Obesity-Related Cancer in Women: A Clinical Review

Weight loss interventions can reduce risk.

ABSTRACT: There is mounting evidence that obesity is linked to numerous types of cancer that affect both sexes. But the incidence of obesity-related cancers is particularly high among women. Obesity is implicated not only in the development of cancer, but also in cancer recurrence, treatment complications, and poor patient outcomes. Nurses, particularly those caring for women, should be aware of these associations so they may provide effective patient teaching about preventing cancer and mitigating its adverse effects. The author discusses the role of obesity in the development and recurrence of cancer in women; describes weight loss interventions that may reduce cancer risk in overweight or obese patients; and suggests interviewing techniques to help nurses sensitively address the topic of overweight and obesity with their female patients.

Keywords: cancer, obesity, obesity-related cancer, overweight, women

Obesity rates have reached an all-time high in the United States, with the latest National Center for Health Statistics prevalence data showing that 39.8% of U.S. adults are obese—38% of American men and 41.5% of American women.[1] Over the past decade, the role that overweight and obesity play in cancer development, recurrence, and related mortality, particularly among women, has become increasingly clear. A population-based study that examined the relationship between body mass index (BMI) and cancer incidence estimated that, in 2012 in North America, of the cancers newly diagnosed in women, 78,984 (9.4%) were attributable to overweight or obesity, compared with 31,792 (3.5%) of the cancers newly diagnosed in men.[2] Furthermore, gynecologic cancers are among those with the strongest evidence for the association with obesity. (For a depiction of overweight-and-obesity–related cancers, see Figure 1.)

When Han and colleagues conducted an analysis of the Atherosclerosis Risk in Communities cohort study, which included nearly 16,000 American men and women ages 45 through 64, they found that being overweight or obese in young adulthood (ages 18 to 29) and weight gain from young to older adulthood increases cancer risk. Specifically, they determined that a woman's BMI at age 25 appears to raise her risk of developing cancer (particularly endometrial cancer) at a later point, regardless of subsequent weight change, and both BMI at age 25 and weight gain from that point forward are associated with an increased risk of postmenopausal breast cancer.[3] The longer a woman is overweight or obese, the greater her risk of developing an obesity-related cancer, with incidence of postmenopausal breast cancer and endometrial cancer rising (after adjustment for degree of overweight) by 8% and 37%, respectively, for every 10 years in which BMI is 10 units above normal weight.[4] From 1997

to 2014, obesity rates rose more rapidly among adult cancer survivors than among the general population, with the annual increase in obesity prevalence among breast cancer survivors and female colorectal cancer survivors estimated to be 3% and 3.1% higher, respectively, than that of adults without a cancer history.[5] Nurses caring for women of all ages need to be aware of the association between obesity and cancer in order to provide appropriate patient teaching and support.

This article discusses the role of obesity in the development and recurrence of breast, gynecologic, and colorectal cancers in women; describes weight loss interventions that may help overweight or obese patients reduce their cancer risk; and explains interviewing techniques that can help nurses better communicate with female patients about the often sensitive topic of overweight and obesity.

