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Healthy and Unhealthy Plant-Based Diets and Body Weight in Breast Cancer Survivors: A Narrative Review

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SUMMARY

Obesity in breast cancer (BC) survivors increase the risk of BC recurrence, second primary BC, BC-specific mortality, and overall mortality. Guidelines for BC survivors encourage healthy lifestyles by promoting healthy diets, engage in physical activity and avoid weight gain to achieve longer survival and improved quality of life. In recent years, there has been a growing interest in the possible beneficial role of plant-based diets in body weight control and in BC risk and prognosis. Plant-based diets can be evaluated using dietary indices which provide a quantitative measure of how closely an individual's diet aligns with a plant-based dietary pattern. However, there is a need to distinguish plant-based diets in healthy and unhealthy. This approach would address a research gap that often overlooks the quality and specific types of plant foods consumed. The aim of this narrative review is to analyze how a plant-based diet may impact on body weight in BC survivors, synthesizing existing evidence and discussing the potential mechanisms and implications. The findings suggest the importance of considering the quality of plant-based diets, as some may include vegetarian foods with a low nutritional profile which may negatively impact on body weight. This aspect could be crucial in preventing weight gain in women with BC, as body weight is considered a risk factor for poor BC prognosis and reduced survival.

Keywords: plant-based diet, dietary patterns, body weight, body mass index, waist circumference, breast cancer

INTRODUCTION

Obesity in breast cancer (BC) survivors, at or after diagnosis, increase the risk of BC recurrence, second primary BC, BC-specific mortality, and overall mortality [1, 2, 3]. Specifically, in postdiagnosis, for every 5 kg/m² of BMI increase, there was an estimated 7% higher risk of all-cause mortality, 10% higher risk of BC-specific mortality, and 14% higher risk of developing a second primary BC [3].

Obesity is commonly defined using body mass index (BMI), which is calculated from the formula body weight (kg) / height (m²). The World Health Organization classifies levels of adiposity based on BMI as follows: underweight, ≤ 18.5 kg/m²; normal, 18.5 – 24.9 kg/m²; overweight, 25.0 – 29.9 kg/m²; obese, ≥ 30 kg/m².

Obesity has a complex relationship with BC risk that differs in pre-menopause versus post-menopause. Higher BMI is associated with a lower risk of BC before menopause and with an increased risk of cancer after menopause, especially among postmenopausal women who have never received hormone replacement therapy [4].

Before menopause, the ovaries are the primary site of estrogen production in women. This is because the enzyme aromatase, which is responsible for converting androgens to estrogens, is predominantly expressed in the ovaries. Only a small portion of estrogen is produced by fat tissue during this stage [5]. After menopause, when the ovaries cease estrogen production, the primary site of estrogen synthesis shifts to adipose tissue, with fat tissue becoming the predominant source of estrogen. Additionally, decreased levels of sex-hormone binding globulin

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result in elevated circulating estrogen levels [6]. Having a higher amount of fat tissue after menopause can result in raised estrogen levels, thereby increasing the risk of developing BC in postmenopausal women with obesity [6].

Body fat deposits are typically located in the upper abdominal region and in lower sites around the hips and thighs. In clinical studies, the waist-to-hip circumference ratio (WHR) is commonly utilized to evaluate body fat distribution, with waist circumference (WC) being identified as a more reliable indicator of visceral abdominal fat distribution [7]. High WC is an indicator of central obesity. In particular, the evaluation of central adiposity may be a more specific indicator of the metabolic effects of obesity and another predictor of BC risk than body weight alone [7]. It was observed that postmenopausal women with BMI $\geq$ 35 kg/m² and WC $\geq$ 90 cm were more likely to develop BC [8]. Intra-abdominal (visceral) adipose tissue is associated with a higher risk of metabolic disorders such as type 2 diabetes, cardiovascular disease (CVD), and insulin resistance [9]. Fat cells in the abdominal area are metabolically active and release higher levels of free fatty acids, as a product of lipolysis, and inflammatory cytokines, which contribute to chronic subclinical inflammation. The levels of adipokines are altered, with an increase in pro-inflammatory leptin and a decrease in adiponectin, resulting in reduced anti-inflammatory and insulin-sensitizing effects [10]. These pathways are associated with the development of highly aggressive biological features in tumors, creating an environment that may promote cancer invasion and metastasis in women with obesity [11, 12].

Exercise and weight loss decrease the inflammatory microenvironment in obese patients, improve antitumor immunity, decrease estrogen levels, and are associated with reduced BC risk, better outcomes and it may indeed improve BC survival [10, 13]. These findings highlight the importance of maintaining a healthy body weight in order to improve the prognosis and outcomes of individuals diagnosed with BC. Long-term lifestyle changes, beyond a single year, may be required for sustained weight loss [13].

