
Cancer in Obese Women: Potential Protective Impact of Bariatric Surgery

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- BACKGROUND:** The use of bariatric surgery has been increasing over the last several years in response to the obesity epidemic, and the objective of this study was to report on the types of cancer in morbidly obese women undergoing bariatric surgery and compare these with types of cancer in obese women without surgery.
- STUDY DESIGN:** A retrospective, observational study was conducted. The bariatric surgery database identified women who underwent operations between 1990 and 2006 at the University of Virginia. Medical records and the institution's and state's cancer registries were searched for demographics and cancer data. Morbidly obese patients not undergoing bariatric surgery were used for comparison.
- RESULTS:** There were 1,482 women who had bariatric surgery, and 53 of these (3.6%) were diagnosed with cancer. The most common cancer site was the breast ($n = 15$, 28.3%) followed by the endometrium ($n = 9$, 17%) and the cervix ($n = 6$, 11.3%). The mean age at cancer diagnosis was 39.4 years. Most cancers ($n = 34$, 64.1%) were diagnosed before the bariatric surgery. Bariatric surgery patients with cancer were older than noncancer patients at time of surgery (mean age 44.7 versus 41.6 years; $p = 0.019$), but otherwise did not differ significantly with regard to race, body mass index, or comorbid conditions. Compared with a control group of 3,495 morbidly obese women who had not undergone bariatric surgery, the surgery patients had fewer cancers (3.6% versus 5.8%, $p = 0.002$), were younger (41.7 versus 46.9 years, $p < 0.001$), and were younger at cancer diagnosis (45.0 versus 56.8 years, $p < 0.001$). The most frequent cancers in the control obese women were endometrial, ovarian, and breast cancer. Both groups of obese women with endometrial, breast, ovarian, and colorectal cancers were younger at diagnosis compared with Virginia Cancer Registry means.
- CONCLUSIONS:** Breast and endometrial cancers remain the most common types in obese women and may occur at young ages; bariatric surgery may decrease cancer development in obese women. (J Am Coll Surg 2009;208:1093–1098. © 2009 by the American College of Surgeons)
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Obesity in the US has become a national public health crisis. Currently about 65% of US adults are overweight and 30% of these individuals are obese, based on body mass index (BMI).¹ Obesity is associated with an increased prevalence of multiple diseases such as hypertension, diabetes, cardiovascular disease, and cancer. Additionally, the in-

creased mortality from diseases associated with excess body mass has also been well established. Recently, poor diet and physical inactivity were calculated to be the second leading cause of death in the US.^{2,3} When looking at obesity-related deaths from cancer alone, Calle and colleagues⁴ estimated that 90,000 deaths a year could be prevented if men and women maintained a normal weight.

Studies of the association of cancer with obesity have identified several sites with increased prevalence and mortality.⁴⁻⁹ Bergstrom and associates⁵ assessed the impact of obesity on cancer in Europe and concluded that cancers of the endometrium, kidney, and gallbladder showed the strongest relationship to excess weight; the most attributable cases were from colon cancer. For women, there is a particularly strong association between obesity and postmenopausal breast cancer and gynecologic cancers, specifically, endometrial cancer.¹⁰ Furthermore, after evaluating

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the prevalence of cancer in Italian morbidly obese patients, Boru and coworkers⁶ concluded that hormone-related tumors were the most prevalent type of cancer and that the breast was the most frequent site. The cause of the increased risk of cancers at these sites is not completely understood, but it is postulated to be secondary to metabolic and hormonal changes from increased food intake and increased adiposity. Factors that may play a role include elevated hormone levels, insulin, and insulin-like growth factor (IGF-1).¹¹

Bariatric surgery is emerging as a popular treatment option for patients who are morbidly obese as the incidence of obesity rises. Unfortunately, diet and exercise alone have proved largely ineffective for attaining significant and sustained weight loss, and experts estimate that people who have a BMI > 50 kg/m² have only a 3% to 5% chance of losing weight with these methods.¹² In contrast, bariatric surgery studies report an average loss of 65% of excess weight 1 year after gastric bypass and an average loss as high as 50% to 60% of excess weight 3 years after adjustable gastric banding.¹² In 2004, there were 121,055 bariatric procedures performed in the US, and demand is continuing to increase.¹³ Early bariatric surgical techniques such as jejunoileal bypass produced unexpected metabolic complications, demonstrating that bariatric surgery results not just in weight loss, but also involves alterations of metabolic processes.¹²

Currently there is a dearth of information about the effects that these metabolic alterations and weight loss may have on development of obesity-related cancers. Although obesity is clearly linked to the development of cancer, what remains unclear is the importance of the timing of obesity and whether subsequent weight loss could decrease risk. The International Agency for Research on Cancer (IARC) Working Group on the evaluation of cancer preventative strategies concluded that there is inadequate evidence in humans for a cancer-preventive effect of intentional weight loss for any cancer site.¹⁴ So it is imperative to study the bariatric surgery population to determine if there is any change in cancer risk after bariatric surgery, or if the risk for obesity-related cancers remains the same. The purpose of this study was to report on the number and types of cancer in morbidly obese women who underwent bariatric surgery at the University of Virginia and to compare them with a control population.

