

Obesity and Cardiovascular Issues: Evaluating the Bariatric Surgery Option

A review of available literature

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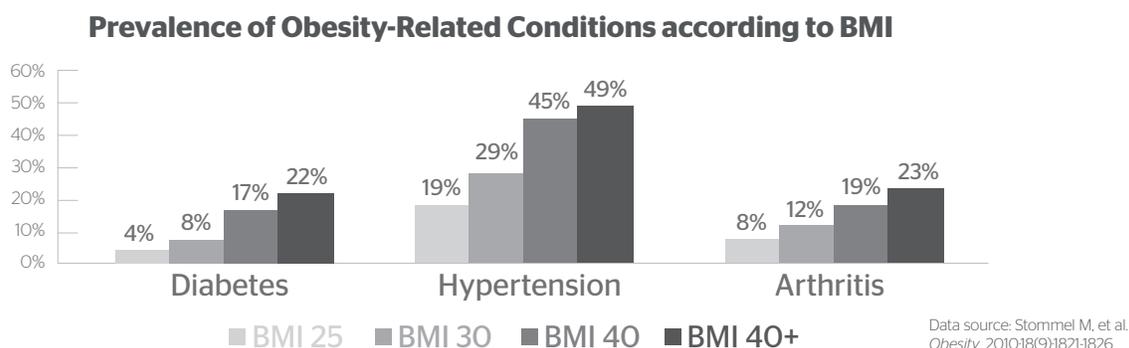
Bariatric surgery is used in the treatment of qualifying obese adult patients for significant long-term weight loss. Individual results following bariatric surgery may vary. Bariatric surgery may be appropriate for some patients and not for others, depending on their specific weight, age, and medical history. Patients and doctors should review all available information on non-surgical and surgical options in order to make an informed treatment decision.

ETHICON manufactures and markets general surgical instruments used in bariatric surgery. The potential benefits discussed are associated with the patient's weight loss and other metabolic effects following bariatric surgery, not with the use of the instruments. ETHICON is offering this information in good faith as an overview to published literature in this area and a starting point for further research. It is not intended to constitute medical advice or recommendations.

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Introduction

Obesity, a chronic disease of substantial public health concern in the United States, is now being classified as an epidemic.¹ More than one third of the American adult population, 75 million adults, is classified as having obesity, with 15 million people classified as having severe obesity (a body mass index (BMI) of ≥ 40 kg/m²).² Often, individuals living with obesity suffer from obesity-related health conditions such as type 2 diabetes (T2DM), hypertension, hyperlipidemia, sleep apnea and arthritis.³ There are over 40 known obesity-related conditions.³ This is particularly problematic because when BMI increases so does the prevalence of obesity-related conditions.⁴ As a result, patients with severe obesity often experience diminished quality of life and increased mortality.^{4,5}



The Link between Obesity and Cardiovascular Events

Clinical studies have found statistically significant associations between obesity and the incidence of cardiovascular morbidities, such as hypertension, insulin resistance, and dyslipidemia and all cardiovascular disease.⁶ Obesity is also linked to coronary heart disease, heart failure, cardiovascular mortality, and all-cause mortality.⁷ These manifestations have been validated by numerous investigators, including a systematic review and meta-analysis of 89 studies by Guh and colleagues.⁸ This study reviewed 20 cardiovascular comorbidities associated with obesity and confirmed statistically significant associations for all cardiovascular diseases measured in the review—except congestive heart failure—even in patients with a BMI of 25-30 kg/m².⁹

One particular manifestation of cardiovascular disease is that hypertension is six times more likely to occur in patients with obesity than in patients with normal weight.¹⁰ In the United States, 30%-50% of hypertension cases are associated with

obesity.⁹ This condition is more prevalent in individuals with obesity due to increased circulating blood volume and cardiac output, as well as decreased vascular relaxation and abnormal vasoconstriction.¹¹ As such, an increasing, linear relationship between hypertension and BMI has been documented.¹² A National Health and Nutrition Examination Survey (NHANES) review (n=4,205) between 1999 and 2004 uncovered an 18.1% incidence of hypertension in individuals with normal weight versus 52.3% incidence for patients with severe obesity, BMI at or above 40 kg/m².¹³ Other studies assert that a BMI of 30-35 kg/m² at age 50 increases incidence of hypertension by 280% and coronary disease by 150%.¹⁴

| Prevalence of Hypertension at Various Weight Classifications ¹³ | | | |
|--|---------------|--------------|---------------------|
| | Normal Weight | With Obesity | With Severe Obesity |
| Hypertension | 18.1% | 30 - 50% | 52.3% |