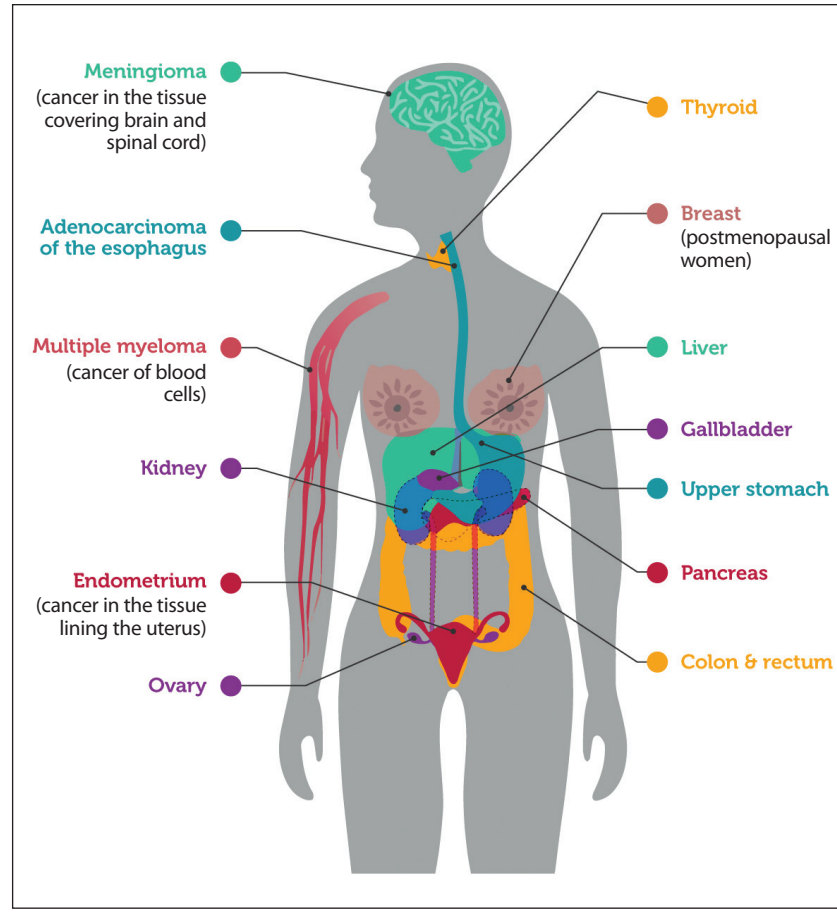

Figure 1. Cancers associated with overweight and obesity. Image courtesy of the National Cancer Institute / Centers for Disease Control and Prevention.

BREAST CANCER

Pathophysiologic links between obesity and breast cancer. Epidemiological data demonstrate a strong, positive correlation between high levels of circulating estrogen and breast cancer in postmenopausal women who do not use postmenopausal hormone therapy. Obese postmenopausal women tend to develop hyperandrogenism and to have increased conversion of androgens to estrogen in adipose tissues. By increasing levels of circulating estrogen, obesity increases cell proliferation, reduces apoptosis, and raises the risk of developing breast cancer.[6] Obesity is also associated with higher levels of circulating and local proinflammatory cytokines, which promote tumor angiogenesis.[7] In addition, the development of breast cancer has been significantly associated with the presence of metabolic syndrome,[8,9] which is defined as the presence of at least three of the following features:

- central obesity
- hypertension
- low levels of high-density lipoprotein cholesterol
- high levels of low-density lipoprotein cholesterol
- high blood glucose levels
- high triglyceride levels

Behavioral factors linking obesity and breast cancer. A Danish study of more than 5,000 women from the Diet, Cancer, and Health Cohort found that obese postmenopausal women were significantly less likely to undergo mammographic screening than women of normal weight, though screening was free of charge.[10] Nonparticipation in such screening could potentially delay breast cancer diagnosis until the disease is advanced and less responsive to treatment. The investigators suggest that this lower rate of participation may be attributable to poorer general health or greater disease burden than that seen in women of normal weight.[10]

Effects of weight on breast cancer prognosis. Central obesity is specifically associated with triple-negative breast cancer (characterized by estrogen receptor–negative, progesterone receptor–negative, and human epidermal growth factor receptor 2–negative tumors), which has a poorer outcome than other types of breast cancer and is more commonly found in African American women.[11]

Women who met the criteria for grade 2 obesity (BMI of 35 to 39 kg/m^2) and grade 3 obesity (BMI of 40 kg/m^2 or higher) were at greater risk for invasive

Motivational Interviewing[60]

- Develop rapport.
- Reframe the issue.
- Ask permission to provide more information.
- Provide new information.
- Ask patients what they think of new information.
- Summarize and discuss next steps.

breast cancer (hazard ratio [HR], 1.58; 95% CI, 1.40–1.79), larger tumor size (HR, 2.12; 95% CI, 1.67–2.69), and lymph node involvement (HR, 1.89; 95% CI, 1.46–2.45) in a secondary analysis of the Women's Health Initiative clinical trials.[12] All are indicators of poor prognosis. But even a weight gain of 15 lbs. in four years has been shown to significantly increase the risk of breast cancer in otherwise healthy premenopausal women.[13]

Risk of breast cancer recurrence and death. A meta-analysis by Chan and colleagues identified 82 studies with a total of 213,075 breast cancer survivors that provided data on BMI before and after diagnosis, as well as total and cause-specific mortality. Their analysis found that, compared with women of normal weight, women who were obese (with a BMI of more than 30 kg/m^2) before diagnosis, within 12 months of diagnosis, and 12 or more months after diagnosis had a 41%, 23%, and 21% higher risk of total mortality and a 35%, 25%, and 68% higher risk of breast cancer mortality, respectively.[14] In a meta-analysis of data from 12 studies with a total of 23,832 women, a weight gain of 5% or more of body weight after breast cancer diagnosis increased risk of death from any cause (HR, 1.12; 95% CI, 1.03–1.22; P = 0.01), and risk was greater when weight gain exceeded 10% of body weight.[15]

Obesity is also associated with breast cancer recurrence after five years, a period of time after which risk of recurrence is generally considered to be substantially reduced.[16] The link between obesity and risk of breast cancer recurrence and death is most clearly established for women with estrogen receptor–positive disease,[17] which suggests that obesity may be so significant to overall health that the harm it causes negates the benefits of many medications, such as endocrine blockers, used to treat women with hormone-sensitive breast cancer.

