Therapy Insight: weight-loss surgery and major cardiovascular risk factors

George L Blackburn* and Edward C Mun

SUMMARY

Weight-loss surgery is an effective treatment for severe, medically complicated and refractory obesity. It reverses, eliminates or significantly ameliorates major cardiovascular risk factors related to obesity. In a large proportion of patients, the therapy produces significant weight loss, reduces the risk of disability and premature death, and improves quality of life. Surgical treatment by gastric-restrictive and malabsorptive procedures started several decades ago in the US. Since the 1970s, accrued clinical experience and advances in technology, particularly in minimally invasive surgical approaches, have changed this therapy. Some procedures have evolved, whereas others have become obsolete. Today's weight-loss operations are safe, effective and potentially life-saving options for severely obese cardiology patients. This review describes weight-loss surgery procedures and their effects on cardiovascular risk factors.

KEYWORDS bariatric surgery, cardiovascular disease, coronary heart disease, obesity, weight-loss surgery

REVIEW CRITERIA

This article is based on personal clinical experience, reviews of the authors' personal libraries, and searches of MESH and MEDLINE for the terms "bariatric surgery", "weight loss surgery", "cardiovascular disease", "coronary heart disease" and "cardiovascular risk factors". All relevant, English-language papers published between January 1980 and April 2004 were retrieved in full.

GL Blackburn is an Associate Professor in and Associate Director of the Division of Nutrition, Harvard Medical School, Boston, MA, USA. EC Mun is Director of Bariatric Surgery, Faulkner Hospital, and an Assistant Professor of Surgery at Harvard Medical School, Boston, MA, USA.

Correspondence
*Beth Israel Deaconess Medical Center, Center for the Study of Nutrition Medicine, Feldberg 880 East Campus, 330 Brookline Avenue, Boston, MA 02215, USA
gblackbu@bidmc.harvard.edu

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INTRODUCTION

Obesity is associated with increased morbidity and mortality.[1] Cardiovascular comorbidities of obesity include coronary artery disease, hypertension, congestive heart failure, pulmonary hypertension, deep-vein thrombosis and pulmonary embolism.[2] The effects of morbid obesity on the risks of hypertension, coronary artery disease and vascular disorders have been well documented.[3]

The WHO has recognized an epidemic of obesity throughout most of the developed and developing world.[4] The prevalence of this condition (defined as BMI >30 kg/m^2), which affects approximately 300 million people worldwide,[5] is increasing in most populations and age-groups.[6] Bariatric surgery is an appropriate treatment for patients with class II obesity (defined as BMI 35–40 kg/m^2) and major comorbidities, or class III obesity (defined as BMI >40 kg/m^2, Table 1).[7] In a hospital-based observational cohort study, Christou *et al.*[3] reported reductions in the relative risk of death of up to 89% in patients who had weight-loss surgery compared with those who did not. In this review, we describe weight-loss surgery procedures and their effects on cardiovascular risk factors. We followed the US Preventive Health Service guidelines, the American Dietetic Association, and other criteria of evidence-based medicine.[8]

HISTORY OF OBESITY SURGERY

Obesity surgery began in the US in 1954, with the first jejunoileal bypass. Although initially performed for the management of hypercholesterolemia,[9] it quickly became apparent that the surgery could induce long-term weight loss. The operation was popular for approximately 20 years, until severe long-term side effects were identified, such as protein–energy malnutrition.

These negative early experiences, including high mortality associated with anesthesia, led to obesity surgery falling out of favor for several decades.[10,11] The worsening obesity epidemic, along with a lack of effective medical treatments

Table 1 Classification of obesity.

Weight class	Obesity class	BMI (kg/m^2)
Underweight	–	<18.5
Normal	–	18.5–24.9
Overweight	–	25.0–29.9
Mild obesity	I	30.0–34.9
Moderate obesity	II	35.0–39.9
Severe obesity	III	≥40.0

Weight class is determined by BMI cut-off points. Obesity is defined as BMI ≥30 kg/m^2. Modified with permission from reference 7 © (1998) National Institutes of Health.

