

Surgical Treatment of Metabolic Syndrome

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Key Words

Obesity · Metabolic disease · Metabolic syndrome · Gastric bypass · Sleeve gastrectomy · Duodenal switch · Lap band · Gastric banding

Abstract

This article explores the surprising finding that bariatric surgery can produce full and durable remission of the metabolic syndrome as well as other comorbidities of obesity including type II diabetes, hypertension, polycystic ovary syndrome, gastroesophageal reflux disease, nonalcoholic steatotic hepatitis, adult asthma and improvement in weight-bearing arthropathy. Such an outcome was previously deemed impossible. One effect of the surgery is the correction of hyperinsulinemia, a common denominator in the various expressions of the metabolic syndrome. Basal insulin levels return to normal levels within a matter of days following surgery, allowing a return of the first phase of insulin secretion. This effect is 'dose related' to the extent of the reduction of contact between food and the gut. The resolution of the spectrum of diseases that comprise the metabolic syndrome following bariatric surgery suggests that hyperinsulinemia may be the common cause that is corrected by lowering contact between food and the gut. If this concept is true, then the cause of the syndrome, including diabetes, could be a diabetogenic signal from the gut that forces the islets to produce excessive and harmful levels of insulin, or the cause could be the removal of a signal that blocks exces-

sive insulin secretion. If either of these mechanisms is proven correct, the current treatment of diabetes with long-term insulin administration deserves review.

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Introduction

The metabolic syndrome is a nebulous concept as evidenced by its multiple names and definitions [1]. It has been called syndrome X, insulin resistance syndrome, and obesity dyslipidemia syndrome among other titles. The various definitions of metabolic disease are usually limited to risk factors for cardiovascular disease and diabetes mellitus [2–5]. There has been some argument as to the qualification of the term 'syndrome' given current evidence [1]. If one considers the components of the current definitions of metabolic syndrome as symptoms of a primary if unknown process that involves multiple systems, then this clinical entity might best be called metabolic failure (MF). MF would therefore be a metabolic derangement likely mediated via the gut that results in life-threatening comorbidities such as obesity, diabetes, hypertension, hyperlipidemia, liver disease, obstructive sleep apnea, polycystic ovarian syndrome, depression, renal failure, weight-bearing arthropathy and certain cancers. No matter what term is used to describe this clinical entity, the only proven durable treatment for its constituent components at this time is bariatric surgery.

Defining the Problem

The metabolic syndrome as a clinical entity was first described in 1988 by Reaven who called it syndrome X [2]. His initial description included hyperinsulinemia, impaired glucose tolerance, low high-density lipoprotein cholesterol and elevated triglycerides. Since that time the constellation of risk factors comprising the syndrome has been modified by various national and international healthcare organizations. The World Health Organization (WHO) produced a definition in 1998 which included obesity based on body mass index (BMI), insulin resistance, microalbuminuria and hypertension as additional risk factors [3]. The most common current definitions are from the National Cholesterol Education Program Adult Treatment Panel III and the National Heart, Lung and Blood Institute, which state that a patient must have 3 of the following risk factors: obesity based on waist circumference; hypertension; elevated fasting glucose; elevated triglycerides, or low high-density lipoprotein [4, 5]. There is debate as to which is the best indicator of obesity as it relates to metabolic syndrome, insulin resistance and cardiovascular risk, with different definitions of metabolic syndrome using either waist circumference or BMI. Research based on the association of these indices with adipokines and diagnostic performance characteristics suggest that BMI should be used as the preferred marker for risk assessment [6].

These definitions are helpful for comparing different groups of patients and assessing risk but do not consider the source of the problem. Metabolic disease or syndrome defines a disease by its symptoms rather than by its cause. For example, myocardial infarction can be defined as ischemia of the heart muscle due to inadequate perfusion. It is not defined as at least the 3 symptoms of chest pain, shortness of breath and elevated cardiac enzymes. While the causal agent of MF is unknown, new evidence in bariatric and metabolic disease suggests that abnormal foregut signaling and inappropriate insulin response to food are key elements.

