term follow-up indicates that the benefit of longer limb length decreases over time and may disappear completely.

RYGB is not without risks. These include the following: infrequent but serious surgical complications, eg, pulmonary embolism, intestinal leak, wound infection, and staple line failure; long-term deficiencies of iron, calcium, vitamin B12, and vitamin D; and the possibility of weight regain. Benefits have been found to outweigh these risks (12).

**LAPAROSCOPIC WEIGHT LOSS SURGERY**

Weight loss surgeons have developed laparoscopic approaches to gastric bypass and other weight loss surgery procedures. Like open procedures, laparoscopic weight loss surgery has proven effective at producing significant and sustained weight loss, along with improvements in comorbid conditions and quality of life. Because it is less invasive than open surgery, it shortens recovery time (14). Additional benefits include decreased rates of wound infection and incisional hernia (14–16).

Laparoscopic surgeons gain access to the abdomen via several small incisions. They insert a tiny video camera through one of the incisions and surgical instruments through the others. They
operate by watching their work on a large-screen monitor. Laparoscopic techniques for weight loss surgery are difficult and associated with a longer and steeper learning curve than equivalent open procedures.

Open and laparoscopic RYGB produce similar short-term weight loss and improvements in comorbid medical conditions. The laparoscopic approach improves short-term recovery from surgery and has a lower incidence of incisional hernias than the open RYGB; long-term data are not yet available. Laparoscopic RYGB, although increasingly common, needs to be performed by appropriately trained and qualified laparoscopic weight loss surgeons.

LAPAROSCOPIC ADJUSTABLE GASTRIC BANDING

In LAGB, an adjustable silicone band is placed around the upper stomach to create a small pouch and a restricted outlet. The diameter of the outlet can be changed by injecting or removing saline through a portal under the skin. If the device is ineffective, or if serious complications develop, the band can be removed.

Although a large body of evidence, especially from European studies, suggests that LAGB is effective and safe for weight loss, long-term data from US patients are still limited. Studies indicate variation in benefits, the source of which remains unclear. Complications from gastric banding include band migration or erosion, gastroesophageal reflux disease, esophagitis, and problems with the subcutaneous port or tubing.

LAGB produces variable short-term weight loss and improvements in obesity-related comorbidities, with lower average mortality rates than RYGB or malabsorptive procedures. Placement of the LABG in the pars flaccida path rather than the retrogastric position appears to reduce the incidence of postoperative complications.

EFFICACY OF WEIGHT LOSS SURGERY

GBP has the most profound effect on reward-based eating, suggesting alteration of the CNS “reward pathways.” It decreases the intensity of hunger and enhances the effectiveness of satiety to decrease food intake. GBP also dramatically alters food preferences and selection independent of specific cravings or aversions. The exact mechanisms for these outcomes have yet to be identified.

Neuroendocrine changes are thought to be key factors in producing weight loss. Gastrointestinal regulators of energy balance include those that promote energy storage [ie, ghrelin, glucose-dependent insulinoetric polypeptide (GIP), galanin, bombesin, and glucagon] and those that promote energy dissipation (ie, peptide YY 3-36, glucagon-like peptide-1, oxyntomodulin, pancreatic polypeptide, urocrinins, cholecystokinin, and insulin). Ghrelin, the 28 amino acid neuroendocrine peptide secreted by the stomach, is the most potent endocrine stimulator of appetite and food intake. Ghrelin has been identified as the natural endogenous ligand for the growth hormone secretagogue receptor (17). It is thought that there may be ghrelin receptors on hypothalamic neurons central to weight regulation.

Weight loss through nonsurgical means increases circulating ghrelin. Plasma ghrelin levels are low after gastric bypass (18–21), although not all studies agree (22, 23). GIP secreted from the duodenum and jejunum is thought to promote fat synthesis and deposition. Whereas absence of GIP signaling appears to protect against obesity, secretion has been found to be acutely stimulated by food intake. GIP response to a meal increases after diet-induced weight loss. Surgery is fundamentally different from dieting. It changes the physiology to reset energy equilibrium, it affects the complex weight regulatory system at multiple levels, and it inhibits environmental influences on weight regulation and defeats powerful mechanisms that are inappropriately active in obesity.

Cummings et al. (24) suggest that the RYGB mediates weight loss and improved glucose tolerance via mechanisms that include following: 1) gastric restriction, which limits energy intake; 2) bypass of the foregut, which impairs ghrelin secretion in the long-limb variants of RYGB; and 3) expedited delivery of nutrients to the hindgut, which enhances the ileal brake and stimulates the release of peptide YY and glucagon-like peptide-1. In some patients, a dumping reaction to ingestion of concentrated carbohydrates may contribute to weight loss.

In addition to promoting weight loss, weight loss surgery is known to improve or resolve hyperlipidemia, diabetes, obstructive sleep apnea, and hypertension (12). Resolution of diabetes has often been found to occur within days of weight loss surgery.

FIGURE 3. Malabsorptive bariatric procedures. Malabsorptive bariatric operations. A, Jejunoileal bypass; B, biliopancreatic diversion; C, duodenal switch. Drawings were rendered by Dr. Alejandro Heffess and generously provided by Edward C. Mun (1). Reprinted with permission from reference 1.
before marked weight loss (25). This effect was more prevalent after the predominantly malabsorptive procedures (bileopancreatic diversion or duodenal switch) and the mixed malabsorptive/restrictive gastric bypass compared with the purely restrictive gastroplasty and gastric banding procedures (12).

The putative extent and time relations of the different operative procedures to diabetes resolution may be related to some of the changes in the gut-related hormones. The hormonal milieu, or the relative balance of foregut mediators, is differently affected when the distal stomach is bypassed or a partial gastrectomy is performed, and the enteric contents are separated from the bilipancreatic stream in the upper small intestinal tract (12).

Current metabolic studies of patients with diabetes undergoing weight loss surgery have shown the following: a recovery of acute insulin response (26); significant decreases of inflammatory indicators (C-reactive protein and interleukin) (27); improvement in insulin sensitivity correlated with increases in plasma adiponectin (28, 29); significant changes in the entero-glucagon response to glucose (30); significant reduction in ghrelin levels after gastric bypass (19) but not gastric banding (31); and significant improvement in $\beta$ cell function after gastric banding (32).

CONCLUSIONS

Surgical therapy is the most effective modality for treatment of severe obesity (1, 3, 4, 12). The most commonly performed procedure, gastric bypass, causes changes in circulating ghrelin and GIP levels that promote weight loss observed after gastric bypass surgery. The reduction in ghrelin and GIP levels are opposite to the increases caused by diet-induced weight loss. These changes are thought to contribute to the greater efficacy of gastric bypass. Other neuroendocrine mechanisms are likely to be involved as well.

Changes in gut-related hormones are believed to be involved in both weight loss and improvement or resolution of obesity-related comorbidities. Improvement or resolution of diabetes has been found to occur within days of weight loss surgery, before marked weight loss (12). The study of the impact of the various weight loss surgical procedures on leptin, ghrelin, resistin, acylation-stimulating protein, adiponectin, entero-glucagon, cholecystokinin, and other gastrointestinal satiety mediators is receiving increasing attention (22, 28, 33, 34).

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