GLOSSARY

GHRELIN
Appetite-stimulating hormone produced by cells lining the stomach

GASTRIC INHIBITORY PEPTIDE
Polypeptide that stimulates insulin secretion in response to a high concentration of blood sugar, and inhibits absorption of water and electrolytes in the small intestine

GALANIN
Neurotransmitter that helps to regulate contraction of gastrointestinal muscle and inhibition of insulin, and is associated with the urge to eat fatty foods

BOMBESIN
Polypeptide that inhibits intestinal motility and causes secretion of substances such as gastrin (which induces secretion of gastric juice)

GLUCAGON
Protein hormone that promotes an increase in the sugar content of the blood by increasing the rate of breakdown of glycogen in the liver

PYY$_{3–36}$
Peptide that has an inhibitory effect on gastric-acid secretion, gastric emptying, digestive-enzyme secretion by the pancreas and gut motility

GLUCAGON-LIKE PEPTIDE 1
An incretin hormone that stimulates insulin secretion, inhibits gastrointestinal secretions and motility, and increases satiety in response to eating

OXYNTOMODULIN
Peptide that is released from the gut during digestion and is considered a putative physiologic regulator of gastric-acid secretion

for the severely obese, brought it back to the attention of the mainstream medical community. Gastric-restrictive and gastric-bypass surgical approaches had, however, been refined in the intervening 20 years, and technologic innovations were being made in the new field of laparoscopic surgery.[8,12]

MECHANISMS OF ACTION IN WEIGHT-LOSS SURGERY

Physiologic changes

There are two major categories of weight-loss surgery: gastric restriction and intestinal malabsorption. Restrictive operations create a small neogastric pouch and gastric outlet to decrease food intake. Malabsorptive procedures rearrange the small intestine in order to decrease the functional length or efficiency of the intestinal mucosa for nutrient absorption. Although the malabsorptive approach produces more rapid and profound weight loss than restrictive procedures,[2] it also puts patients at risk of metabolic complications, such as vitamin deficiencies and protein–energy malnutrition. Restrictive procedures are considered simpler and safer than their malabsorptive counterparts, despite inferior long-term weight loss in many cases.[2] The various types of bariatric operations are illustrated in Figures 1 and 2.

Neuroendocrine changes

Neuroendocrine changes that result from surgery are thought to play a key role in producing weight reduction. Gastrointestinal regulators of energy balance include those that promote energy storage (i.e. GHRELIN, GASTRIC INHIBITORY PEPTIDE, GALANIN, BOMBESIN and GLUCAGON) and those that promote energy dissipation (i.e. PYY$_{3–36}$, GLUCAGON-LIKE PEPTIDE 1, OXYNTOMODULIN, UROCORTINS, 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. Its characteristics make it unique among gut-derived signals.[13]

Ghrelin has been identified as the natural endogenous ligand for the growth hormone secretagogue receptor.[14] Data suggest ghrelin receptors are present on hypothalamic neurons central to weight regulation. Several studies have shown reductions in plasma ghrelin levels after gastric-bypass surgery, which could be due to a favorable effect directly related to the procedure.[15–17] Gastric inhibitory peptide,[18] which is secreted from the duodenum and jejunum, is thought to promote fat synthesis and deposition. Like ghrelin, its concentration is favorably altered as a result of weight-loss surgery.

Gastric bypass induces physiologic and neuroendocrine changes that appear to affect the weight-regulatory centers in the brain. Gastric bypass impacts reward-based eating more than any other procedure, suggesting alteration of the reward pathways in the central nervous system. The intensity of hunger decreases and the effectiveness of satiety increases, leading to lower levels of food intake. Gastric bypass also dramatically alters food preferences and selection, independent of specific cravings or aversions. The exact mechanisms for these outcomes have yet to be identified.

WEIGHT-LOSS SURGERY METHODS

ROUX-EN-Y GASTRIC BYPASS (RYGB) is the most common bariatric operation in the US, although laparoscopic adjustable GASTRIC BANDING (LAGB) is the procedure most widely performed worldwide. Long-term data from US patients are still limited,[19] but substantial evidence, especially from European and Australian studies, suggests that LAGB is effective and safe for weight loss. Since its introduction in the US in 2001, LAGB has become increasingly popular as a main restrictive procedure and has largely replaced VERTICAL BANDED GASTROPLASTY.