Many practice guidelines for the treatment of obesity in adults have been made [7–9]. The current paradigm of treatment for this disease process is to treat each individual symptom. Diabetes is treated with insulin or medication, hypertension with medications, sleep apnea with continuous positive pressure ventilation at night, obesity with diet and exercise and so on. This is analogous to treating myocardial infarction with morphine for the pain and oxygen for the shortness of breath. Of course we do those things but we also address the ischemia with

coronary stenting or bypass. We should think of MF in the same way and treat the cause whenever possible as well as manage its symptoms.

The metabolic syndrome is a global epidemic and effective treatment is of increasing importance. For example, the prevalence of the metabolic syndrome in the USA is about 23% [10] and in China the prevalence is 9.8% in men and 17.8% in women [11]. Obesity was once considered a disease of wealthy industrialized nations but that is no longer the case as evidenced by the rise in obesity [11, 12] and other comorbidities of metabolic syndrome worldwide [13–15]. The WHO estimates that the number of obese and overweight individuals has increased from 1.1 million to 1.7 million based on the WHO classification of overweight being a BMI >25 [12]. Worldwide obesity, defined as a BMI >35, is estimated at 14.1%, i.e. 400 million people suffer from obesity globally [13]. Cardiovascular disease is now the leading cause of death in the developing world with the exception of sub-Saharan Africa [14]. In 2003 the WHO estimated that 16.7 million people die of cardiovascular disease annually comprising more than 29% of global deaths. They also reported that 171 million people in the world had type II diabetes in 2000, which will double by 2030 [15]. As a point of comparison, 33.2 million people in the world are living with HIV and there are 2.1 million annual deaths from AIDS [16]. The National Health and Nutrition Examination Survey found that 34% of adults in the USA have metabolic syndrome as defined by the National Cholesterol Education Program Adult Treatment Panel III guidelines as shown in table 1.

The metabolic syndrome, therefore, is a costly disease in terms of life, productivity and expenditure. A study by Boudreau et al. [17] showed that patients with metabolic syndrome had annual healthcare costs that were 1.6 times that of those without and that the costs increased by 24% with each additional risk factor assessed. The direct cost of obesity in the USA was estimated at 194 billion dollars in 2010 [18].

Bariatric Surgery is an Effective Treatment for the Metabolic Syndrome

Bariatric surgery is an effective, durable and safe treatment for obesity and associated comorbidities. Diet modification, lifestyle interventions, exercise regimens and medical therapy are rarely curative and weight regain is common. Patients rarely achieve their weight loss goals and often regain weight. Diet and exercise plans

Table 1. Definitions of metabolic syndrome

Clinical risk factor	WHO definition	NCEP/ATPIII
Obesity	BMI ≥ 30 kg/m ²	waist circumference: ≥ 102 cm (≥ 40 inches) in men ≥ 88 cm (≥ 35 inches) in women
Elevated triglycerides	≥ 150 mg/dl	≥ 150 mg/dl
Low HDL	< 35 mg/dl < 39 mg/dl	< 40 mg/dl < 50 mg/dl
Hypertension	$\geq 140/90$ mm Hg	$\geq 130/85$ mm Hg
Elevated fasting glucose	impaired glucose tolerance impaired fasting glucose type II diabetes	≥ 100 mg/dl
Insulin resistance	hyperinsulinemic euglycemic clamp	not included
Microalbuminuria	present	not included

NCEP = The National Cholesterol Education Program; ATPIII = Adult Treatment Panel III; HDL = high-density lipoprotein.