While there is a well-established association between being overweight or obese in menopause and having a sedentary lifestyle with an increased risk of BC [4], the relationship between diet and BC risk is not yet fully understood. The impact of diet on BC risk, recurrence, and mortality is still an active and ongoing area of research. It is estimated that 30% to 50% of all cancers could be prevented through a healthy lifestyle by being at a healthy weight, being physically active, and making sustainable long-term changes to dietary habits [14]. Therefore, nutritional interventions play a critical role in determining cancer prognosis, improving patient quality of life, and enhancing the effectiveness of anti-tumor therapies. Among BC patients, diet, physical activity, and weight management, are indeed essential to improving survival rates. In these patients, nutritional intervention should be considered as an integral part of the multimodal therapeutic approach in oncology to reduce the risk of recurrence, mortality and the development of BC co-morbidities (e.g., obesity, hypertension, hyperlipidemia, and diabetes mellitus) [14,15]. A healthy lifestyle and dietary habits are advised to BC patients before, during, and after treatment in order to have better long-term survival and quality of life [15]. The dietary pattern promoted by the World Cancer Research Fund / American Institute for Cancer Research (WCRF / AICR) to improve the survival of women with BC after diagnosis emphasizes a diet rich in plant-based foods such as vegetables, fruit, whole grains, and legumes, especially soy. Conversely, it de-emphasizes the consumption of refined grains and animal products. In particular, the WCRF / AICR guidelines recommend limiting consumption of red meat (e.g., beef, pork, and lamb) and avoiding processed meat by limiting consumption of "fast foods" and other processed foods high in saturated fatty acids (SFA), starches, or sugars (e.g., sweets, desserts). Additionally, it suggests reducing the consumption of sugar-sweetened beverages (SSBs), avoiding alcohol, and not using supplements for cancer prevention [11, 16, 17].

PLANT-BASED DIET AND BREAST CANCER

In recent years, there has been growing interest in the potential protective effects of plant-based diets against BC. The term "plant-based diet" may both be used to describe a diet rich in plant foods or as an umbrella term for various types of vegetarian patterns that excludes some or all animal foods [18, 19]. Despite the increasing popularity of vegetarian or vegan diets, the majority of individuals in Western countries still consume a combination of foods from both animal and plant sources [20].

Evaluating diets only as a dichotomy of vegetarian and omnivorous, categorizing study populations into participants who do or do not consume some or all animal foods, has several limitations that are overcome by using dietary indices that evaluate progressive adherence to a plant-based dietary pattern [18]. It is important to understand whether the gradual reduction of animal food intake with a concomitant increase in the consumption of plant-based foods can reduce the risk and recurrence of BC. If effective, this approach could have broader implications, as it may be more feasible and sustainable for individuals compared to the complete exclusion of animal foods [21]. Another limitation in studies focusing on vegetarian diets is that all plant-based foods are treated equally, but the nutritional quality is not equivalent across all plant foods [19]. Satija et al. [22] proposed three different approaches for plant-based dietary indices, which are numerical scores designed to assess adherence to an overall pattern of plant-based eating (Figure 1). An overall plant-based diet index (PDI) was created,

equivalent to the original pro-vegetarian dietary pattern, which emphasizes consumption of all plant foods while reducing intake of animal foods. Another plant-based dietary index is the healthful plant-based diet index (hPDI), which focuses on the intake of healthy plant foods that have been associated with improved health outcomes. This includes whole grains, legumes, vegetables, fruits, nuts, vegetables oils, and beverages like tea and coffee. The last index, the unhealthful plant-based diet index (uPDI), places emphasis on the consumption of less healthy plant foods, which have been linked to a higher risk of various diseases. Examples of these foods include refined grains, potatoes, fruit juices, sweets, desserts, and SSBs [23]. These three indices provide a quantitative measure of how closely an individual's diet aligns with a plant-based dietary pattern. This approach is particularly interesting as it addresses a significant gap in current research, which often overlooks the quality and specific types of plant foods consumed in comparison to the proportion and frequency of animal food intake within a plant-based diet. Plant-based diets have been associated with lower risk of chronic diseases, such as type 2 diabetes, with a stronger inverse association for hPDI and a positive association for uPDI [22], CVD [19], and some cancers [24]. Recent studies have provided evidence suggesting the potential benefits of plant-based diets in reducing the risk and recurrence of BC. The Nurses' Health Studies have shown that healthful plant-based diets were significantly associated with lower BC risk, especially for ER-negative BC [21, 25] where a healthful plant-based diet adherence was not a full vegetarian diet, but one composed of both plants and some animal foods. Furthermore, adopting healthful plant-based dietary patterns has been found to potentially improve overall survival among BC survivors [23]. While some studies suggest potential benefits of plant-based diets in reducing BC risk and promoting BC prevention and survivorship, the specific relationship is still unclear although some suggest a dose-response with the highest prevalence of overweight and obesity found among omnivores compared to semi-vegetarians, lacto-vegetarians, and vegans [26]. Other randomized controlled trials have demonstrated that a vegetarian diet is an effective intervention for weight loss, with vegan dietary treatments achieving the greatest weight loss among different vegetarian dietary patterns [27, 28]. However, only a few studies investigating BMI in women with BC have made the distinction between healthy and unhealthy plant-based diets. The assessment of the quality of plant-based food using three plant-based dietary indices (PDI, hPDI, and uPDI) is a fairly new concept and has been defined by Satija et al. [19, 22]. PDIs are numerical scores designed to measure adherence to an overall pattern of plant-based dietary patterns. These scores are designed to understand common dietary patterns that incorporate a range of progressively increasing proportions of plant foods while reducing the consumption of animal foods.

