SURGERY FOR OBESITY AND RELATED DISEASES

Surgery for Obesity and Related Diseases 16 (2020) 713–724

ASMBS Guidelines/Statements

ASMBS position statement on the relationship between obesity and cancer, and the role of bariatric surgery: risk, timing of treatment, effects on disease biology, and qualification for surgery

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Received 13 March 2020; accepted 16 March 2020

Preamble

The following position statement is issued by the American Society for Metabolic and Bariatric Surgery in response to numerous inquiries made to the Society by patients, physicians, Society members, hospitals, health insurance payors, the media, and others, regarding the relationship between obesity and cancer. This includes the increased incidence of cancer in patients with obesity, how obesity can impact conventional cancer screening, recommended cancer screening before bariatric surgery, the beneficial impact of weight loss not only on future cancer risk but on prolonged survivorship after cancer treatment, the timing of cancer treatment related to bariatric treatment in specific patients, and whether patients with active cancers may, in fact, be considered for bariatric surgery despite older guidelines to the contrary. This statement will also discuss ethical issues related to patients who decline cancer screening before bariatric surgery. In this statement, a summary of current, published, peer-reviewed scientific evidence, and expert opinion is presented. The intent of issuing such a statement is to provide available objective information about these topics. The statement is not intended as, and should not be construed as, stating or establishing a local, regional, or national standard of care. The statement will be revised in the future as additional evidence becomes available.

Increased fat mass—particularly visceral fat—has been associated with an elevated incidence of a number of malignancies including cancers of the breast, endometrium, cervix, prostate, thyroid, stomach, liver, kidney, pancreas, gallbladder, and some ovarian subtypes [1–3]. Overweight and obesity are also found to be associated with esophageal adenocarcinoma, colon and rectal cancer, multiple myeloma, non-Hodgkin's lymphoma, and more recently melanoma [2,3]. GLOBOCAN, a comprehensive cancer surveillance database managed by the International Association of Cancer Registries, estimated in 2012 approximately 28,000 (3.5%) new cases of cancer in men and 72,000 (9.5%) in women were because of obesity as identified by elevated body mass index (BMI) [4]. This incidence

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https://doi.org/10.1016/j.soard.2020.03.019
1550-7289/

varied by cancer type, but elevated weight contributed to as many as 44% of esophageal cancers in men and 54% of gallbladder cancers in women. A large prospective cohort study of >500,000 U.S. adults estimated that overweight and obesity contributed to 14% of all cancer deaths in men and 20% in women [5].

Of further concern is the finding that several cancers traditionally found in patients >50 years of age are now being diagnosed with increasing frequency in younger age groups. This includes breast, colorectal, kidney, endometrial, thyroid, liver, gastric, meningioma, ovarian, and esophageal adenocarcinoma [6]. Obesity promotes the development of cancer through multiple mechanisms, including proinflammatory cytokines, elevated amounts of reactive oxygen species and growth factors, increased conversion of androgens to estrogens, reduced growth-controlling adipokines, changes in gut microbiota with an increase in tumor-promoting species, as well as mechanical effects, such as gastroesophageal reflux, which may increase risk for esophageal adenocarcinoma. It is likely the shift of other malignancies to younger populations will continue in the future as obesity continues to increase [6].

An analysis of population-based cancer registries in the United States from 1995 to 2014, examining 14,672,409 cancer cases, showed the incidence of 6 obesity-related cancers (multiple myeloma, colorectal, endometrial, gallbladder, kidney, and pancreas) increased significantly in young adults (25–49 yr), with a steeper rise in successively younger generations. While the incidence of some cancers (including smoking- and HIV-associated cancers) is decreasing in younger patients, the dramatic rise in the prevalence of overweight and obesity in young adults is expected to negate these gains and increase the future burden of cancer overall [7].

In a study from Canada, where the average reported wait time from referral of a patient with obesity to bariatric surgery was 5.2 years [8], the most common cause of death in patients awaiting bariatric surgery was cancer, and the mortality rate in this wait-listed group was 1.57%; 3 times higher than the nationally reported rate of .49% in the general population at the time [9].

It is clear from these, and many other studies, there is a relationship between overweight and obesity, and certain forms of cancer. All the biological mechanisms for this relationship are still under intense study. As background for this position statement, we will examine the complex clinical interrelationship between obesity and cancer, including the impact on screening and treatment, weight loss through bariatric surgery, and its effects on cancer prevalence and outcomes, the timing of bariatric versus cancer surgery, and other related questions.