are considered successful with weight loss of 5–10%. Pharmacologic treatment of obesity is considered successful if there is a weight loss of 15%. Studies have shown that a modest reduction in weight of 5% or more can improve the indices of metabolic disease; however, this is not curative [19, 20]. Bariatric surgery has been shown in multiple studies to produce substantial durable weight loss and improve or cure many of the symptoms of metabolic syndrome including type II diabetes, hypertension, sleep apnea and hyperlipidemia [21–23]. Moreover, there are multiple studies that have shown a decreased mortality in patients undergoing surgical weight loss [24–26]. For example, a large meta-analysis led by Buchwald et al. [27] showed a 78% resolution of type II diabetes following bariatric surgery. The National Institutes of Health Consensus Development Conference on Gastrointestinal Surgery for severe obesity in 1991 recommended that surgical intervention be considered for patients with a BMI ≥ 35 who have comorbid conditions of obesity or patients with a BMI ≥ 40 without comorbid conditions. They suggest that gastric restrictive or bypass procedures should be considered for well-informed surgical candidates in the setting of a multidisciplinary team approach [28]. The Food and Drug Administration advisory committee on obesity recently changed their guidelines to include any patient with a BMI > 30 .

All bariatric procedures have some component of restriction, which limits the amount the patient can eat. More importantly these procedures produce early satiety [29] whereby the patient eats a small portion of food and feels satisfied. The laparoscopic adjustable gastric band (LAGB) is a purely restrictive procedure. The other commonly performed bariatric procedures, including laparoscopic Roux-en-Y gastric bypass (LRYGB), sleeve gastrectomy and pancreatic diversion with duodenal switch, also divert nutrients from the duodenum and alter the endocrine and absorptive characteristics of the gut as shown in table 2. There are many theories regarding the mediation of the beneficial effects of bariatric surgery. The diversion of the nutrients from the duodenum as well as weight loss may both be important in the mechanisms of the surgical correction of diabetes. Nutrient diversion increases the release of gastrointestinal hormones such as peptide YY and glucagon-like peptide. Some research has shown that early remission of type II diabetes mellitus occurs via early increase in insulin secretion mediated through these hormones. Additional research suggests that progressive weight loss following diversionary surgery results in increased insulin sensitivity and later remissions of type II diabetes [30]. A study at our institution of postprandial insulin levels in obese type II diabetic patients following gastric bypass showed a significant decrease in insulin levels at 1 week and 3 months.

Fig. 1. Preoperative postprandial insulin levels. A comparison of postprandial insulin levels in lean controls, nondiabetic obese patients and type II diabetic obese patients after a midcaloric meal.

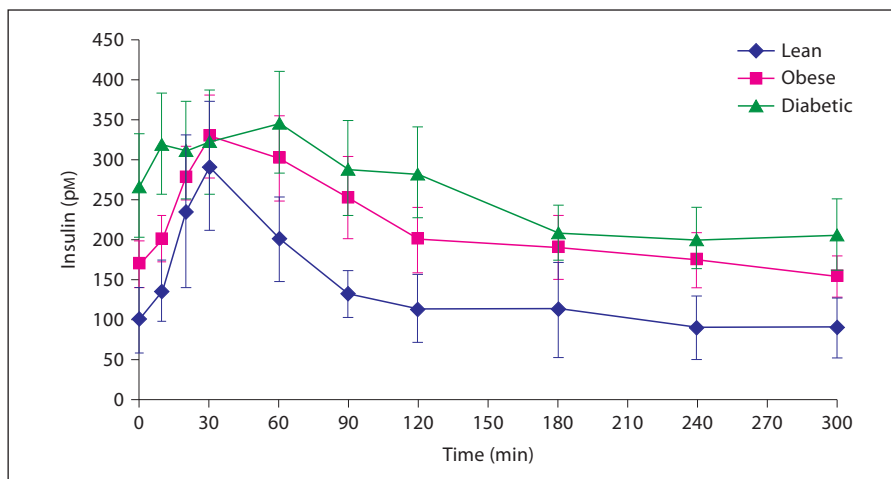


Table 2. Comparison of bariatric procedures

Procedure	Mechanism of action	EWL	Short-term complications	Long-term complications	Mortality
Gastric bypass	restrictive and malabsorptive	59.53%	leak, DVT, PE, pulmonary, bleeding, infection	marginal ulcers, anastomosis, strictures, gastrogastic fistula, metabolic derangement	0.5%
Gastric banding	restrictive	46.17%	bleeding, infection	band slippage, erosion or infection	0.1%
Biliopancreatic diversion with duodenal switch	restrictive and malabsorptive	63.61%	leak, DVT, PE, pulmonary, bleeding, infection	marginal ulcers, anastomosis, strictures, bowel obstruction, metabolic derangement	1.1%
Sleeve gastrectomy	restrictive	55.53%	bleeding, leak, infection	stricture	0.6%