Advances in technology and surgical skills, along with growing demand from patients, have also led to increases in the number of LAGB procedures performed. Gastric bypass, which accounts for approximately 70% of bariatric surgeries in the US,[20] produces greater weight loss than purely restrictive procedures, such as vertical banded gastroplasty.[21]

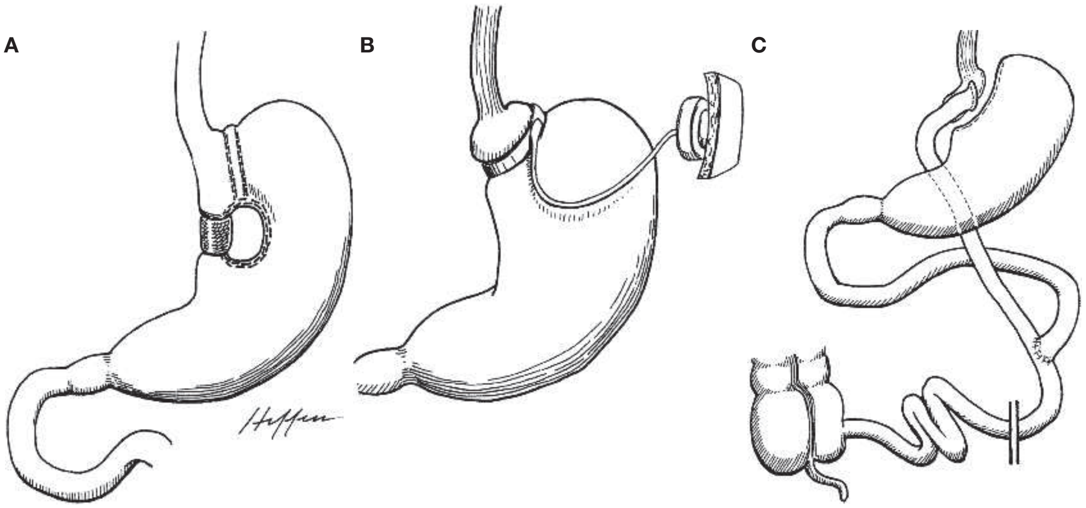

Figure 1 Restrictive weight-loss surgery procedures. (**A**) Vertical banded gastroplasty. Both a band and staples are used to create a small stomach pouch. (**B**) Adjustable gastric banding. A band made of a special material is placed around the stomach near its upper end, creating a small pouch of the upper stomach and a narrow passage into the larger remainder of the stomach. (**C**) Roux-en-Y gastric bypass. A restrictive procedure in which a small proximal gastric pouch is created, followed by the creation of a jejunojejunostomy in a 'Y' configuration to allow an end of the jejunum to be brought up and anastomosed to this proximal pouch.[2] Drawings were rendered by A Heffess and generously provided by EC Mun. Reproduced with permission from reference 2 © (2001) the American Gastroenterological Association.

GLOSSARY

UROCORTINS
Peptides of the corticotropin-releasing factor family with roles in gastric-emptying inhibition and distal colonic motor-function stimulation

CHOLECYSTOKININ
Peptide that stimulates delivery of digestive enzymes into the small intestine of the pancreas and bile from the gallbladder

ROUX-EN-Y GASTRIC BYPASS (RYGB)
A tiny stomach pouch is created and a portion of the digestive tract is rerouted to reduce absorption of food in the intestine

GASTRIC BANDING
A band is placed around the stomach near its upper end to create a small pouch and a narrow passage into the remainder of the stomach

VERTICAL BANDED GASTROPLASTY
Both a band and staples are used to create a small stomach pouch

BILIOPANCREATIC DIVERSION
Portions of the stomach are removed and a small remaining pouch is connected directly to the small intestine, bypassing the duodenum and jejunum

DUODENAL SWITCH
Biliopancreatic diversion that keeps the pyloric valve intact, retaining a portion of the duodenum in the food stream

BILIOPANCREATIC DIVERSION, with or without DUODENAL SWITCH, also produces excellent sustained weight loss and significant improvement of comorbidities.[22,23] These malabsorptive procedures are effective in the management of extreme obesity (BMI >50 kg/m^2). The use of these procedures in the US has been restricted, however, by limited data on long-term safety and adverse metabolic effects.[24]

Roux-en-Y gastric bypass

The most important features of RYGB are the small neogastric pouch and tight stoma that limit oral intake, making restriction the primary mechanism for weight loss.[2] In addition, the distal stomach and proximal small bowel are bypassed in the RYGB configuration, which results in dumping syndrome and mild malabsorption. RYGB anatomy is also shown to cause alterations in ghrelin and PYY_{3-36} responses in favor of appetite control and weight loss. Perhaps due to its multiple mechanisms, the RYGB procedure results in notable long-term weight loss and marked improvement or resolution of obesity-related comorbidities, including cardiovascular disorders.[1,11]