Effect of obesity on cancer screening

Cancer is a major health problem and one of the leading causes of mortality, accounting for up to 25% of deaths in the United States [10]. The early detection of presymptomatic cancer through screening is a key step in reducing cancer-associated morbidity and mortality. However, obesity may decrease the frequency and quality of cancer screening, and may therefore contribute to increased cancer-related mortality in patients with obesity. Although individuals with obesity may have frequent medical visits for obesity-related co-morbidities, healthcare providers, including bariatric surgeons, should not assume these individuals are obtaining appropriate cancer screening, as this population may face challenges that reduce the occurrence of such screening.

Breast cancer

A history of having undergone bariatric surgery has been found to be associated with decreased incidence of breast cancer and its associated mortality [11–14]. On the other hand, women with obesity are at higher risk for morbidity and mortality from postmenopausal breast cancer but are less likely to undergo screening mammography. In a systematic review of studies examining the relationship between weight and mammography, Maruthur et al. [15] found increasing weight was related to lower likelihood of undergoing mammography consistently across the studies. Women with a BMI $\geq$40 kg/m^2 were significantly less likely than those of lower BMI (combined odds ratio [OR] = .79, 95% confidence interval [CI]: .068–.92) to have undergone mammography in the prior 2 years. This relationship appeared stronger in white women. A lower screening rate may partly account for increased breast cancer mortality in women with severe obesity [16].

In a study designed to identify patient barriers to mammography, Feldstein et al. [17] found obesity was associated with lower mammogram completion rates (OR = .67, $P < .0001$). Of note, women with obesity in this cohort were much more likely to report "too much pain" from mammograms [17]. Obesity and breast density may also impact the sensitivity and specificity of mammography. In an analysis of 100,622 screening mammograms, the risk of false-positive results was increased by 20% in women with obesity compared with underweight or healthy weight women. The authors concluded that weight loss may improve the tolerance for and accuracy of mammography [18].

Cervical cancer

As with breast cancer, women with obesity undergo screening for cervical cancer less frequently. Most studies on cervical cancer screening found a negative association between increasing weight and screening, and this negative association was again most consistent in white women [16,19]. Data from the National Cancer Institute's 2005 Health Information National Trends Survey showed women aged 25 to 64 years with obesity were significantly less likely to adhere to recommended cervical cancer screening guidelines (OR = .3 for class III obesity, 95%CI: .15–.59) [20]. In a meta-analysis of studies evaluating the relationship between weight and Papanicolaou testing in the United States, Maruthur et al. [21] reported an inverse relationship between cervical cancer screening and obesity. Compared with women with a healthy BMI, the combined OR for Papanicolaou testing was .75 (95%CI: .64–.88) for class III obesity. In this systematic review, 3 of 4 studies that considered race as a factor found this inverse relationship held true for white women, but no study found this for black women. The authors concluded lower screening rates may partly explain the higher cervical cancer mortality in white women with obesity [21].

Colorectal cancer

Obesity also increases the risk for colorectal cancer (CRC) and may have a negative impact on CRC screening. The relationship between weight and CRC screening in men is inconsistent, while there is a trend toward lower CRC screening in women of higher weight [22]. The data for 8550 respondents aged 50 to 75 years in the 2010 National Health Interview Survey showed men with a BMI ≥40 kg/m^2 were significantly less likely to adhere to screening guidelines compared with men of healthy weight (adjusted OR = .35, 95%CI: .17–.75); were less likely to have had an endoscopic examination (adjusted OR = .37, 95% CI: .18–.79); and had a trend toward lower fecal occult blood test use (adjusted OR = .42, 95% CI: .14–1.27) [23]. Men with obesity were more likely to state "lack of physician recommendation" as a reason for nonadherence to screening (29.7% obese class III versus 15.4% nonobese, P = .04). The odds of adherence and use of different screening modalities for women were similar across all BMIs, yet for nonadherent women, more women with class III obesity reported "pain" and "embarrassment" as the reasons for nonadherence to screening compared to women of healthy weight (11.6% versus 2.6%, P = .002) [22]. When patients are screened, adenomatous polyps are detected at a higher rate as BMI increases [23].