DVT = Deep venous thrombosis; PE = pulmonary embolism.

Insulin levels in lean, nondiabetic obese, and type II diabetic obese patients after a midlevel caloric meal are shown in figure 1. Obese type II diabetic patients have increased insulin levels compared to the other groups. However, as shown in figure 2, 1 week after surgery postprandial insulin levels decrease in both nondiabetic obese and type II diabetic obese patients to normal levels. This change to normal is sustained after 3 months when the patients are eating a more normal diet as shown in figure 3. The exact mechanism of this reduction is an area of intensive study [31].

Patients maintain substantial weight loss after all forms of bariatric surgery. Many patients also improve or resolve type II diabetes, hyperlipidemia, obstructive sleep apnea and hypertension following surgery. A large meta-analysis reviewed over 10,000 patients and revealed a

mean weight loss of 61.2% for all procedures. Type II diabetes resolved in 77% of patients, hyperlipidemia improved or resolved in more than 70% of patients, hypertension resolved in 62% of patients and sleep apnea resolved in 85% of patients [27]. It has also been observed that patients maintain their weight loss. A review study by O'Brien and Mcphail [32] showed greater than 50% excess weight loss (EWL) maintained for gastric banding and gastric bypass at 8 and 10 years, respectively. A long-term follow-up study performed at our institution showed the maintenance of weight loss at 14 years after gastric bypass [33].

Bariatric surgery is performed in high-risk patients who are morbidly obese with multiple health problems, although operative mortality is very low. A large review by Buchwald et al. [34] showed that the mortality was

Fig. 2. Postprandial insulin levels at 1 week. A comparison of postprandial insulin levels in lean controls, nondiabetic obese patients and type II diabetic obese patients 1 week following bariatric surgery.

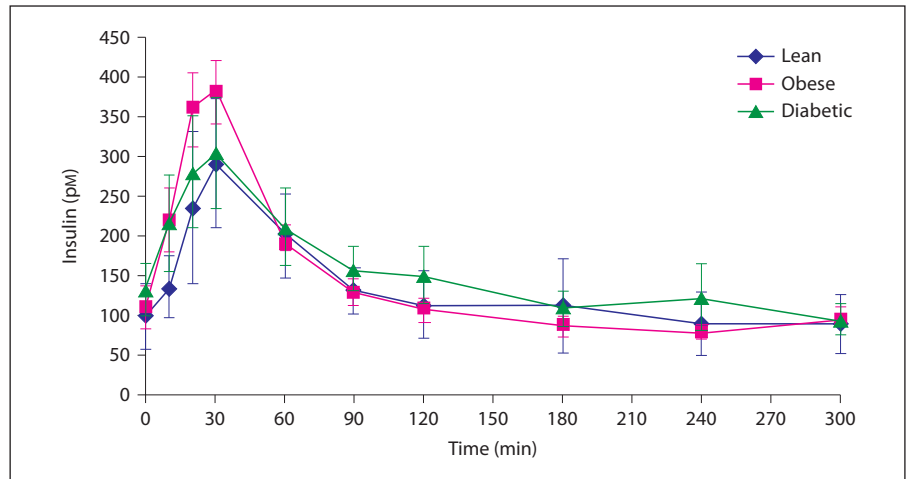
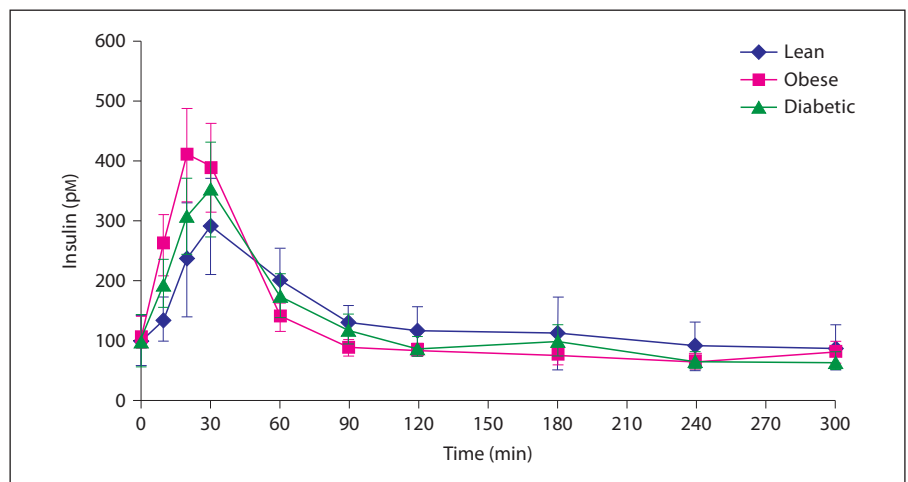