GYNECOLOGIC CANCERS

Endometrial cancer. Obesity and overweight increase both a woman's lifetime risk of developing endometrial cancer and her risk of developing it earlier in life.[18] The increased risk is associated not only with adult obesity but also with childhood and adolescent obesity.[19] High BMI at age 18 is associated with a nearly 30% increased risk of developing endometrial cancer (hazard rate ratio [HRR], 1.29; 95% CI, 1.12–1.49) for each five-unit increase in BMI, and adult weight gain raises the risk by more than 80% (HRR, 1.81; 95% CI, 1.66–1.98) per five-unit increase in BMI.[20]

Treatment for endometrial cancer is often effective, especially if the cancer is diagnosed early; the most common cause of death in endometrial cancer survivors is cardiovascular disease.[21] Weight loss, an intervention that nurses can encourage in overweight or obese patients, is well known to help reduce the risk of cardiovascular disease. In addition, weight loss has been shown to reduce the risk of developing endometrial cancer by as much as 44%.[22]

The risk of cervical cancer is also increased in overweight (odds ratio [OR], 1.25; 95% CI, 0.79–2) and obese (OR, 1.70; 95% CI, 1.10–2.63) women.[23] The reason for this is not clear, as cervical cancer is usually associated with human papillomavirus.

COLORECTAL CANCER

While it is widely recognized that overweight and obesity significantly raise the risk of developing colorectal cancer, obesity is also associated with poorer outcomes, including cancer recurrence, cancer-specific mortality, and a lower rate of disease-free survival.[24] Obesity in early life (adolescence and young adulthood) appears to further increase risk of colorectal cancer in women in later life.[25] National data have shown that obese patients with colorectal cancer have more surgical complications, a greater prevalence of comorbidities and perioperative mortality, and greater health care utilization.[26] In some studies, obese patients undergoing rectal cancer surgery had increased conversion rates of laparoscopic to open surgery and increased postoperative morbidity.[27] Although laparoscopic surgery is considered superior to open procedures in obese patients, the risks of infection and anastomotic leak from laparoscopic surgery are significantly greater in obese patients than in patients of normal weight.[28]

CHALLENGES IN TREATING CANCER IN OBESE WOMEN

Because chemotherapy doses are calculated on the basis of body surface area (BSA) and generally capped at a BSA of 2 m^2 to prevent toxicity, obese women may receive insufficient chemotherapy to treat their cancer effectively.[29,30] Increased visceral fat (the "apple-shaped" body type) in postmenopausal women receiving neoadjuvant chemotherapy for breast cancer is associated with poorer outcomes, including shorter disease-free survival.[31]

Posttreatment complications. Breast cancer survivors, especially women who were premenopausal at breast cancer diagnosis and received a long course of chemotherapy, are significantly more likely to gain 5% or more of their prediagnosis body weight within 23 months after diagnosis.[32] This weight gain is believed to result from treatment-induced menopause

and such associated changes as fat accumulation, altered fat distribution, and reduced lean body mass. Compared with women of normal weight, obese women experience more wound complications (seroma, hematoma, skin dehiscence, and delayed healing), perfusion complications (fat and flap necrosis), and infections with surgical treatment, as well as face significantly higher costs related to complications of breast reconstruction following mastectomy.[33]

Gynecologic cancer surgery complications, such as venous thromboembolism, wound infection, 30-day readmission, and delayed wound healing, are more likely to occur when the patient is obese.[34,35] When operating on obese women, it may be more difficult for surgeons to visualize the operative field.[36] Estimated blood loss, operating time, and hospital length of stay are all greater for obese women treated surgically for endometrial cancer.[37] Using minimally invasive surgical techniques may minimize complications for obese women.[35]

Obesity complicates radiation therapy, particularly when the radiation is directed at the pelvis, because the beams must travel a greater depth to reach targeted organs, thereby exposing healthy organs to more radiation.[38] Obese women treated with radiation for endometrial cancer experience significantly more severe radiation toxicity affecting both skin and internal organs.[39] Obese women whose breast cancer is treated with radiation therapy have been found to experience more severe treatment-related symptoms, poorer quality of life, and worse functional well-being, both during treatment and for long periods afterward.[40]