Ferrante et al. [24] reviewed the rate of CRC screening in 22 suburban primary care practices. Among 1297 patients age ≥50 years, 39% of patients had obesity and 29% received CRC screening. After controlling for age, sex, total number of co-morbidities, number of visits in the past 2 years, and number of years in the practice, patients with obesity had 25% lower odds of being screened for CRC compared with patients without obesity (OR = .75, 95% CI: .62–.91, P = .004). The relationship between obesity and CRC screening was similar for men and women [24]. Using the Centers for Disease Control Behavioral Risk Factor Surveillance System, Rosen and Schneider [25] examined the rates of self-reported CRC screening with fecal occult blood testing within the past year or endoscopic screening (sigmoidoscopy or colonoscopy) within the past 5 years among 52,886 respondents. After statistical adjustment for potential confounders, women with severe obesity were less likely than women of healthy weight to undergo CRC screening (adjusted rate difference −5.6%; 95% CI: −8.5 to −2.6). Screening rates for men in different weight groups did not differ significantly [25].

Endometrial cancer

Obesity is very strongly associated with the development of endometrial cancer, in a dose-response relationship with BMI. Approximately 57% of endometrial cancers in the United States are thought to be attributable to overweight and obesity [26]. Given the adverse effect of obesity on the prevalence and mortality of cervical and other cancers, it is important to emphasize screening efforts, particularly for women. Bariatric treatment programs, with a mostly female patient population, could be in a position to recommend appropriate screening in selected patients before their undertaking elective surgery. In a survey sent to 1503 U.S. bariatric surgeons, 80% of the 263 respondents obtained gynecologic histories, but 56% and 49% did not require Papanicolaou testing or mammograms, respectively, before bariatric surgery. Only 21% of respondents had ever referred a patient for endometrial evaluation, and 20% of surgeons did not consistently counsel their patients about increased cancer risks due to obesity [27]. Bariatric surgeons correctly identified postmenopausal bleeding (99%), obesity (97%), irregular or heavy periods (69%), hereditary nonpolyposis colorectal cancer (21%), infertility (20.2%), diabetes (14.1%), and hypertension (4.9%) as signs and risk factors of endometrial cancer [27].

Prostate cancer

Obesity may be associated with reduced risk of low-grade nonaggressive prostate cancer but increased risk for more aggressive disease [28] and there is emerging evidence of periprostatic white adipose tissue inflammation as a driver of higher Gleason Score [29]. Interestingly, studies suggest men with obesity are more likely than individuals of healthy weight to undergo prostate-specific antigen testing [30,31]; it is not clear if this is related to a decreased likelihood of having had an actual prostate examination. Using the 2001 Centers for Disease Control Behavioral Risk Factor Surveillance System data for men aged ≥50 years, Fontaine et al. [32] reported that obesity was associated with increased OR for obtaining prostate-specific antigen test (class I obesity OR = 1.26, 95%CI: 1.06–1.36; and class II obesity OR = 1.14, 95%CI: 1.02–1.26) after adjusting for age, race, smoking, education, employment, income, and health insurance status [32].

Impact of obesity, bariatric surgery, and weight loss on cancer prognosis and recurrence

Weight loss in persons with obesity reduces cancer risk. Multiple studies have shown bariatric surgery results in a significant decrease in cancer risk and cancer mortality in patients with obesity, notably in women [33–37], leading some authors to suggest treating metabolic dysfunction may be the next frontier in cancer prevention [38]. The reduction in the incidence of cancer after bariatric surgery was found to be related to the weight loss itself and not to the effect of simply having undergone surgery. In a recent study, Schauer et al. [39] found, "in adjusted models, the association between bariatric surgery and cancer risk was explained by weight loss and was not independently associated with surgery."

Baseline obesity has been linked to poor prognosis in breast cancer patients [40]. Furthermore, weight gain after initial cancer treatment has been associated with disease recurrence and cancer death in several types of cancer, such as breast [41], prostate [42], and CRC [43]. However, prior bariatric surgery has also been shown to improve the outcomes of CRC patients in the perioperative period [44].

Winder et al. [45] concluded bariatric surgery results in a decrease in the incidence of endometrial cancer. Linkov et al. [46] have also shown bariatric surgery can result in changes in hormone receptor markers on endometrial cells, which could become the target of novel therapies for endometrial cancer.

It is important to distinguish the impact of intentional versus unintentional weight loss on cancer survivorship when assessing the literature. Intentional weight loss in the general population is linked to increased survival while unintentional weight loss has been associated with decreased survival. Most studies assessing weight loss in cancer survivors have been conducted in breast cancer patients. A systematic review [47] assessing the effect of weight loss in breast cancer survivors managed to identify only 5 observational studies, all with lower-level evidence, but all of which suggested significant weight loss or gain after treatment could lead to an increased risk of death [48–52]. None of the included studies limited their study sample to posttreatment breast cancer survivors nor did they differentiate between the stages of disease or intentional versus unintentional weight change; unfortunately, this makes drawing robust conclusions difficult and the authors suggest only attempts to maintain stable weight may improve survival in cancer patients.