Fig. 3. Postprandial insulin levels at 3 months. A comparison of postprandial insulin levels in lean controls, nondiabetic obese patients and type II diabetic obese patients 3 months following bariatric surgery.



0.1% for restrictive procedures, 0.5% for gastric bypass and 1.1% for biliopancreatic diversion. Patients with MF are at substantially increased risk of morbidity and mortality from their primary disease without intervention. A large Canadian study, comparing morbidly obese patients who undergo bariatric surgery and those who do not, showed a reduction of relative risk of death of 89% in those patients undergoing surgery [35].

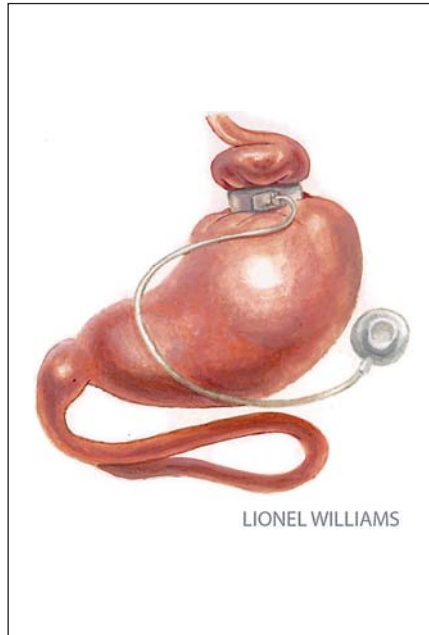
Prevalence of Bariatric Surgery

An estimated 344,000 bariatric procedures were performed worldwide last year. The most commonly performed bariatric procedures were LRYGB (47%), LAGB (42%), sleeve gastrectomy (5%) and biliopancreatic diversion (92%) [36]. Bariatric procedures have leveled off at

113,000 annually in the USA due in part to a lack of access [37]. The current indications for bariatric surgery are a BMI >40 or >35 with significant obesity-related comorbidity. Preoperative evaluation and preparation should involve a multidisciplinary approach including surgical, nutritional and psychological evaluation. The patient must be an acceptable surgical candidate who is capable of understanding the operation and its consequences and agrees to long-term follow-up. The choice of procedure depends on the patient's medical condition and preference. Follow-up is lifelong involving surveillance for nutritional and metabolic derangement and long-term complications.