METHODS

Institutional Review Board approval was obtained from the University of Virginia Health System and from the Virginia Department of Health. The University of Virginia Surgery Department Database was used to identify all

female patients who underwent bariatric surgery from 1990 to 2006. Data abstracted from the University of Virginia Surgery Department Database included date of birth, date of operation, height, weight, BMI, procedure performed, and postoperative complications. The weight and height from the time of operation were used to calculate BMI in kg/m². The World Health Organization defines normal body weight as a BMI of 18 to 24.9 kg/m², overweight is 25 to 29.9 kg/m², obese class I is 30 to 34.9 kg/m², obese class II is 35 to 39.9 kg/m², and obese class III is > 40 kg/m². Additional health information about postoperative complications, comorbid diagnoses, and race was obtained from patient charts and from the University of Virginia's Clinical Data Repository (CDR). The CDR is a research data warehouse that integrates clinical, administrative, and financial data from multiple information systems within the University of Virginia Health System.¹⁵ Additionally, a convenience control population of women with a diagnosis of morbid obesity was created through the CDR between 2001 and 2006 and assessed for the most frequent cancers and age at cancer diagnosis for a comparison group.

Patients diagnosed with cancer were identified through the University of Virginia's Cancer Registry, the CDR, and the Virginia Cancer Registry. The Virginia Cancer Registry is maintained by the Virginia Department of Health and is a statewide registry of data on individuals diagnosed or treated in Virginia or Virginia residents who received cancer care out of state. Data abstracted from the University of Virginia's Cancer Registry and the Virginia Cancer Registry records included diagnosis date, age at diagnosis, tumor site, and histology. Patients with a history of cancer were also identified through the CDR, and patient charts were used to provide additional information about diagnosis date, site, and histology. Unfortunately, no weight data are collected as part of these databases so a statewide control population of overweight women is not available.

Statistical analysis was performed using SPSS 16.0 (SPSS Inc). Independent sample *t*-tests and chi-square tests were used to evaluate differences between groups. For all tests, *p* < 0.05 was considered statistically significant.

RESULTS

Between 1990 and 2006, 1,482 women had bariatric surgery at the University of Virginia. The mean patient age was 41.7 years (range 18 to 69 years), the majority were Caucasian (86%), and the most common bariatric procedure performed was a laparoscopic gastric bypass (62%) (Table 1). The mean BMI was 51.6 kg/m² (range 26.3 to 105 kg/m²). Of the 1,480 patients with BMI recorded, 1,405 (94.9%) were morbidly obese at the time of opera-

Table 1. Clinical Characteristics of Women Undergoing Bariatric Surgery

Characteristic	n	%
Mean age 41.7 y (range 18–69 y)	1,482	100
Race		
Caucasian	1,278	86.2
African American	199	13.4
Other	4	0.3
Unknown	1	0.1
BMI range, kg/m ²		
25–29.9	1	0.1
30–34.9	4	0.3
35–39.9	70	4.7
40–49.9	659	44.5
50–59.9	480	32.4
60 or higher	266	17.9
Unknown	2	0.1
Comorbid conditions		
Hypertension	672	45.3
Type 2 diabetes	333	22.5
Dyslipidemia	221	14.9
Asthma	146	9.9
Heart disease	53	3.6
More than 2 conditions	414	27.9
Procedures		
Laparoscopic gastric bypass	915	61.7
Gastric bypass	405	27.3
Laparoscopic conversion gastric bypass	66	4.5
Laparoscopic adjustable gastric band	57	3.8
Vertical banded gastroplasty	26	1.8
Revision of previous procedure	9	0.6
Laparoscopic vertical banded gastroplasty	2	0.1
Reverse jejunal bypass	2	0.1

BMI, body mass index.

tion (BMI > 40 kg/m²). We were unable to obtain records of patient BMI from the time of cancer diagnosis, so the BMI from the time of bariatric surgery was used for statistical analysis.

Of the 1,482 bariatric surgery patients, 53 (3.6%) were diagnosed with invasive cancer. The most common cancers found mirrored previous findings for obesity-related cancers, with breast (15 patients) and endometrium (9 patients) being the most common sites. The site-specific cancers are reported in Table 2. The mean age at time of cancer diagnosis was 39.4 years and the median age was 40 years.