The following are ongoing trials assessing the effect of intentional weight loss on cancer survival and recurrence, again mainly in breast cancer patients: the Moving Forward trial [53] (United States), the ENERGY trial [54] (North America), the BWEL trial [55] (North America), the SUCCESS-C trial [56] (Germany), and the DIANA-5 trial [57] (Italy). These studies are all based on lifestyle intervention, with specific diets and physical activity regimens prescribed to recruited patients. Although the hormonal and antiinflammatory benefits of weight loss in cancer patients have been demonstrated in bench research, it will take time to show these benefits clinically because of the longitudinal nature of the studies required.

As 38.4% of individuals in the United States will be diagnosed with cancer in their lifetime, it is not uncommon for patients who are seeking bariatric surgery to have undergone prior cancer treatments [58]. Bariatric surgery has been shown to result in overall improvement of diet, lifestyle, co-morbidities, and quality of life. In addition, there is evidence to suggest cancer is associated with a worse prognosis in patients with severe obesity. There are no data to suggest cancer patients who undergo bariatric surgery have a better or worse prognosis as it relates to disease-specific or overall survival. Nevertheless, the American Society of Clinical Oncology position statement on cancer and obesity recommends a comprehensive approach to help cancer survivors adopt healthy lifestyle changes and improve access to weight loss services, including bariatric surgery [59].

Timing of bariatric surgery in relation to cancer screening

Cancer is known to involve genetic change, in the form of DNA mutations. Most cancers are acquired and not directly inherited, and as such, can be influenced by potentially modifiable environmental factors, such as obesity. The timing of bariatric surgery in eligible patients who are cancer-free, who currently have cancer, or who have already undergone cancer treatment and are considered to be in remission, warrants discussion. Bariatric surgery has well-established benefits in terms of significant and sustained weight loss and improvements in co-morbidities and quality of life. Emerging evidence shows weight loss after bariatric surgery to be associated with decreased risk of cancer [33–37,43,47]. As the evidence of association between obesity and cancer expands, bariatric surgery should be discussed with patients as a means to modify and manage cancer risk.

A substantial percentage of patients seeking weight loss surgery are at an age where they are candidates for cancer screening, such as for breast, endometrial, and CRC. Some patients will decline such screening at the time of seeking bariatric surgery. While those diagnosed with cancer often proceed to have their cancer treated first, others, for personal reasons, may wish to proceed with bariatric surgery and have their cancer treated later; this presents a unique discussion and informed consent challenge.

In certain circumstances, weight loss may theoretically decrease the risks associated with a subsequent cancer operation, depending on the nature and location of the cancer, the necessary access, and the extent of resection and required reconstruction. In some situations, surgeons and patients may therefore want to consider bariatric surgery first. Prior bariatric surgery has been related to improved postoperative outcomes in CRC patients [11,43]. In other circumstances, cancer may be identified intraoperatively during bariatric surgery, and this may change the surgical plan. As noted earlier, there is little long-term prognostic data on disease-free or overall survival of cancer patients after bariatric surgery. Screening or surveillance methods and treatment approaches for cancer after bariatric surgery may differ depending on the type of cancer and the type of bariatric procedure that was performed; this would be the case, for example, in evaluation for gastric cancer in Roux-en-Y gastric bypass (RYGB) patients.

Therefore, even with studies showing that bariatric surgery-associated weight loss can result in notable decreases in cancer risk and mortality, the timing of bariatric surgery, in relation to cancer screening efforts, remains an important clinical consideration. Patient-centered values must be considered, and detailed counseling needs to be conducted as a starting point for management. Guidelines for cancer screening for patients of average risk are available and presented here (see Appendix) and bariatric surgery visits offer the opportunity to counsel patients on the elevated risk of malignancy associated with obesity and the importance of screening and treatment timing. This is an important practice for bariatric surgeons to consider; a recent study showed only 66% of surveyed bariatric surgeons reported engaging in counseling for obesity-related cancer risk and prevention [26]. Yet, cancer screening typically falls in the domain of primary care providers, rather than surgical specialists, such as bariatric surgeons, and it is not clear that this additional burden should fall on the shoulders of bariatric surgeons.

An algorithm to help guide primary care practitioners and bariatric surgeons in approaching cancer screening, surveillance, or treatment timing in patients with clinically severe obesity is outlined in Fig. 1.

Specific examples of cancer screening implications for bariatric surgery procedures

Breast cancer

Risk- and age-appropriate breast cancer screening is recommended both before and/or after bariatric surgery. As mentioned previously, weight loss after bariatric surgery may aid in the earlier detection of breast cancer by self-examination or mammography. In addition, lower radiation doses are reported to be needed for mammography after bariatric surgery [60].