After an initial rapid increase there has been a decline in the number of bariatric surgeries performed. Less than 1% of the patients who would benefit from these procedures undergo surgery. In the USA this is usually a

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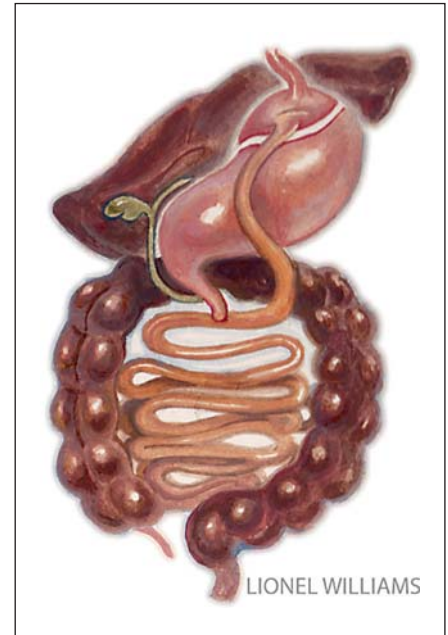


Fig. 4. LAGB.

Fig. 5. Roux-en-Y gastric bypass.

result of insurance denial. Bariatric surgery is excluded from many basic insurance coverage packages and denied by Medicaid in some states. This is true in North Carolina where we practice. Moreover, this area has one of the poorest and most overweight populations in the country. Inclusion criteria can also be difficult for patients to meet. Many insurance carriers require documentation of morbid obesity for 5 years and documented failure of diet and lifestyle intervention prior to consideration for surgery.

Laparoscopic Adjustable Gastric Banding

LAGB is a purely restrictive bariatric procedure. The procedure is performed laparoscopically by placing a plastic band with an internal saline-adjustable balloon around the upper portion of the stomach to create a small pouch as shown in figure 4. The balloon is attached to a reservoir that is placed subcutaneously on the abdominal wall [38]. The patient then undergoes serial percutaneous adjustments to create a small outflow channel through the band. The goal is to achieve early satiety via distention of the pouch and delayed emptying via the small outflow channel. Complications include band slippage, band erosion, foreign body infection and inability to achieve early satiety through adjustment. A large study by O'Brien et al. [39] examining the results of 709 patients undergoing LAGB resulted in 52% EWL at 2 years. This study also reported significant improve-

ment or cure of comorbidities associated with the metabolic syndrome such as diabetes dyslipidemia and hypertension at 1 year. The percentage of patients with resolution or improvement of diabetes is lower after LAGB (47%) compared to gastric bypass (83%) or biliopancreatic diversion (98%) [34, 40].

Laparoscopic Roux-en-Y Gastric Bypass

This procedure was initially described as an open abdominal procedure by Edward Mason and Ito [41] in 1967. However, in 1994 Wittgrove et al. [42] described how this procedure is safely done laparoscopically as well. This allows for less pain, a shorter postoperative stay and decreased risk of wound complication. The Roux-en-Y gastric bypass entails the creation of a 20- to 30-ml gastric pouch usually with a linear stapling device. The stomach is routinely divided completely. A 30- to 50-cm jejunal biliopancreatic limb is measured from the ligament of Treitz. The bowel is divided, the distal Roux limb is created and an anastomosis is made to the gastric pouch. The Roux limb can be placed in an antecolic or retrocolic fashion. An enteroenterostomy is then created 75–150 cm distally to the gastroenterostomy to reinsert the biliopancreatic limb and form a common channel as depicted in figure 5.

A meta-analysis by Buchwald et al. [34] reviewed the results of bariatric procedures in over 22,000 patients. Patients undergoing gastric bypass lost 68% of their excess

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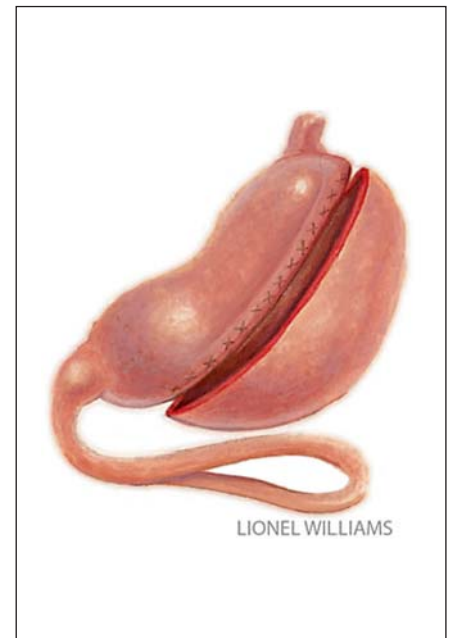


Fig. 6. Biliopancreatic diversion with duodenal switch.