Thirty-four cancer patients (64.1%) were diagnosed and treated before their bariatric surgery and for these patients, the mean age at the time of cancer diagnosis was 35.8 years. The average interval between cancer diagnosis and bariatric surgery was 9.9 years. Seventeen cancer patients (32%) were diagnosed after bariatric surgery was

performed and the average interval between cancer diagnosis and bariatric surgery was 4.2 years. One patient (1.9%) was diagnosed during the preoperative workup, and the time of cancer diagnosis was unknown for one patient (1.9%). The majority of gynecologic cancers were diagnosed before the operation (85% preoperative diagnosis); breast cancers were almost equally distributed (46.7% preoperative and 53.3% postoperative).

Clinical characteristics of bariatric surgery patients with and without cancer were compared using *t*-tests and chi-square analysis. The only statistically significant difference found between groups was that cancer patients were older than noncancer patients at the time of bariatric surgery (mean age 44.7 versus 41.6 years; *p* = 0.019). No significant differences were found between the groups for race, BMI at time of operation, type of operation, or comorbid conditions.

A control population of 3,495 women with morbid obesity who had not undergone bariatric surgery was identified using the CDR. The average age of this control population (from the date of first recorded diagnosis of morbid obesity) was significantly older than the bariatric surgery population (46.9 versus 41.7 years; *p* < 0.001), and a higher percentage of the control women were diagnosed with cancer (5.8% versus 3.6%; *p* = 0.002). For the entire population of women with cancer, women undergoing bariatric surgery were younger (39.4 versus 56.8 years; *p* < 0.001) and had an increased BMI (52.2 versus 46.1 kg/m²; *p* < 0.001) when compared with women who had not had bariatric surgery. Obese women with cancer in both of these populations were compared with the Virginia State Cancer Registry average age of cancer diagnosis for the most common cancers identified (Table 3). The obese women with cancer (both with and without bariatric surgery) were younger than the Virginia Cancer registry average age at diagnosis for virtually all cancers.

DISCUSSION

The results of this study demonstrated that hormonally responsive tumors, specifically gynecologic and breast, are the most prevalent cancers in this population of obese women. These findings are consistent with previous reports on the prevalence of site-specific cancers in obese patients.^{1,4-11} The most frequent cancer in our bariatric surgery population was breast (28.3%), followed by endometrial (17%), and this was mirrored in our control group, in which the most common cancers were endometrial (62.3%), breast (9.4%), and ovarian (9.9%). Two notable findings were the strikingly young age of the endometrial cancer patients with bariatric surgery (mean age, 35.3 years), and the exceedingly high BMI of those same patients (mean BMI,

Table 2. Sites of Cancer in 53 Bariatric Surgery Patients

Site	n	Age, y (SD)*	BMI, kg/m ² (SD) [†]	Time of diagnosis in relation to bariatric surgery [‡]
Gynecologic	20	33.8 (9.1)	55.1 (11.2)	17 pre, 3 post
Endometrium	9	35.3 (5.8)	60.1 (6.4)	8 pre, 1 post
Cervix	6	32.5 (9.2)	53.9 (12.9)	5 pre, 1 post
Vulva	3	27.6 (3.1)	46.7 (4)	3 pre
Ovary	2	39.5 (26.1)	49.2 (2.6)	1 pre, 1 post
Breast	15	46 (5.6)	51.1 (11.2)	7 pre, 8 post
Melanoma	4	44.3 (11)	50.4 (11.8)	2 pre, 2 post
Skin, other	3	37.5 (3.5)	43 (6.2)	1 pre, 1 post, 1 unknown
Cranial meninges	2	43 (24)	50.8 (5.4)	1 pre, 1 work-up
Colorectal	2	44 (1.4)	52.5 (19)	1 pre, 1 post
Thyroid	2	25 (17)	46 (2.8)	2 pre
Parotid gland	1	34	55	1 pre
Kidney	1	46	60	1 pre
Craniopharyngeal duct	1	42	55	1 post
Spinal cord	1	47	49	1 pre
Unknown primary	1	45	57	1 post

*Mean age at time of cancer diagnosis.

[†]Mean BMI at time of bariatric surgery.

[‡]Cancer diagnosis made either pre (before bariatric surgery was performed) or post (after bariatric procedure), or work-up (during the preoperative work-up). BMI, body mass index.