In the setting of diagnosed breast cancer before bariatric surgery, treatment of the cancer first is generally recommended and may include adjuvant therapies that can be completed before weight loss surgery is undertaken, allowing time for wound healing and the ability to meet nutritional needs during the cancer treatment phase. Bariatric surgery patients may be asked to defer breast reconstructive surgery until after their weight loss. Patients with obesity who undergo breast reconstruction (whether by autologous tissue or implant) tend to develop more complications than do patients after weight loss. Additionally, weight loss provides patients with other reconstructive options, such as vascularized flaps with reduced risk [14].

Another therapeutic consideration relating to breast cancer treatment revolves around the use and absorption of hormonal and other chemotherapeutic agents. Bariatric procedures, especially those where segments of the intestine are bypassed, alter drug pharmacokinetics. There have been reports of tamoxifen malabsorption after RYGB and the need to measure serum drug levels to better guide treatment [61]. Treating a bariatric patient who has altered drug absorption may pose a challenge to the oncologist, and parenteral anticancer therapies may need to be considered in the presence of malabsorption. Communication between the bariatric and oncology teams is recommended to enhance understanding of the type of bariatric procedure and its potential challenges for the oncology treatment team.

Upper gastrointestinal cancer

Routine use of preoperative upper gastrointestinal (UGI) endoscopy before bariatric surgery is not uniformly practiced, but some authors have recommended it to evaluate the esophagus and stomach and assess for the presence of preoperative Barrett's esophagus (BE) or other abnormalities [62]. Obesity, gastroesophageal reflux disease and BE are identified risk factors for UGI malignancies, commonly lower esophageal cancers [63,64]. Vague UGI symptoms after bariatric surgery, such as nausea, dysphagia, or reflux, may cause delayed cancer diagnosis, as these can be common postbariatric surgery complaints; this can result in more advanced tumors at the time of diagnosis [65]. Periodic endoscopic surveillance in patients with known BE and early evaluation in patients who develop new symptoms, such as upper abdominal pain, dysphagia, reflux, or anemia, after bariatric surgery are also strongly encouraged [66].

A diagnosis of esophageal adenocarcinoma is a contraindication to proceeding with bariatric surgery [67]. Diagnosis of esophageal and GE junction adenocarcinoma after bariatric surgery presents a challenging management scenario and requires close collaboration between the surgical oncologist and the bariatric surgeon. One center presented 9 cases where esophageal cancer developed after bariatric surgery. The mean age was approximately 60 years, and 60% of cases were stage 3 or 4 at the time of diagnosis. Only 50% had a symptomatic presentation, and 50% had concurrent BE. Three of 4 cases found to have incidental BE had a localized disease that was well treated with endoscopic resection or esophagectomy. The rest had a more unfortunate course [68].

Surgical management of an UGI cancer poses particular challenges because of anatomic alterations after bariatric surgery. After sleeve gastrectomy (SG), it is impossible to use the stomach for reconstruction after esophagectomy. In such circumstances, an esophagojejunostomy or colon interposition is necessary, likely increasing postoperative

1. Patients not seeking bariatric surgery

A. Screening-eligible patients

i. Do not want screening

a. Establish appropriate informed consent and document refusal of screening

b. Refer to primary care physician/specialists to further discuss screening

c. Counsel on benefits of bariatric surgery if indicated

ii. Screening negative

a. Discuss appropriate surveillance and offer weight loss counseling

b. Consider bariatric surgery

iii. Screening positive

a. Discuss timing of cancer therapy in relation to bariatric surgery if patient is interested in the latter (see 1.B. below)

B. Patients diagnosed with cancer

iv. Do not want cancer therapy

a. Counsel on the role of cancer-specific therapy and document refusal

b. Refer to primary care physician/specialists for further evaluation and counselling

c. Consider if there is a role for bariatric surgery

v. Discuss timing of cancer therapy

a. Determine need for neoadjuvant or adjuvant therapies

b. Determine timing of surgical cancer therapy and how it may affect future bariatric options and surveillance