Fig. 7. Sleeve gastrectomy.

body weight. The operative morbidity for the gastric bypass ranges from 0.5 to 2%. A review of long-term results by O'Brien et al. [43] reveals mean EWL of 62.5% at 3 years and 52.5% at 10 years. Immediate postoperative complications include anastomotic leak, remnant stomach leak, thromboembolic events, pulmonary complications, hemorrhage and infections. Long-term complications include marginal ulcer, anastomotic stricture, gastrogastic fistula, cholelithiasis, internal hernia and metabolic derangement.

Biliopancreatic Diversion with Duodenal Switch

Biliopancreatic diversion constitutes only about 2% of bariatric procedures worldwide. The biliopancreatic diversion produces the greatest weight loss and resolution of comorbidity of all bariatric procedures at a cost of moderately increased morbidity and mortality. The procedure entails a partial gastrectomy creating a tubular stomach based on the lesser curve followed by division of the duodenum in the first portion. A Roux-en-Y duodenal ileostomy is created resulting in a 100-cm common channel and 150-cm alimentary limb as illustrated in figure 6. Immediate postoperative concerns are similar to those for LRYGB such as anastomotic or staple line leak and thrombotic complications. Late postoperative complications of anemia, marginal ulceration and vitamin deficiency are more frequent than with LRYGB. Durable weight loss of 70–80% of excess body weight is

achieved with a resolution or improvement of diabetes of 98% [40].

Sleeve Gastrectomy

Sleeve gastrectomy is a less commonly performed bariatric procedure. It can be performed alone or as part of a staged procedure in which biliopancreatic diversion with duodenal switch is performed after initial weight loss has occurred. A partial gastrectomy which removes the greater curve of the stomach is done leaving a 100- to 150-ml tubular gastric conduit based on the lesser curvature of the stomach as shown in figure 7. There are fewer studies reviewing the results of sleeve gastrectomy. This procedure is complicated by leaks at the relatively long staple line in more than 1% of patients. Short-term reviews do show efficacy with EWL of 55% and acceptable safety profiles comparable to other bariatric procedures [44].

Complications

While infrequent, the short-term complications include bleeding, infection, leak and deep venous thrombosis/pulmonary embolism. Some patients also experience aversion effects to high caloric foods commonly called dumping following diversion procedures which can be a helpful complication. The lifelong monitoring for long-term complications such as neuropathy, internal hernia, marginal ulcer, anastomotic stricture and psychological effects is mandatory following all of these procedures.

Conclusion

A different view of the metabolic syndrome and its treatment is overdue. Obesity is only 1 symptom of an underlying medical condition rather than a separate disease. Research in bariatric and metabolic disease suggests that obesity and related comorbidities such as diabetes, hypertension and hyperlipidemia stem from a central process that may be related to signaling pathways in the foregut. 'Metabolic failure' is a more appropriate title for this broad disease process. Hyperinsulinemia plays a role in this process and deserves continued investigation as

well. MF is an expensive problem with increasing global prevalence. At present, the only durable treatment for MF is bariatric surgery. Gastric bypass, LAGB, biliopancreatic diversion with duodenal switch and sleeve gastrectomy are all safe and effective procedures. Most patients with MF will fail medical therapy and lifestyle intervention. These patients should be offered bariatric surgery if they are a surgical candidate. Patients with MF who do not have surgery have decreased life expectancy due to their comorbid disease. Denial of the only effective treatment of metabolic disease to those who need it most is unfair.

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