Various infrequent but potentially serious surgical complications are associated with RYGB; namely, 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. Lifelong surveillance of micronutrient and electrolyte levels, particularly calcium, thiamin and various vitamins, is essential to ensure the cardiovascular and general health of patients after surgery. Laparoscopic RYGB is associated with a longer and steeper learning curve for physicians than equivalent open procedures.[25] When performed by experienced surgeons, however, laparoscopic RYGB reduces recovery time[26] and decreases rates of wound infection and incisional hernia.[25,26]

Laparoscopic adjustable gastric banding

LAGB involves placement of an adjustable silicone band around the upper stomach to create a small pouch and a narrow outlet. The aperture of the outlet can be changed by injection or removal of saline through a port under the skin. If the device is ineffective or serious complications develop the band can be removed. The adjustability and reversibility of LAGB make it an attractive alternative to other conventional bariatric procedures.

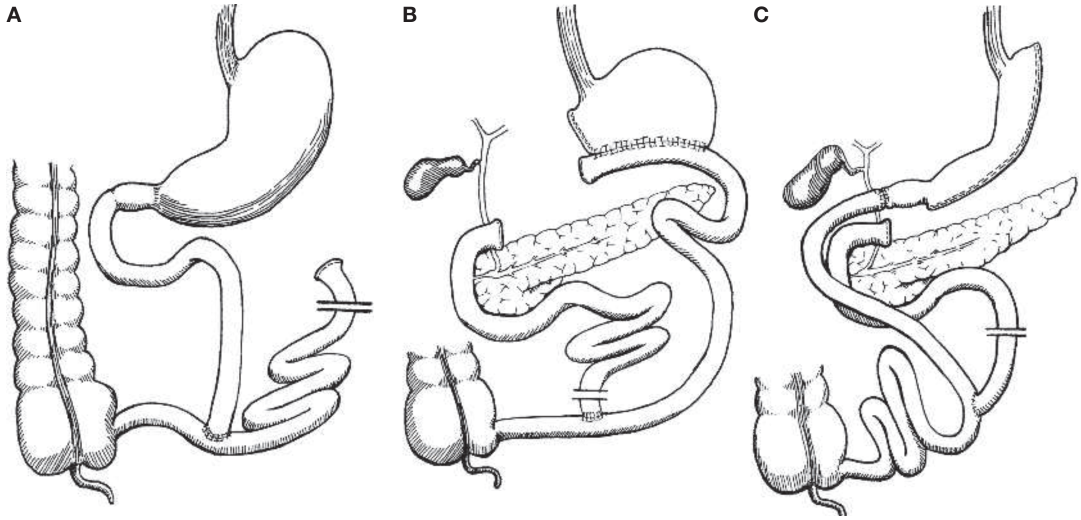

Figure 2 Malabsorptive bariatric procedure. (**A**) Jejunoileal bypass. The first part of the jejunum is connected to the last portion of the ileum to bypass the area of the intestine where nutrients are absorbed; this procedure is no longer used. (**B**) Biliopancreatic diversion. Portions of the stomach are surgically removed. The small pouch that remains is connected directly to the last segment of the small intestine, bypassing both the duodenum and jejunum. (**C**) Duodenal switch. Biliopancreatic diversion that keeps the pyloric valve intact, maintaining a portion of duodenum in the food stream.[2] Drawings rendered by A Heffess and generously provided by EC Mun. Reproduced with permission from reference 2 © (2001) the American Gastroenterological Association.

Weight loss achieved after LAGB varies,[19] but is generally less than that after RYGB or malabsorptive procedures, although data indicate that outcomes are improving.[19] The procedure, like other bariatric surgeries, improves obesity-related comorbidities and quality of life.[27–32] LAGB is also associated with lower average mortality rates than RYGB or malabsorptive procedures. Complications from gastric banding (including band migration or erosion, gastroesophageal reflux disease, esophagitis and malfunction of the subcutaneous port or tubing) can, however, lead to removal or revisional surgery in as many as 10–38% of patients.[10]

CARDIOVASCULAR RISK FACTORS AND OBESITY

Obesity causes cardiac and vascular disease through well-known mediators, such as hypertension, type 2 diabetes and dyslipidemia (Box 1). There is evidence that less-well-characterized mediators also have a role in obesity-related cardiovascular risk, such as chronic inflammation and hypercoagulation,[33] C-reactive protein, lipoprotein (a), fibrinogen and homocysteine.[34]

Excess body weight is an independent risk factor for coronary heart disease, ventricular dysfunction, congestive heart failure, stroke and cardiac arrhythmias.[35] Droyvold *et al*.[36] reported an independent relation between changes in BMI and changes in systolic and diastolic blood pressure. They noted that individuals in whom BMI increased had a raised risk of developing hypertension.