The NHANES review found that with increasing degrees of obesity there was also an increase in the prevalence of dyslipidemia, another type of cardiovascular disease.¹³ Obesity is strongly associated with atherogenic dyslipidemia, characterized by increased triglyceride levels, apolipoprotein B, small low-density lipoprotein (LDL) particles, and low high-density lipoprotein (HDL) cholesterol levels.⁷

Although obesity puts patients at an increased risk for conditions such as cardiovascular disease, even in the absence of underlying heart disease, a high BMI can lead to alterations in cardiac structure and function.¹⁵ Obesity is often associated with the degradation of left ventricular systolic and diastolic function, leading to heart failure and subsequent left ventricular remodeling.¹⁶ Additionally, blood lipid abnormalities are commonly found in individuals with obesity. Elevated levels of total cholesterol, LDL cholesterol, and triglycerides are common, as well as decreased levels of HDL cholesterol.¹¹ Elevated triglyceride levels or hypertriglyceridemia is caused by increased hepatic very low density lipoprotein (VLDL) secretion.¹¹ Increased delivery of free fatty acids to the liver from visceral and upper body subcutaneous fat also contributes to elevated VLDL levels.¹¹ These heightened VLDL levels may indirectly affect the lipid profile of individuals with obesity, resulting in high LDL and low HDL cholesterol levels.¹¹ Cardiovascular abnormalities observed in individuals with obesity are ultimately believed to be a result of many factors, such as increased sodium retention, increased sympathetic nervous system activity, insulin resistance, and renin-angiotensin system alterations.¹⁶

The Bariatric Surgery Treatment Option for Weight Loss

Traditional approaches to weight loss, including changes in diet and physical activity, are important for a healthy lifestyle. However, a landmark Swedish study found that on average, a 200-pound patient fighting obesity with diet and exercise alone would only be able to achieve a sustained weight loss of 4 pounds over 20 years.¹⁷ Weight loss resulting from behavioral interventions generally leads to a “starvation response”.¹⁷ The body seeks to defend its body weight by increasing appetite while lowering the metabolism.¹⁷ This limits weight loss and promotes weight regain.¹⁷

Bariatric surgery helps to reset the body’s ability to effectively manage weight by altering the complex relationship the body has with food and its metabolism.

New research indicates that with procedures that alter the stomach or intestine, surgery has metabolic and hormonal impacts that enable the body to regulate itself down to a lower set point for body fat. Following bariatric procedures such as sleeve gastrectomy and gastric bypass, the digestive tract is altered in a way that decreases appetite due to modification of gastrointestinal (GI) hormone levels including ghrelin, glucagon-like peptide-1, peptide YY, cholecystokinin, amylin, leptin, insulin, and adiponectin.¹⁸ Many patients experience a decrease in hunger, increased satiety, and even healthier food preferences.¹⁰

Bariatric surgery is the most effective long-term treatment option for qualifying patients with obesity. It has been shown to improve associated conditions through weight loss, or in some cases such as T2DM, through metabolic processes that can complement or replace the need for other treatment.¹⁹ According to the American Heart Association Scientific Statement from 2011, “...it is clear that obesity surgery today offers the only effective long-term treatment option for the severely obese patient.”¹⁰ Bariatric surgery has been shown to provide the greatest amount of excess weight loss with greater than 45% one year post surgery compared to 10% or less for lifestyle and pharmacological treatments.^{20,21,22} Obesity-related health conditions have been resolved in up to 80% of patients.²³ Approximately 179,000 bariatric procedures were performed in 2014 in the US.²⁴

Cardiac Improvements with Weight Loss Post Bariatric Surgery

Bariatric surgery has been identified by medical societies such as the Academy of Nutrition and Dietetics and the American Heart Association as the most successful therapy for severe obesity.¹⁰ In 2014 there were 179,000+ procedures completed.²⁴ The risk of cardiovascular disease is lowered by weight loss from any means.²⁵ For instance, a weight loss of 2.25kg or more in individuals over 16 years of age, was associated with a decrease in the sum of cardiovascular risk factors in both men (48%) and women (40%).¹² Some of the improvements associated with weight loss include reductions in blood volume and hemodynamic demands on the heart, along with decreased left ventricular mass, chamber size, and septal wall thickness.¹²

According to the American Heart Association, “it is clear that obesity surgery today offers the only effective long-term treatment option for the severely obese patient.”¹⁰

Evidence has demonstrated that bariatric surgery improves cardiovascular risk in individuals with obesity, and the American Heart Association has stated “bariatric surgery resulting in a weight loss of 20 to 30 kg maintained up to 10 years was associated with a reduction of comorbidities with an overall mortality rate <1%.” High blood pressure was resolved in 42% of patients after gastric banding,²⁶ 50% of patients after sleeve gastrectomy,²⁷ and 66% after gastric bypass.²⁸

