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BREAST CANCER DISPARITIES (LA NEWMAN, SECTION EDITOR)

Mitigating Breast Cancer Disparities by Addressing the Obesity Epidemic

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Abstract

Purpose of Review Obese breast cancer patients have poorer outcomes compared to non-obese patients. The intent of this review is to discuss recent studies and analyses regarding the status of the obesity epidemic and its effect on breast cancer incidence and outcomes. Subsequently, we will introduce a program implemented at a New York City hospital to reduce the morbidity and mortality of breast cancer patients with obesity.

Recent Findings The prevalence of obesity among adult Americans is 42%, spanning all racial and socioeconomic groups. Importantly, obesity is associated with multiple chronic diseases including cancer. Among breast cancer patients, obesity is linked to higher mortality and poorer clinical outcomes, including but not limited to distant recurrence and secondary malignancies.

Summary Current treatment of breast cancer patients does not address the link between obesity and poorer prognosis. Here, we present a general strategy for reducing the morbidity and mortality of obese breast cancer patients by addressing the obesity epidemic.

Keywords Obesity · Breast cancer · Disparities · Weight loss · Bariatric surgery

Introduction

Obesity is associated with severe health risks [1] and costs to the American healthcare system [2, 3]. Its prevalence has been steadily increasing in the twenty-first century. Obesity is characterized by an excess of adipose tissue and is defined as a body mass index (BMI) that is greater than or equal to 30, and severe obesity is defined as a BMI greater than or equal to 40 [4]. With a worsening obesity epidemic in the USA, it is important to understand the epidemiology of this disease, to review its multifactorial causes and its effect on people's health, and to discuss modern day solutions and interventions.

Among American adults, the prevalence of obesity is now 42.4%, which is about a 12% increase since 2000 [4]. Prevalence is 40.0% among younger adults aged 20–39, 44.8% among middle-aged adults aged 40–59, and 42.8% among older adults 60 and over. Additionally, about 9.2% of American adults have severe obesity, an increase from 4.7% in 2000.

The epidemiology of obesity is also characterized by differences in prevalence among different racial and ethnic groups. Among adults, non-Hispanic Black adults are more likely to have both obesity and severe obesity compared to other racial groups. Prevalence is lowest among non-Hispanic Asian adults (17.4%) compared to non-Hispanic Whites (42.2%), non-Hispanic Blacks (49.6%), and Hispanic (44.8%) adults [4]. Of note, non-Hispanic Black women have the highest prevalence of obesity at 56.9%. These racial disparities are apparent even at younger ages [5, 6].

Factors that could account for disparities in obesity prevalence include socioeconomic status (SES), diet, physical activity, genetics, psychosocial factors, stress, and discrimination. These factors contribute to the higher rates of obesity among Hispanics and non-Hispanic Blacks [7–10]. Socioeconomic status is known to be a major contributor to an unhealthy diet and is associated with the consumption of calorie-dense food with less nutritional value [7, 8]. Those in a higher

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socioeconomic class are more likely to have a balanced, healthier diet consisting of fruits and vegetables. Of note, people with a lower SES are knowledgeable about healthy food choices but are more likely to have a perception that these foods are more expensive [9]. Globally, the prevalence of obesity has increased regardless of levels of development, suggesting that income or wealth does not influence prevalence alone [11]. Thus, several factors, with intricate cause-and-effect relationships, contribute to the disparities in obesity prevalence.

While a serious disease on its own, obesity is a risk factor for numerous chronic diseases across all populations, including cardiovascular disease, diabetes mellitus, chronic kidney disease, musculoskeletal disorders, and many cancers [1, 12–14]. With respect to breast cancer, studies show that the relative risk for postmenopausal breast cancer is approximately 1.1 per 5 BMI units [12], and the relative risk of death from breast cancer is 2.12 [13]. Obesity has now even been associated with poorer outcomes, including death, in COVID-19 infections [15]. Globally, studies show that excess body weight accounted for about 4 million deaths, with more than 66% of these deaths being related to cardiovascular disease [16].

With a growing obese population, more people are likely to develop chronic comorbidities. It is imperative that we tackle this epidemic with interventions at multiple levels to have the greatest effect. While individuals can focus on lifestyle changes, healthcare workers can reinforce this change in behavior, promote public health interventions within their communities, and refer patients to other services that may promote further weight loss such as a nutritionist or a bariatric surgeon. Bariatric surgery has proven to be the most effective treatment for weight loss and is associated with curing comorbidities such as diabetes [17•]. We will describe how we incorporate these multiple strategies into our program to reduce breast cancer disparities.

Obesity and Breast Cancer

Obesity is a global disease and its link to cancer has become a growing area of interest. It confers a greater risk for the development of 13 types of cancer, including estrogen receptor positive (ER+) breast cancer in postmenopausal women [18, 19]. Obesity was first reported to have an impact on breast cancer diagnosis and outcome in 1976 when Abe et al. reported that obese breast cancer patients had worse overall survival compared to normal-weight patients. One reason for this is obese patients were likely to present with a higher stage of disease. Meta-analyses have reported an approximately 30% increased risk of recurrence or death in obese versus normal-weight women diagnosed with breast cancer and all-cause mortality of 41% independent of menopausal status [20, 21].