60.1 kg/m²). This younger age may reflect an age migration secondary to the impact of obesity or may be a surrogate marker for a dose response for obesity given the average BMI of 60 kg/m². Compared with either our control population of morbidly obese women or the Virginia Cancer State Registry, the average age of endometrial cancer diagnosis in bariatric surgery patients was still 20 years younger (35 years versus 58 years versus 63 years, respectively). Studies in the 1970s report only 2% to 3% of endometrial cancers in women younger than 40 years of age.^{16,17} But

another recent report from Kentucky found that although the mean age of women diagnosed with endometrial cancer was 63 years, the percentage of women under 40 years was now 5.6%.¹⁸ Taken together, these data underscore the importance of heightened awareness of the potential for cancer in young obese women, especially those women undergoing bariatric surgery because they may have the most profound risk.

Obesity results in a profound change in the hormonal milieu, with effects on circulating peptide and steroid hor-

Table 3. Comparison of Ages at Cancer Diagnosis in Different Populations

Selected cancer sites	UVA bariatric surgery population* (n = 53), mean age at diagnosis, y	UVA morbidly obese control population [†] (n = 203), mean age at diagnosis, y	Virginia Cancer Registry, [‡] mean age at diagnosis, y
Gynecologic			
Endometrium	35.3	57.9	62.6
Cervix	32.5	46.8	49.8
Vulva	27.6	62.8	58.3
Ovary	39.5	51.0	61.9
Breast	46	57.3	60.2
Melanoma	44.3	None diagnosed	57.2
Colorectal	44	55.0	68.6
Thyroid	25	53.2	47.4
All cancers	39.4	56.8	N/A

*Derived from 1,482 women undergoing bariatric surgery who were diagnosed with cancer.

[†]Derived from 3,495 women diagnosed with morbid obesity at UVA between 2001 and 2006 who were also diagnosed with cancer.

[‡]Average age of diagnosis from Virginia Cancer registry from 2001 to 2005, accessed May 2008.

UVA, University of Virginia.

mones and their binding factors, and these changes may be partially corrected with weight loss. Obese patients have increased estrogen levels because of conversion of circulating androgens by increased aromatase activity in peripheral adipocytes. Also, there is an increase in adrenal and ovarian secretion of hormones and decreased progesterone production because of decreased ovulation. Increasing BMI also results in a linear increase in circulating levels of insulin, which causes chronic hyperinsulinemia and subsequent inhibition of hepatic synthesis of sex hormone-binding globulin. With a decrease in the production of sex hormone-binding globulin there is an increase in free steroid hormone levels. Overall, there is an increase in unopposed estrogen that can promote cancer in hormonally responsive tissue.^{10,11}

Patients who achieve weight loss from bariatric surgery have demonstrated improvements in a variety of metabolic conditions such as hypertriglyceridemia, low levels of high-density lipoprotein (HDL), elevated cholesterol, and type 2 diabetes.¹⁹ Adams and colleagues²⁰ reported that bariatric surgery patients had a 40% decrease in longterm mortality from any cause, and a 60% decrease in longterm mortality from cancer. But the prevalence of cancer in the postbariatric surgery patient population was not reported and it is unknown if metabolic changes related to weight loss resulted in lower rates of cancer development, or if having a lower BMI resulted in earlier diagnosis or improved treatment outcomes. Our finding that one-third of our patients were diagnosed with cancer after their bariatric surgery, and presumed metabolic improvements, points to the need for continued and careful screening of this patient population to ensure early tumor detection. Although not conclusive, the fact that most of our women with bariatric surgery were diagnosed before their operation and the fact that fewer bariatric patients were diagnosed with cancer compared with their obese counterparts may lend support to the hypothesis that bariatric surgery could be protective for obesity-related cancers.

Certain limitations are present in this study. We were unable to obtain BMI and weight of patients at the time of their cancer diagnosis, so we do not know if the patients were obese when they were diagnosed with cancer. Additionally we do not have information about weight loss after operation, so it was not possible to examine the impact that weight loss may have had on reducing the prevalence of cancer. Finally, we obtained cancer diagnosis information only from Virginia-based cancer registries and the medical records at our institution. It is possible that patients were treated for cancer in different states, and we were unable to access that information.

This study highlights the fact that morbid obesity places women at risk for cancer and those cancers may occur at earlier ages. Physicians may want to consider increasing their index of suspicion for cancers in their morbidly obese patients. Breast and endometrial cancers remain the most common types in obese women and may occur at young ages; bariatric surgery may decrease cancer development in obese women. This supports previous findings of hormone dependent tumors in obese patients and illustrates the continued need for information about the effects of metabolic alterations and weight loss on the development of obesity-related cancers.

Author Contributions

Study conception and design: Modesitt
 Acquisition of data: McCawley, Ferriss, Geffel, Northup
 Analysis and interpretation of data: Modesitt, McCawley
 Drafting of manuscript: McCawley, Modesitt
 Critical revision: McCawley, Ferriss, Geffel, Northup, Modesitt

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