The specific distribution of excess fat can influence the relation between obesity and cardiac disease. Individuals with increased fat accumulation in the abdominal region often have atherogenic lipid profiles and are at increased cardiovascular risk.[37,38] Excess abdominal adipose tissue, particularly visceral fat, and excess triglyceride content in heart tissues are associated with impaired ventricular function and increased coronary heart disease.[20]

Effect of weight-loss surgery outcomes on cardiovascular risk

Weight-loss surgery is the most effective therapy available for people who are extremely obese (Table 1).[1,20] It reverses, ameliorates or eliminates major cardiovascular risk factors, including hyperlipidemia,[11,39] hypertension[11] and other lipid disturbances.[1] RYGB is known to achieve long-term (>14 years of follow-up) and significant weight loss (>50% of excess body weight) in 90% of patients who undergo the operation.[40] Ventricular function can be improved, significantly decreasing cardiac risk and medication requirements in 80–92% of patients.[10] Data at 2 and 10 years of follow-up from the Swedish Obese Subjects (SOS) study[1] show more favorable rates of recovery from all studied risk factors (i.e. hypertriglyceridemia, low HDL cholesterol, diabetes, hypertension and hyperuricemia) in the surgery group than in the control group.

Obesity leads to abnormal remodeling of the heart, and is associated with higher biventricular mass and end-diastolic volume in adults and adolescents, as seen clearly on MRI.[41,42] Moreover, obesity is associated with enlargement of the aorta and decreased aortic elasticity.[43] Such structural abnormality might contribute to the increase in cardiovascular risks related to underlying obesity. Weight reduction, even when achieved by diet, has been shown to improve left-ventricular diastolic filling and ejection fraction.[44] In addition, substantial weight loss produced by bariatric surgery appears to reverse many of the electrocardiographic abnormalities associated with morbid obesity.[45]

Most patients with congestive heart failure symptoms show improvement within 1–2 weeks of surgery, after diuresis of the mobilized fluid (typically within 4–8 weeks) or on achievement of 10% weight loss.[10] Weight loss of around 10% of initial body weight improves endothelial function as well as inflammatory and procoagulant states.[46] The data show a direct association between weight loss and the incidence of coronary heart disease.[47]

Weight-loss surgery resolves type 2 diabetes in 75–85% of patients, with significant improvement in 95%.[48] This surgery normalizes lipid profiles and improves ventricular function in 100% of patients.[10]

Obstructive sleep apnea is a common finding among morbidly obese patients and has a potentially serious impact on cardiovascular fitness. In almost all cases, however, weight loss achieved by bariatric procedures improves obstructive sleep apnea to the point of eliminating the need for continuous positive airway pressure, with no apnea in 40% of patients and minimal episodes in 60%.[49] These findings were clearly confirmed by a meta-analysis of all bariatric surgical procedures: 83.6% of total surgical patients enjoyed either complete resolution or significant improvement in obstructive sleep apnea.[50]

Weight-loss surgery in morbidly obese individuals produces significant decreases in concentrations of inflammatory indicators (C-reactive protein and interleukin-6).[51] QTc duration is shortened effectively and the prevalence of left-ventricular hypertrophy is decreased.[52] Data show rises in recovery rates for patients with hypertriglyceridemia, low levels of HDL cholesterol, hypertension and hyperuricemia, compared with individuals who have not undergone weight-loss surgery.[1]

Around 10–15% of patients fail to achieve long-term success after gastric bypass. Many patients lose weight initially, but slowly regain it over the next 5 years. Such patients require ongoing medical monitoring and treatment. Some also need intense diet, exercise and lifestyle changes, as well as adjunctive weight-control medications.[10]

Box 1 A case in point of improvements in cardiac and vascular disease after Roux-en-Y bypass surgery in a severely obese patient.