The pathways implemented in the link between obesity and cancer are numerous. The first relates to the reprogramming of metabolically active adipose tissue in an obese person [22•, 23]. This active and hypertrophied adipose tissue sets off a release of inflammatory cytokines and other mediators such as IL-6, TNF-a, and IL-1b which can promote tumor growth [22•, 23]. This pro-inflammatory state can lead to hormonal dysregulation, changes in cellular proliferation and differentiation, and impact DNA repair mechanisms [23]. Secondary insulin resistance and increased leptin levels can have a direct impact on tumor growth as well. These various changes will enhance the tumor microenvironment allowing the tumor to thrive. Metabolic pathways involving PI3K–AKT, HIF1α, LKB1–AMPK, and p53 are key regulators of breast cancer cell metabolism and growth [24]. Fat is a metabolically active tissue with elevated levels of the aromatase enzyme which converts androgen to estrogen. Excess estrogen production from expanded adipose tissue has been proposed as a mechanism for the adverse outcomes in obese women with breast cancer [25]. Several meta-analyses and prospective studies, including the Nurses' Health Study and the European Prospective Investigation into Cancer (EPIC), have shown that increased body weight is associated with an increased risk of developing ER+ breast cancer in postmenopausal women [26–28].

There have been inconsistent reports of the effect of obesity on breast cancer risk in premenopausal women. Although obesity was not associated with increased ER+ breast cancer in premenopausal women, one meta-analysis revealed that obese premenopausal women had a higher risk of Triple Negative Breast Cancer (TNBC) [23, 28]. This suggests that mechanisms other than elevated levels of endogenous estrogens contribute to a higher risk of breast cancer and recurrence. There are also reports of an association between obesity and risk of inflammatory breast cancer regardless of menopausal and ER status [29, 30]. Black breast cancer survivors are 70% more likely to be obese than are white breast cancer survivors [31].

Adverse Effects

There are many contributing factors that account for the adverse effects of obesity on breast cancer patients. Psychosocial factors such as lower socioeconomic status, access to medical care, and stigma of obesity create challenges in diagnosing and treating obese women with breast cancer [32•, 33]. Education and access to healthy foods and physical activity are noted to be barriers in Black breast cancer survivors compared to other racial groups [34]. Recognition of the impact of obesity on breast cancer risk by healthcare providers is also important. Education of healthcare providers on the link between obesity and breast cancer is a key step in overcoming disparities that obese people may face in access to care.

It has been found that lower adherence to mammography screening and diagnostic difficulties are seen in obese patients. This may be due to multiple reasons including feelings of low self-worth, embarrassment, and perception of lack of reassurance by their healthcare team [35].

Increased BMI has been associated with the risk of surgical complications for obese breast cancer patients. These include potential problems with anesthesia, bleeding, surgical site infections, and asymmetry in breasts esthetically [32•]. Reconstruction may also be deferred for multiple reasons including additional co-morbidities and difficulty attaining favorable cosmetic outcomes.

Obesity is also associated with higher rates of post-operative lymphedema which can be attributed to surgical complications such as wound healing, infection or seroma, and extent of axillary node dissection [36].

A discrepancy in rates of local recurrence post lumpectomy has also been reported in obese breast cancer patients compared to those with normal BMI with some reports showing increased rates of local recurrence in obese patients [32•, 37].

Obese patients with large breasts may also experience higher rates of skin toxicities associated with radiotherapy due to the size of the breasts and positioning. To avoid increased doses of radiotherapy, prone positioning is used in patients with higher BMI and/or large breasts [32•, 38].

It can be challenging to dose chemotherapy correctly for obese breast cancer patients. Often the BSA (body surface area) is capped at 2m2 for fear of overdosing patients and secondary toxicities. There is conflicting data on whether higher doses of chemotherapy are needed to achieve therapeutic levels of tumor suppression. One study suggests the benefits of adjuvant chemotherapy were significantly less in the obese population, including those who received appropriate doses [32•, 39].

Adherence to endocrine therapy in the adjuvant setting is difficult for many patients due to potential side effects. In obese breast cancer patients who were taking aromatase inhibitors, it has been reported that postmenopausal breast cancer survivors with a BMI > 35 kg/m2 had a significantly higher rate of breast cancer recurrence [40] and had a 60% increased risk of disease recurrence compared to normal BMI survivors [41].

Program Development

With the increasing evidence associating obesity to breast cancer, we felt it was important to educate and create awareness surrounding this critical issue. Our goal was to establish a unique program that allows obese breast cancer patients to navigate through oncology, bariatric surgery, and obesity medicine while integrating healthy lifestyle changes.

Our immediate aims were to (1) to educate patients on the role of obesity in the development of breast cancer and its implications on risk of recurrence; (2) to offer the opportunity for obese patients with breast cancer to receive sustainable weight loss care, beyond their cancer treatment; (3) to define and address the psychological and nutritional weight loss needs of this patient population through the medical and surgical pathways; and (4) to measure adherence and satisfaction through weight-loss parameters and questionnaires.