2. Patients seeking bariatric surgery

A. No prior cancer diagnosis

i. See considerations in section 1.A. above

B. Diagnosed with cancer

i. During work-up

a. See considerations in section 1.B. above

ii. Intraoperative incidental finding

a. Consider type of cancer and develop appropriate cancer-specific plan, with intraoperative oncologic consultation. Options:

i. i. Abort bariatric procedure

ii. ii. Surgical cancer therapy first with adjuvant therapy to follow (Informed consent considerations)

iii. iii. Continue bariatric procedure as planned, with concurrent or delayed cancer therapy

iii. Previously diagnosed cancer

a. Not yet treated

i. i. See considerations in section 1.B. above

Fig. 1. Outline of cancer screening considerations in patients with clinically severe obesity.

b. Treated

i. i. Patient undergoing current therapy

ii. ii. Patient in remission

a. Consider surveillance when selecting bariatric procedure

iii. iii. Patient has recurrence

a. Identify goals of cancer treatment and/or bariatric options

3. Cancer after bariatric surgery

A. Considerations relating to screening or surveillance approaches

B. Considerations relating to the changed anatomy:

i. Reconstructive options

ii. Risks of adjuvant therapy and GI side effect

iii. Changes in pharmacokinetics

Fig. 1. (*continued*).

morbidity [65]. In cases of esophageal cancer after prior RYGB, experienced surgeons advise a close collaboration between bariatric and cancer surgeons to address a technically nuanced complex procedure for cancer resection and reconstruction [69].

Gastrointestinal stromal tumors (GIST) can be found incidentally and can often be treated concurrently with complete resection during bariatric procedures, particularly with SG. One study found incidental pathologic lesions identified in 2% of patients at the time of bariatric procedures, with GIST accounting for almost one quarter of these [70]. Curative resection with negative margins is the recommended therapy for localized gastric GIST, with >5-year survival in large case series [71]. In the performance of RYGB, it is foreseeable that GIST could be missed; attention to UGI symptoms helps with evaluation and detection.

Development of gastric cancer has been only rarely described after bariatric procedures. Identification of *Helicobacter pylori* and treatment of this infection are particularly advised as a preventive measure when one is considering performing RYGB. However, the mean time from bariatric surgery to the finding of gastric carcinoma in case reports averaged 8.2 years, and there is no good evidence relating bariatric surgery to the development of gastric adenocarcinoma. As such, there are currently no postoperative screening guidelines for gastric cancer after bariatric surgery [72].

Hepatocellular cancer

Fatty liver disease is defined as a triglyceride content amounting to >5% of the organ's weight [73]. Nonalcoholic fatty liver disease and its sequela, nonalcoholic steatohepatitis, are increasingly recognized risk factors for development of gastrointestinal cancers, particularly of the liver. The dysfunction of excess visceral adipose tissue leads to impaired production of adipocytokines. This, in turn, favors an increase in proinflammatory cytokines and a decrease in antiinflammatory cytokines. An overall proinflammatory state creates an environment conducive to neoplastic growth. The associated increase in insulin resistance can also contribute to cancer development. Bariatric surgery can reverse the pathologic liver changes found in patients with nonalcoholic steatohepatitis and nonalcoholic fatty liver disease [74]. It can also be safely performed in patients with early-stage or well-compensated cirrhosis, although data supporting this have only been found in cohort studies [75]. The Nationwide Inpatient Sample (1998–2007) showed bariatric surgical mortality in patients with compensated cirrhosis was .9%, while in patients whose cirrhosis was decompensated, it was as high as 16.3% [76]. There are no current reports recommending bariatric surgery as a first step in treatment of known hepatocellular carcinoma.

Thyroid cancer

There is an association between increasing obesity and increased risk of papillary thyroid cancer [77]. Bariatric patients who have undergone a malabsorptive operation and who later require total thyroidectomy are at additional risk for hypocalcemia. For example, RYGB has been identified as a risk factor for postoperative hypocalcemia after thyroidectomy and such management can be challenging [78,79]. Compared with patients without prior weight loss surgery, postthyroidectomy hypocalcemia in bariatric surgery patients tends to be delayed and severe, resulting in greater odds of hospitalization. There is a 2-fold risk of hypocalcemia after RYGB compared with either SG or adjustable gastric banding [79]. Hypocalcemia in general can be difficult to treat because of the relatively poor absorption of oral supplements after RYGB. Careful monitoring of such patients is recommended.

Pancreatic cancer

Pancreatic cancer is also an obesity-associated malignancy. There is no described role for bariatric surgery in the treatment plan of recently diagnosed pancreatic cancer. However, there are case reports of patients undergoing various modifications of the Whipple procedure for pancreatic cancer diagnosed after RYGB or SG. The technical challenges involved in these procedures require close collaboration between the surgical oncologist and a bariatric surgeon to assure complete resection along with appropriate reconstruction [80–83].