Case report

A woman (age 64 years, height 1.6 m, weight 126 kg, BMI 49 kg/m^2) presented with hypertension, diabetes, hypercholesterolemia, peripheral vascular disease, three-vessel coronary artery disease treated by percutaneous transluminal coronary angioplasty and stent, and a history of knee osteoarthritis. Left-ventricular ejection fraction was 62% and stress MIBI[a] test was negative. Additional medical history included gastroesophageal reflux disease with anemia, diverticulosis and a 1.7 cm × 2.4 cm midsigmoid-colon polypoid mass. She needed bilateral knee replacement, but it would be possible only after major weight loss. Nonsurgical weight loss had been unsuccessful.

Cholelithiasis was detected on ultrasonography, as well as multiple ventral incisional hernias from previous appendectomy and other pelvic operations. She had also previously undergone aortic endarterectomy and renal artery stent placement. She was taking once-daily doses of the following medications: 30 mg pioglitazone, 40 mg atorvastatin, 25 mg atenolol, 20 mg omeprazole, 160 mg fenofibrate, 12.5 mg hydrochlorothiazide combined with 160 mg valsartan, 5 mg glyburide combined with 500 mg metformin, 81 mg aspirin and 400 μg folic acid.

Open Roux-en-Y gastric bypass was performed (Figure 1B). Surgery was uncomplicated and the patient's postoperative course was uneventful. An open gastrostomy tube was placed to avoid potential complications from her gastric remnant. At 3 weeks, blood pressure was 142/76 mmHg, the abdomen was soft without distension or tenderness and the midline incision had healed well. The gastrostomy tube was removed and a soft-solid diet was started. At 1 year, the patient weighed 82.1 kg and her BMI was 32 kg/m^2. Blood pressure was normal on minimum-dose atenolol, she was euglycemic without diabetic medications and her serum lipid profile was normal with atorvastatin therapy. At 17 months postoperatively, the patient was a further 4 kg lighter and successfully underwent bilateral knee replacement without complications.

Discussion

Despite high surgical risk, the operation proceeded because other weight-loss options were exhausted and the patient was highly motivated, well informed and committed to long-term care. Roux-en-Y gastric bypass surgery was chosen because of its low related mortality. Postoperatively, the patient was monitored at 2, 6, 9 and 12 months, then annually, for potential long-term complications from surgery. She was required to take a multivitamin, iron, vitamin B12 and calcium supplement for the rest of her life.[60]

[a]Stress MIBI, nuclear imaging stress test using 2-methoxy isobutyl isonitrile as a marker.

If patients return to initial body weight, they generally regain their original degree of cardiovascular risk; sometimes the risk worsens because of advancing age. Certainly, patients do not continue to enjoy the initial improvements. The anatomic changes that are a consequence of RYGB surgery do not usually affect the absorption of cardiac medications, thus the efficacy of pharmacologic treatment is unaltered in these patients.

CLINICAL CONSIDERATIONS

Although highly effective and often life-saving, bariatric surgery still carries significant risks and adverse effects.[53] Patients at unacceptably high operative risk include those with unstable or severe coronary heart disease, severe pulmonary disease, and other conditions thought to seriously compromise anesthesia, wound healing or adherence to postoperative follow-up and self care.[10,54–56] Active collaboration between staff from multiple medical disciplines is required to address risks and potential complications.[43]

MORTALITY

Laparoscopic gastric-bypass surgery takes longer and is more complex to learn than other advanced laparoscopic techniques.[19] A review of patients undergoing laparoscopic RYGB showed 1.5% mortality.[55] In a population-based analysis, Flum and Dellinger[57] reported 1.9% mortality at 30 days in patients undergoing this procedure. Published studies indicate that laparoscopic gastric-bypass surgery has a mortality of 0.05% compared with 0.5% for open gastric-bypass surgery.[58,59]

CONCLUSION

The effects of obesity on cardiovascular health and disease are numerous.[37] Serious consequences of severe obesity, including cardiac dysfunction,[6] markedly reduce the probability of attaining a normal lifespan and raise the annual risk of mortality at least 10-fold.[43] Whereas medical management for the severely obese has failed to provide effective long-term treatment for obesity, there is increasing evidence that bariatric surgery could be the best option.

Weight-loss surgery is fundamentally different from dieting. Changes in physiology resulting from the surgery reset energy equilibrium, affect the complex weight-regulatory system at multiple levels, inhibit environmental influences on weight regulation and defeat powerful mechanisms that are inappropriately active in obesity. For extremely obese patients, bariatric surgery offers a second chance. For their physicians, it provides another needed weapon in the armamentarium of cardiology.

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Competing interests
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