Obesity and Cancer: 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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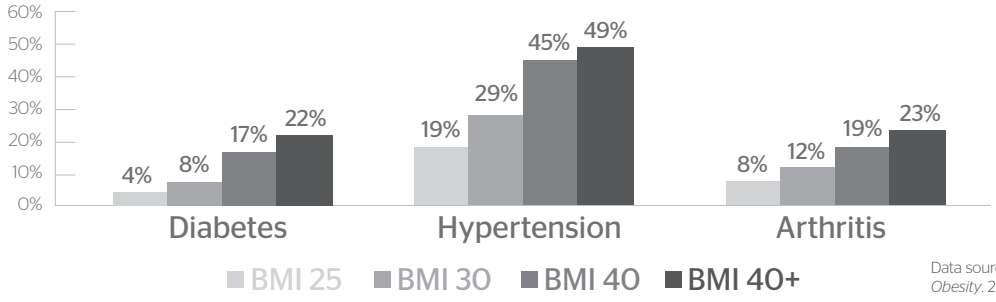
Introduction

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/m^2).[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]

Prevalence of Obesity-Related Conditions according to BMI



Data source: Stommel M, et al. *Obesity*. 2010;18(9):1821-1826.

The Link between Obesity and Cancer

There is growing evidence supporting the association between obesity and cancer. According to a recent document produced by the American Society of Clinical Oncology, "Obesity is linked to poorer cancer outcomes, including higher risk of recurrence and cancer-specific and overall mortality".[6] There is a clinical association between obesity and most common types of cancer including post-menopausal breast cancer, colorectal cancer, and cancers of the endometrium, kidney, esophagus, thyroid, and gallbladder.[7] The strongest associations have been seen with breast, prostate and colorectal cancers".[6] The American Society of Clinical Oncology (ASCO) identifies obesity as a health risk—responsible for nearly 25% of the relative contribution to cancer incidence[8]—that is quickly overtaking tobacco as the second leading preventable cause of cancer.[9] It is thought that 34,000 incident cases of cancer in men and 50,500 in women in 2007 were due to obesity, though some cancers such as endometrial and esophageal, may be more attributable to obesity than others.

Each 5 kg/m2 in BMI increases the risk for:[7]
Men: esophageal (by 52%), thyroid (by 33%), colon (by 24%) cancer
Women: endometrial (by 59%), gall bladder (by 59%), and postmenopausal breast cancer (by 12%)

Notes from the American Society of Clinical Oncology's new publication on Obesity and Cancer state that:

- "Obesity at diagnosis is linked to a 33% increase in the risk of breast cancer related mortality and overall mortality in pre- and post-menopausal women with early stage breast cancer."[10]
- "Obesity is associated with the development of biologically more aggressive and advanced prostate cancer"[11]
- "Obesity is associated with reduced response to prostate cancer treatment."[12]

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The exact mechanism for the link between obesity and cancer has not been fully established; however, adipose tissue is known to function extensively as an endocrine organ, and these properties are what may contribute to cancer risk.[13] Fat cells produce substances such as estrogen and adipokines (such as leptin), and they may affect other biochemical signals such as inflammatory signals or tumor growth regulators.[13] Estrogen has been linked to breast and endometrial cancers, and leptin promotes cell proliferation.[14] Individuals with obesity generally display enhanced baseline levels of insulin and insulin-like growth factor- that may play a role in the development of tumors.[15] These signals are not problematic in average-sized individuals, but with the greatly enhanced fat mass that exists in patients with obesity and especially in those with severe obesity, these factors are more likely to be uncontrolled.

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.[16] Weight loss resulting from behavioral interventions generally leads to a "starvation response".[16] The body seeks to defend its body weight by increasing appetite while lowering the metabolism.[16] This limits weight loss and promotes weight regain.[16]

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.[17] Many patients experience a decrease in hunger, increased satiety, and even healthier food preferences.[18]

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 treatments.[19] According to the America 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."[18] 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]

Cancer Related Improvements with Weight Loss Post Bariatric Surgery

Weight reduction is helpful to reducing cancer risk in individuals with obesity. However, traditional weight-loss therapies (i.e., caloric restriction and increasing exercise levels) are frequently inadequate for weight management for individuals with severe obesity.[25] Aggressive treatment of obesity to lower weight and therefore lower the incident risk of cancer is thought by many to be a necessary step for many patients with severe obesity.[25,26] The American Society of Clinical Oncology includes bariatric surgery as a treatment citing that weight loss has been shown to help cancer patients, and bariatric surgery has been shown to help with weight loss.[8]

Bariatric surgery has been shown to be an effective weight-loss therapy for individuals with obesity, and in some cases effective at reducing the prevalence of diabetes, hyperlipidemia, hypertension, and obstructive sleep apnea in a substantial majority of patients and alleviating symptomology.[27] There were 179,000 bariatric procedures performed in the US in 2014.[24] Bariatric surgeries' effectiveness for weight-loss is matched by its safety profile; in terms of overall mortality, bariatric surgery is about 0.1%,[28] which is less than cholecystectomy (0.7%) and hip replacement (0.93%), and overall likelihood of major complications is about 4.3%[29] While there are risks involved in bariatric surgery, clinical evidence shows that the overall risks of severe obesity outweigh the risks of metabolic and bariatric surgery.[30]

Bariatric surgery allows for a reduction in weight which may be an effective long-term solution to reducing the likelihood of cancer incidence. Specifically, Christou et al.

showed that 2.0% of patients who received bariatric surgery (n=1,035) versus about 8.5% of the non-surgery group (n=5,746) displayed cancer incidence, a statistically significant reduction.[31] Reductions were observed in breast and colon cancer, reduced by 85% and 70%, respectively.[31]

A meta-analysis by Yang and colleagues of 5 observational studies established a 57% lower risk of obesity-related cancer diagnosis in severely obese individuals that underwent bariatric surgery. In the same meta-analysis, researchers observed a 58% reduced risk of breast cancer, 14% reduced risk of pancreatic cancer, 88% reduced risk of kidney cancer, 40% reduced risk of myeloma, 25% reduced risk of melanoma, and 43% reduced risk of non-Hodgkin's lymphoma.[32]

Meta-analysis by Yang and colleagues Post-surgery results[32]	
Breast cancer	58% reduced risk
Pancreatic cancer	14% reduced risk
Kidney cancer	88% reduced risk
Myeloma	40% reduced risk
Melanoma	25% reduced risk
Non-Hodgkin's lymphoma	43% reduced risk

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.[30]

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.[33] 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%,[28] which is less than cholecystectomy (0.7%)[34] and hip replacement (0.93%)[35] 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%[28]	0.7%[34]	0.93%[35]

The overall likelihood of bariatric surgery major complications is 4.3%.[36] 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.[37,38]

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.[39] Sleeve gastrectomy may be associated with gastric leak, intra-abdominal abscess, pulmonary embolism, delayed gastric emptying, splenic injury, stricture, and late choledocholithiasis.[40] Gastric banding risks can include gastric perforation, port rotation or leak, band or port-site infection, band obstruction, malposition, nausea/vomiting, and band erosion.[39]

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.[41] Bariatric surgery can be considered as an aid in reducing weight, which has been shown to improve cancer outcomes and lower cancer risk.[42]

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 patents 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.[31] 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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