Renal cell carcinoma

Obesity is a significant risk factor for renal cell carcinoma, with a 2.5 and 3.3 relative risk for men and women, respectively [84]. The prevalence of renal cell carcinoma in postbariatric surgery patients is currently unknown, but the risk appears to remain higher than in the general population [85]. Therefore, preoperative screening and postoperative surveillance of bariatric patients are worthy of consideration.

Timing of bariatric surgery in patients with concurrent cancer

Many of the improvements in morbidity and mortality related to obesity after bariatric surgery are also seen in cancer patients, and weight loss may reduce risks inherent to cancer treatments and improve diagnostic efforts; as such, concurrent cancer may not be an absolute contraindication to bariatric surgery [86]. Adams et al. [87] have found that bariatric surgery can lead to approximately a 60% decrease in long-term mortality from cancer and a 24% reduced risk of cancer in RYGB patients compared with control patients with obesity. In addition, bariatric surgery in cancer patients may decrease the risk of development of second primary malignancies and of noncancer-related death from cardiovascular disease and diabetes [86].

The optimal timing of bariatric surgery in individuals diagnosed with both cancer and obesity has not been fully elucidated, and several factors must be included in the decision-making process. The type and stage of the malignancy, risk of recurrence, life expectancy, and appropriate screening to rule out recurrence are ideally considered in a multidisciplinary approach in patients with a history of malignancy before proceeding with bariatric surgery [86]. Depending on the natural history of a given cancer type, patients with a personal history of cancer need not be routinely required to demonstrate 5 years of disease-free survival before undergoing bariatric surgery [88].

Summary and recommendations

1. Obesity increases the risk for development of many types of cancer, and successful treatment of obesity by various methods, including bariatric surgery, can mitigate this risk.
2. Patients with obesity may be less likely to undergo cancer screening than leaner individuals.
3. The primary care system often performs suboptimally regarding routine health maintenance issues, like cancer screening in patients with obesity. As a result, bariatric treatment programs may be in a good position to encourage such patients to undergo recommended health screening.
4. A diagnosis of past, recently treated, or concurrent cancer may not be an absolute contraindication to undergoing bariatric surgery, and demonstration of 5-year, disease-free survival is often not necessary.
5. The influence of various bariatric procedures on cancer risk, screening, management, and surveillance in both the short- and long-term are important areas for preoperative consideration and patient counselling.

6. The decision to refuse or delay cancer screening is a personal healthcare choice and therefore a patient's refusal to undergo recommended health screening should not be used as a sole determinant of whether that patient may undergo bariatric surgery.
7. Further research is needed to evaluate the effects of bariatric surgery on survival in cancer patients.

Cancer and bariatric surgery position statement and standard of care

This Position Statement is neither intended to provide inflexible rules or requirements of practice and is not intended, nor should it be used, to state or establish a local, regional, or national legal standard of care. Ultimately, there are various appropriate treatment modalities for each patient, and the surgeon must use his or her judgment in selecting from among the different feasible options. The American Society for Metabolic and Bariatric Surgery cautions against the use of this Statement in litigation in which the clinical decisions of a physician are called into question. The ultimate judgment regarding appropriateness of any specific procedure or course of action must be made by the physician in light of all the circumstances presented. Thus, an approach that differs from this Statement, standing alone, does not necessarily imply the approach was below the standard of care. To the contrary, a conscientious physician may responsibly adopt a course of action different from that set forth in the Statement when, in the reasonable judgment of the physician, such course of action is indicated by the condition of the patient, limitations on available resources, or advances in knowledge or technology. All that should be expected is that the physician will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of this Position Statement was to assist practitioners in achieving this objective.

Disclosures

The authors have no commercial associations that might be a conflict of interest in relation to this article.

Appendix. Cancer Screening Guidelines for Average-Risk Individuals

The following is a synthesis of cancer screening recommendations based on clinical guidelines by the leading medical professional and cancer organizations for average-risk populations.

While a variety of screening tests are available for many types of cancer, the following important factors should be considered in choice of a screening test: the magnitude of the effect in reducing the incidence or mortality from the cancer, evidence for its effectiveness, cost and cost-effectiveness in terms of cost per year of life saved, safety and comfort, availability, and potential harm. The desirable screening strategies should provide high value where the benefits clearly outweigh the harms and cost. Healthcare providers should actively engage patients in informed and shared decision-making about screening options.