High Blood Pressure Resolution following bariatric surgery

| Sleeve Gastrectomy ²⁷ | Gastric bypass ²⁸ |
|----------------------------------|------------------------------|
| 50% | 66% |

In a long-term Swedish Obese Study (SOS), patients who received surgery had a 33% reduction in relative risk of first time fatal or non-fatal myocardial infarction or stroke, a larger reduction than in patients who did not receive surgery.²⁹ The study asserted that significant cardiovascular improvement over 10 years requires a very large and sustained weight loss of around 10 to 40 kg, which typically cannot be achieved with traditional lifestyle interventions alone.³⁰

The SOS study also associated gastric bypass with lowered systolic (mean: -5.1 mmHg) and diastolic pressure (-5.6 mmHg), differing significantly from both vertical banded gastroplasty (VGB)/adjustable gastric banding (AGB) (-1.5 and -2.1 mmHg, respectively; $P<.001$) and controls (+1.2 and -3.8 mmHg, respectively; $P<.01$).³¹ In a recent Retrospective Matched Cohort Database Study by G. Li, S. Kashyap, A.D. Patkar, J.G. Seare, A. Yoo use of medications for hypertension and hyperlipidemia also declined significantly in diabetic patients—down 45% and 55% at 12 months, respectively ($P<0.0001$).³² Bariatric surgery was also associated with a lower number of cardiovascular deaths at follow-up.¹⁷ Post-surgical adverse cardiovascular outcomes were related to the baseline level of insulin rather than BMI. The outcomes of surgery are predicted in a major way by the baseline metabolic state and its amenability to correction via surgery.²⁹

At 36 months post-surgery with medical therapy, the Cleveland Clinic Ethicon sponsored STAMPEDE study showed significant improvement in HDL and Triglycerides compared to the medical therapy treatment alone.³³

| STAMPEDE Endpoints at 36 Months ³³ | | | |
|---|-------|-------|--------------------------|
| | RYGB | SG | Control/ Medical Therapy |
| % change in HDL | +34.7 | +35.0 | +4.6 |
| % change in Triglycerides | -45.9 | -31.5 | -21.5 |

Of note, all options included intensive medical therapy. The control group included ONLY intensive medical therapy.

Bariatric surgery also can lead to better physical function, higher energy levels and better perception of general health.³³ The incidence of chest pain and shortness of breath may be reduced, as well as the prevalence of cardiovascular abnormalities such as hypertension, dyslipidemia, and diabetes.²⁹

In patients with cardiovascular events, weight loss may cause reduction in blood pressure due to reduced total circulating and cardiopulmonary blood volume, as well as reduced sympathetic nervous system activity. Reduction in plasma catecholamines and renin activity may also play a role.³⁴ Echocardiographic studies show decreased left ventricular hypertrophy and improved function after surgery.²⁵ In addition to improved blood pressure measurements, oxygen consumption is reduced with weight loss, signifying the ability to perform more strenuous tasks.³⁵ The reduction of coagulability and blood pressure along with improvements in lipid profile may synergize to reduce risk of intravascular catastrophe.^{29,33}

Following surgery, results from the Cleveland Clinic’s STAMPEDE study showed a reduction in medications used following surgery for gastric bypass and sleeve gastrectomy compared to little change with medical therapy alone.³³

| Cardiovascular Medications at Baseline and Month 36 patients (%) ³³ | | | |
|--|-----------------|----------------------------------|--------------------------------------|
| CV medications | Medical therapy | Gastric Bypass + Medical Therapy | Sleeve Gastrectomy + Medical Therapy |
| Baseline | | | |
| None (%) | 0(0) | 3(6.3) | 2 (4.1) |
| 1 - 2 (%) | 19 (47.5) | 17 (35.4) | 28 (57.1) |
| ≥ 3 (%) | 21 (52.5) | 28 (58.3) | 19 (38.8) |
| At 36 months | | | |
| None (%) | 1 (2.5) | 33 (68.8) | 21 (42.9) |
| 1 - 2 (%) | 18 (45) | 14 (29.2) | 25 (51) |
| ≥ 3 (%) | 21 (52.5) | 1 (2.1) | 3 (6.1) |

Data Source: Supplement to: Schauer PR, et al. *N Engl J Med*. 2014;370:2002-13.