We designed a program to empower women to accomplish their weight loss goals, potentially mitigate their breast cancer risk, and improve their overall health. BOLD was created: Breast Cancer and Obesity, a Lifestyle Development program.

We began with referrals of appropriate candidates to Bariatric Surgery. New York-Presbyterian Queens (NYPQ) has an established Bariatric Program accredited as a Comprehensive Center by the American College of Surgeons through the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP).

As per the guidelines of the American Society for Metabolic and Bariatric Surgery, those with a BMI greater than or equal to 40 or those with a BMI greater than or equal to 35 with at least one of more obesity-related co-morbidity (type 2 diabetes, hypertension, obstructive sleep apnea, hyperlipidemia/hypercholesterolemia) and the inability to achieve a healthy and sustained weight loss for a prolonged period despite prior weight loss efforts are candidates for Bariatric Surgery.

Analysis of our institutional data from 2020 revealed that 27 of our 236 breast cancer patients met the criteria for Bariatric Surgery referral. We divided our breast cancer patients into 2 groups: active treatment and survivors. All our active treatment patients, regardless of BMI, are referred to the Oncology Nutrition service. The obese patients who are in the survivorship period would be referred to the BOLD program.

We were conscious of the emotional and mental toll that a breast cancer diagnosis can have on a patient and were mindful of when to introduce the program. The goal was to empower patients with the ability to control something—their weight—in a treatment environment that is out of their control. We used the National Accreditation Program for Breast Centers (NAPBC) definition of survivorship to determine when we would begin to introduce the program to those who qualified. Stage 0–III breast cancer, within 6 months of completing active treatment, no later than 1 year from date of diagnosis, up to 18 months for those receiving hormonal and targeted therapy.

Patients were identified by their breast surgical and medical oncologists. In office, education regarding obesity and breast cancer was provided. The program was

introduced. For those who were interested, a referral was made to Bariatric Surgery. For those who declined, the reason was documented. The patients were followed by a breast center Nurse Navigator throughout pre-op weight counseling, consults, and surgery to track their progress (Chart 1).

Our pilot program was launched in March 2021. At the time of manuscript submission, 21 patients had been offered referrals to BOLD. Thirteen patients had a BMI of 40 or greater. Seven patients had a BMI 35–39.9 with one or more qualifying co-morbidities. One with BMI less than 35 (34.7) but with multiple qualifying co-morbidities. Seventeen have accepted and enrolled. One has had bariatric surgery, five are in process, six are pending appointment, one was not a candidate based on insurance criteria, one preferred a non-surgical route after consultation, two desired medical management over surgical, and one patient is still contemplating which track she would like to pursue. We continue to collect this data and improve the logistics of referrals, making entry into BOLD seamless and efficient.

Discussion

There is sufficient evidence to support that obesity is a risk factor for the development of breast cancer and is associated with increased morbidity and mortality. Poorer outcomes in obese breast cancer patients may be due to lower SES, barriers to education and physical activity, and a higher TNM stage at diagnosis. Various pathways contribute to the molecular link between obesity and breast cancer and its resistance to treatment. These may include suboptimal dosing of chemotherapy and anti-estrogen therapy and lack of targeted therapies that could potentially have direct effects on breast cancer cells and the tumor microenvironment. More studies are needed to establish the link between obesity and breast cancer progression, response to therapy, and metastasis. Prevention of obesity or identifying metabolically obese patients who are normal weight may be one way to get ahead of the obesity and the disparities obese breast cancer patients face. Community outreach to primary care physicians and patients is necessary to provide widespread education on the overall effects of obesity and its link to breast and other cancers. The creation of an obesity cancer team may be needed to integrate the key specialties which will focus on prevention and reducing the risk of breast cancer.

BOLD was developed to overcome barriers such as access to education and resources: nutritional support, physical activity programs, and weight loss programs. After a successful BOLD pilot, we identified the need to further develop a non-surgical track that incorporates pharmaceutical management as well as lifestyle changes. The initial discussion with our patients opens an opportunity to refer patients to the various tracks of our program. This involves a partnership with obesity medicine, dieticians, exercise programs, and education. In the future, the program will also be offered to our high-risk breast patients and possibly expanded and reformatted to meet the needs of other cancer types. The choice between the lifestyle, medical, and surgical tracks can be used interchangeably and/or in concert with one another. This provides multiple avenues to increase the chance of successful weight loss and improvement in overall health and breast cancer risk.

The BOLD program will allow us to study these patients closely and design clinical trials to help identify additional markers and targets to provide further insight into the link between obesity and breast cancer. Further research will allow for the development of targeted treatment to decrease morbidity and mortality in this patient population.

Conclusion

By addressing the obesity epidemic in our breast cancer patients, we hope to improve their overall health and potentially their breast cancer outcomes. Our long-term goals are to look at breast cancer recurrence, incidence, and disease-specific survival as it relates to the implementation of our BOLD program and sustained weight loss.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12609-022-00460-4.

Declarations

Conflict of Interest The authors declare no competing interests.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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