Colorectal cancer screening

Screening is recommended in individuals aged 50 to 75 years with 1 of the following strategies [89–94]:

1. Annual high-sensitivity guaiac-based fecal occult blood test on 3 stool samples or fecal immunochemical test (FIT) on a single stool sample. The cost of FIT is higher than guaiac-based tests but is more convenient with better performance and the potential to be more cost-effective as fewer follow-up colonoscopies may be needed.
2. Sigmoidoscopy every 5 years.
3. Computed tomographic colonography every 5 years.
4. Combination of high-sensitivity fecal occult blood test or FIT every 3 years with sigmoidoscopy every 5 years.
5. Colonoscopy every 10 years.

Screening in average-risk adults <50 years or >85 years of age, or those with an estimated life expectancy of <10 years are not recommended. Screening of adults aged 76 to 85 years should be individualized and take into account their health and screening history. In the absence of prior colorectal screening, a 1-time screening colonoscopy for those up to age 83 years or sigmoidoscopy up to age 84 years is reasonable. Individuals at increased risk of colorectal cancer may start screening at an earlier age and/or more frequently.

The U.S. Food and Drug Administration has approved a new FIT-DNA stool test, Cologuard assay (Exact Sciences), for which more comparative effectiveness data are needed.

Breast cancer screening

While a large number of breast cancers are brought to attention by patients, the majority of breast cancers in the United States are diagnosed through screening. Because screening is of greatest value for those most likely to develop breast cancer, it is important to determine the patient's risk of developing breast cancer. Various tools for calculation of breast cancer risk, such as the Gail Model (available at the National Cancer Institute website), are available [95]. Breast cancer risk is very low in those <40 years but increases with age.

Clinical breast exam, while important for evaluation of women with breast complaints or abnormalities, should not be the only screening method, and its adjunct role to mammography is not universally accepted. Some expert groups do not recommend breast self-examination for screening, but as a way to educate women about breast health and raise breast self-awareness. Mammography, digital or film, is the primary breast cancer screening modality in average-risk women. The sensitivity and specificity of mammography are age-dependent and higher in older women [96]. Because of both substantial benefits and risks of harm, such as false-positive results, associated with screening, a full discussion and shared decision-making with the patient is essential. Other techniques, including ultrasound and magnetic resonance imaging, are reserved as adjuncts to screening certain high-risk patients or for further evaluation of findings on mammography [97]. There is near universal agreement regarding screening mammography or discussions about screening at least every 2 years for women aged 40 to 74 years. The American College of Physicians advises the following high-value screening principles [98]:

1. After discussing benefits and harms of screening mammography with average-risk women aged 40 to 49 years, biennial screening mammography should be ordered at the request of an informed woman.
2. Biennial mammography screening in average-risk women aged 50 to 74 years should be encouraged.
3. Average-risk women $<$40 years, or $\geq$75 years of age, and those with a life expectancy $<$10 years should not undergo screening for breast cancer.
4. Average-risk women of any age should not undergo breast cancer screening with magnetic resonance imaging or tomosynthesis.

Cervical cancer screening

Cervical cancer is related to infection with human papillomavirus. Most cervical cancers develop in women who have never been screened or only sporadically. Therefore, cervical cancer screening decreases its incidence and mortality. The following are the screening recommendations [99–101]:

1. Screening of average-risk women $<$21 years or women of any age with a history of hysterectomy with removal of the cervix is unnecessary.
2. Average-risk women aged 21 to 29 years should be screened once every 3 years with Papanicolaou cytology test.
3. Average-risk women aged $\geq$30 years may continue the Pap cytology test every 3 years or use a combination of Pap and human papillomavirus testing once every 5 years.
4. It is reasonable to stop screening average-risk women $>$65 years who have had 3 consecutive negative cytology results or 2 consecutive negative cytology plus human papillomavirus test results within 10 years, with the most recent test done within 5 years.

Prostate cancer screening

Screening through prostate-specific antigen (PSA) can reduce mortality but the absolute risk reduction is very small, and there is concern about the potential benefits of screening versus harm to quality of life from overdiagnosis or treatment complications. Therefore, major societies and expert groups, including American Urologic Association, American College of Physicians, and the U.S. Preventive Services Task Force, strongly recommend discussion of risks and benefits of screening for informed decision-making by the patient, who should clearly state his preference for screening [102–104]. The following are high-value care advice from the American College of Physicians [98]:

1. A discussion about the limited potential benefits and considerable harms of screening using the PSA test with average-risk men aged 50 to 69 years who inquire about PSA-based prostate cancer screening.
2. Screening with the PSA test in average-risk men aged 50 to 69 years only if they express a clear preference for screening after an informed discussion.
3. No PSA test in average-risk men $<$50 years or $>$69 years or those with a life expectancy of $<$10 years.

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