Cost Effectiveness of Bariatric Surgery

Following bariatric surgery, patients may have substantially lower costs associated with reduced medications and a reduced interaction with all levels of the healthcare system as their obesity-related conditions improve.³⁶ In a published study, there was a 65% cost savings for hypertension medications at 12 months following gastric bypass.³⁷

The cost of surgery may begin to be recouped within the first four years, and related cost savings for antidiabetic, antihypertensive and dyslipidemic agents continue through six years.³⁸ According to the American Journal of Managed Care (AJMC), a peer-reviewed journal on health outcomes research, health insurers recover their costs for bariatric surgery in about two years for laparoscopic surgery and in about four years for open surgery.³⁹ The analysis covered six months of pre-surgical evaluation and care, the surgery itself, and up to five years of post-surgical care. Bariatric surgery appears to be a clinically effective and cost-effective intervention for moderately to severely obese people compared with non-surgical interventions.

Bariatric Surgery Risks

All surgeries have risks, such as adverse reactions to medications, problems with anesthesia, problems breathing, bleeding, blood clots, inadvertent injury to nearby organs and blood vessels, even death. According to outcomes data from Bariatric Surgery Centers of Excellence, bariatric surgery has an overall mortality of about 0.1%,⁴⁰ which is less than cholecystectomy (0.7%)⁴¹ and hip replacement (0.93%)⁴² surgeries. The success of bariatric surgery is highly correlated with the experience of both the surgeon and the health center.

| Mortality Rate for Surgical Procedures | | |
|--|--------------------|---------------------|
| Bariatric Surgery | Cholecystectomy | Hip Replacement |
| 0.1% ⁴⁰ | 0.7% ⁴¹ | 0.93% ⁴² |

The overall likelihood of bariatric surgery major complications is 4.3%.⁴³ The risk for serious complications depends on the type of bariatric surgery, the patient's medical condition, and age, as well as the surgeon's and anesthesiologist's experience. General risks associated with bariatric surgery include a failure to lose weight, nutritional or vitamin deficiencies, inflammation of the gallbladder, gallstones, dilated pouch, dysphagia, GERD, incisional hernia, malnutrition, and weight regain. Bariatric surgery may also

cause changes to the autonomic nervous system, specifically to the processes that regulate energy balance and metabolic function. While these changes may help to sustain a lower weight set point, they also could induce changes to circulating bile acids, distribution of bacteria in the gut microbiota, and altered vagal and sympathetic neural activity.^{44,45}

Each type of bariatric surgery is associated with its own risks. Risks related to gastric bypass may include nutrient deficiency, anastomotic stenosis, leak or fistula, marginal ulcer/gastritis and stenosis, bowel injury or obstruction, nausea/vomiting, internal/incisional hernia, and pouch dilation.⁴⁶ Sleeve gastrectomy may be associated with gastric leak, intra-abdominal abscess, pulmonary embolism, delayed gastric emptying, splenic injury, stricture, and late choledocholithiasis.⁴⁷ Gastric banding risks can include gastric perforation, port rotation or leak, band or port-site infection, band obstruction, malposition, nausea/vomiting, and band erosion.⁴⁶

Identifying Candidates for Bariatric Surgery

Bariatric Surgery can be considered for weight reduction in patient that are 18 years of older with a BMI of >40 or ≥ 35 with an obesity related condition. Bariatric surgery is a viable alternative when diet exercise and other behavioral interventions are not effective. Bariatric surgery has been shown to produce +25% weight loss at 5 years.⁴⁸

Bariatric surgery can be considered for patients with obesity that have a cardiovascular condition or symptoms of a cardiovascular condition. According to the SOS "compared with usual care, bariatric surgery was associated with reduced number of cardiovascular deaths and lower incidence of cardiovascular events in obese adults"³⁰ and therefore could be considered for patients with obesity.

Since bariatric surgery is a life changing event it is important to ensure patients are well informed, motivated and cognizant of the operative risk. It is also important to advise patients on the need for long term follow up. Clinical evidence suggests that the overall risks of severe obesity often outweigh the risks for bariatric surgery.⁴⁹ Bariatric surgery results may vary and surgery may or may not be appropriate for particular patients depending on their specific age, weight and medical history. Patients and doctors should review all available medical information on surgical and non-surgical options in order to make an informed decision.

How to Refer Patients

After discussing a patient's candidacy for surgery, it is important to emphasize behavioral and psychological readiness for the procedure, discuss benefits and possible complications, manage post-operative expectations, as well as emphasize the long-term responsibilities associated with bariatric surgery. Additionally, encourage them to check with their current health insurance plan to determine specific requirements for surgery and proactively provide them with the necessary documentation that will be required for their surgical consultation. These documents may include weight loss attempts, medical records, and a pre-surgery health evaluation.

Additional Resources

Online resources are available at ethicon.com/obesity, or ASMBS.com for those healthcare professionals interested in learning more about bariatric surgery or realize.com for patients who are interested in finding a surgeon for a consultation.

Patients can receive more information and answers to common questions about obesity and bariatric surgery by calling: Ethicon's Obesity Patient Hotline at **1 (855) 273-2549**.

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