DISCUSSING WEIGHT AND WEIGHT LOSS IN CANCER

Broaching the subject of weight loss with a patient is challenging under any circumstances, but it may be even more so when the patient has been diagnosed with or treated for cancer. Both patients and their families may believe that maintaining weight, or even having some weight "to spare," is somehow protective in cancer. While cachexia associated with cancer is obviously a concern, intentional weight loss by an overweight or obese patient is another matter entirely, and family and friends who don't realize this may actively discourage weight loss in cancer survivors, believing that weight loss indicates disease progression.

The weight of the health care provider—and the patient's response to that weight, or the response the provider anticipates—are also potential barriers to initiating a discussion of weight loss. Nurses and other health care providers who are themselves overweight or obese may hesitate to introduce the subject of weight loss with patients.[41] How patients perceive and respond to a provider's weight seems to vary. One study found that patients were less likely to follow weight loss suggestions from an overweight or obese physician,[42] but another found that overweight patients may identify more readily with and be more motivated by health care professionals whose weight status is similar to their own.[43] Overweight nurses have reported feeling self-conscious about the way they are perceived by patients but have also reported being more critical of overweight patients, perhaps because they are critical of their own weight status.[44] Nevertheless, the overweight or obese health care provider may be able to build a therapeutic alliance with the patient by virtue of their empathy and understanding of the fact that losing weight can be a struggle. When a health care provider talks to patients in a nonjudgmental manner about the health risks of excess weight, patients are more likely to attempt to lose weight.[45] Patient–provider rapport is important. Studies have shown that when health care practitioners demonstrate empathy and provide reassurance, patients are more satisfied and more likely to attempt weight loss.[46]

A diagnosis of cancer provides a teachable moment for many patients and their families. In the face of a life-threatening illness over which the patient and their loved ones have little control, changing behaviors or lifestyle is often a means of achieving control. Patients may be encouraged to learn that there is good evidence weight loss in overweight breast cancer survivors lowers levels of estrone and estradiol, both of which are associated with cancer recurrence,[47] and weight loss has been found to lower the risk of cardiovascular disease in postmenopausal breast cancer survivors.[48]

The terms used to discuss overweight, obesity, and weight management affect how the patient receives the message. The public has been shown to prefer terms such as "weight" and "unhealthy weight" to terms like "morbidly obese," "obese," or "fat."[49] In an attempt to seem less judgmental, health care providers may use vague terms or euphemisms when speaking about weight, but this choice to "soften" the terminology used to characterize a patient's weight

The Brief Negotiation Interview[59]

Step 1: Ask permission of patients to discuss the topic in order to reinforce their autonomy.
Step 2: Provide feedback on the patients' responses to the information provided.
Step 3: Enhance motivation with one or more of the following strategies:

- Ask patients why they want to make the change.
- Assess patients' motivation by asking how ready they are to make the change (on a scale of 1 to 10).
- In response to their level of motivation, ask why they didn't pick a lower number.
- Focus on motivation rather than resistance.

Step 4: Ask patients what their next step is.

The 5 A's Model[61]

Ask about patients' knowledge and feelings about their weight.
Assess their willingness to make changes.
Advise patients about how their present weight affects their health and well-being.
Assist patients in finding the help they need.
Arrange for a referral to a nutritionist or weight loss program and plan for follow-up.

problem may not sufficiently motivate the patient to attempt weight loss. In one study of primary care providers, physicians avoided using the word "obese" to describe their patients' obesity and instead used such phrases as "your weight may be damaging to your health."[50] However, patients in the study reported that the word "obesity" highlighted the seriousness of their health issue and considered the term less upsetting than the euphemism.

The importance of nutrition. Nurses have been shown to have limited awareness of the importance of good nutrition in cancer survivorship.[51] For this reason, many may not raise the topic with their patients, even though commonsense advice to follow the American Cancer Society recommendations (see www.cancer.org/healthy/eat-healthy-get-active/acs-guidelines-nutrition-physical-activity-cancer-prevention/summary.html) can prompt patients to initiate lifestyle changes. While nurses aren't expected to provide detailed weight loss interventions to patients, they can certainly discuss the risks of being overweight or obese in the context of cancer prevention and survivorship, as well as the benefits of maintaining a healthy weight and participating in physical activity.

Interventions to address overweight and obesity. While counseling patients on intensive weight loss strategies is beyond the scope of practice for most nurses, there are some evidence-based interventions that can be encouraged. Although little research has been conducted on weight control interventions for cancer survivors,[21] Chlebowski and Reeves reviewed randomized controlled trials of weight loss interventions and concluded that telephone-based interventions are feasible and effective in motivating female cancer survivors; in all trials reviewed, however, weight loss maintenance was the biggest challenge.[52]

A review of commercial weight loss programs found that, after 12 months, Weight Watchers and Jenny Craig were more effective in producing weight loss in participants than education and counseling,[53] though this review did not target trials that specifically included cancer survivors.

Pharmacologic agents and bariatric surgery have proven effective in reducing weight in noncancer populations,[54] but their role in cancer survivors has not been established.

Whether exercise in addition to weight loss improves outcomes in cancer survivors has also not been established,[55] but 150 minutes of moderate to vigorous physical activity with two sessions of strength training per week, which is deemed safe for cancer survivors and effective in both alleviating fatigue and improving quality of life,[56] may also aid in weight loss. Furthermore, research presented at the 2018 Cancer Survivorship Symposium found that exercise can have both short- and long-term benefits for patients undergoing anticancer treatment, including chemotherapy.[57]

Discussion techniques. There are a number of techniques nurses can use to initiate a discussion about weight loss with patients. These include motivational interviewing[58] and the brief negotiation interview,[59] both of which may be helpful, though they are somewhat complex and time consuming (see *Motivational Interviewing*[60] and *The Brief Negotiation Interview*[59]). Another technique, the 5 A's model (see *The 5 A's Model*[61]), is mandated by the Centers for Medicare and Medicaid Services when counseling patients about weight.[62] It is simple to use and familiar to many health care providers because of its use in tobacco cessation counseling. The 5 A's are ask, assess, advise, assist, and arrange.

THE PATIENT PERSPECTIVE

Many women, even those who have been diagnosed and treated for cancer, don't realize that obesity raises the risks of developing cancer and of cancer recurrence.[63] In a study of women with endometrial cancer, fewer than half knew that obesity was a risk factor for their cancer (44.4%) or about the association between obesity and breast cancer (49.6%) or obesity and colorectal cancer (48.1%).[63] Only 38% had discussed their weight with an oncologist. Research suggests, however, that gynecologic cancer survivors are eager to receive information from their health care providers about weight management, including weight loss and lifestyle changes that can aid in weight loss. In fact, of 244 patients with gynecologic cancer who responded to a survey on this subject, 79% reported that they would try to lose weight if a physician suggested they do so.[64]

Social factors may influence a woman's receptivity to the suggestion of weight loss. The fat acceptance movement, which promotes the acceptance of overweight and obesity, has gained increasing support over the past decade.[65] Demographic data and responses to a survey concerning beliefs about personal weight were collected from 150 women who self-identified as African American.[66] Of the participants, one (0.7%) was underweight, 34 (23%) were normal weight, 36 (24%) were overweight, 57 (38%) were obese, and 22 (15%) were morbidly obese. Although more than three-quarters of the sample were overweight, obese, or morbidly obese,

51% of the entire sample reported feeling good about themselves, and only 50% recognized their weight as a risk factor for serious health problems. (The survey did not specifically ask about cancer.)

Emotional eating is not uncommon in the context of depression or posttraumatic stress disorder.[67] Cancer survivors may experience symptoms of posttraumatic stress,[68] and this may prompt them to reach for unhealthy food to self-medicate and reduce their bad feelings. It is important for nurses to talk about this openly and help patients find more effective coping strategies to deal with stressors and to encourage them to seek out family members and friends who support their weight loss efforts.

HEALTH CARE PROVIDERS' RESPONSIBILITY

Evidence linking obesity to the development and recurrence of cancer, as well as to cancer treatment complications, is strong. Associations such as the American Society of Clinical Oncology[69] recognize this link and have prioritized initiatives focused on obesity prevention and treatment. The responsibility for addressing this issue, however, lies with all health care providers, especially those who care for women, in whom nearly 10% of new cancer diagnoses are associated with obesity.[2] Lifestyle changes are challenging to make, but nurses who recognize and take advantage of teachable moments can do much to raise awareness of the importance of maintaining a healthy weight for overall good health. ▼

For 137 additional continuing nursing education activities on women's health, go to www.nursingcenter.com/ce.

Anne Katz is a clinical nurse specialist at CancerCare Manitoba, Winnipeg, Canada. Contact author: anne.katz@cancercare.mb.ca.
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