In an analysis of the combined data from the Nurses' Health Study I and II and the Health Professionals' Study, 3 ongoing US prospective cohort studies involving healthy women and men, three variations of plant-based diet indices (overall, healthful, and unhealthful), and weight fluctuations were investigated over 4-year intervals spanning more than 20 years. The authors found that different types of plant-based diet indices were associated with different amounts of weight gain or loss and that healthier plant-based diets were associated with less weight gain over 4-year intervals, whereas unhealthful plant-based diets were associated with greater weight gain during midlife [29].

A systematic review, summarizing findings from 9 prospective cohort studies of adults 18 years and older, without BC, on the association between the level of adherence to a plant-based dietary patterns and obesity risk, demonstrated that adherence to a plant-based diet, especially if rich in healthy plant foods, was associated with lower obesity risk, lower body adiposity, and better body weight management [18]. In this review, no significant association was found between the uPDI and the risk of overweight or obesity, but a positive association was observed with the risk of central obesity [18].

Another study demonstrated that adherence to a healthful plant-based diet was associated with favorable long-term changes in adiposity-related inflammatory and metabolic biomarkers concentrations in women [30]. Higher hPDI score was significantly associated with lower plasma concentrations of leptin, insulin, and higher plasma concentrations of adiponectin. On the other hand, a higher uPDI score was significantly associated with higher concentrations of leptin and insulin [30].

Findings suggest broad variations in nutritional quality of plant foods, with the healthier options showing higher levels of diet quality indicators, while the less healthy ones are poorer in quality [31]. The observations align with the results of a prospective cohort study conducted in a Mediterranean population, emphasizing the significant importance of considering the diverse nutritional quality of plant foods within plant-based diets, particularly for BC prevention [31]. Not all plant foods offer equal nutritional benefits, making it essential to prioritize fiber-rich, micronutrient-dense options like fruits, vegetables, whole grains, and legumes to maximize health benefits [31].

Within plant-based diets, carbohydrates play a major role, and their quality has been investigated in relation to body weight changes in a reanalysis of the 3 prospective cohort studies of the Harvard group, highlighting the importance of carbohydrate quality and source for long-term weight management [32]. These authors found that a 10 unit increase in glycemic index was associated with 1.2 kg greater weight gain, and a 100 g/day increase in starch or added sugar was associated with 1.5 kg and 0.9 kg greater weight gain, respectively, over four years. Conversely, a 10 g/day increase in dietary fiber was associated with

0.8 kg less weight gain. These associations were stronger among participants with overweight or obesity compared with those with normal weight and were also stronger among women than men [32].

Plant-based diets may have benefits beyond body weight control. They have also been associated with a lower risk of chronic diseases such as type 2 diabetes, CVD, and some cancers [19, 22]. Healthful plant-based dietary patterns have been directly associated with greater overall survival in BC survivors [23] as well as in healthy individuals, as the analyses of the large UK Biobank data on a quarter million women demonstrated [33].

Potential Mechanism

The possible inverse associations of a healthful plant-based dietary score with BMI in women with BC could be partly explained by higher intake of several beneficial components of plant-based foods, which may indicate a better diet quality compared to an unhealthy plant-based diet.

A diet high in healthful plant-based foods would be rich in dietary fiber, unsaturated fatty acids (MUFA and PUFA), antioxidants, and micronutrients such as calcium, magnesium, potassium, but low in SFA [22]. For example, vegetables and fruits are the main sources of fiber and antioxidants, nuts are rich in PUFA, soy and pulses are main sources of plant protein, and coffee and tea are rich in antioxidants, theaflavins and chlorogenic acid respectively [33, 34]. These food groups have been suggested to promote weight loss/maintenance, reduce adiposity, and potentially lower the risk of obesity through various pathways and intermediate factors, including satiety, inflammation, oxidative stress and gut microbiome modulation [18, 22, 34]. Studies have shown that dietary fiber increases satiation and satiety at a low caloric density and regulates lipid metabolism to reduce adiposity and promoting weight loss/maintenance [18], it is also associated with reduced levels of inflammatory markers [35]. High intakes of unsaturated fatty acids and low intakes of SFA in diets have also been shown to have anti-inflammatory properties [22]. In addition, plant-based dietary patterns have been shown to enhance insulin sensitivity, improve glycemic control, lower blood pressure, reduce long-term weight gain, and mitigate systemic inflammation [19, 21, 36], all factors linked to BC risk and recurrence [14, 11]. The abundance of antioxidants, vitamins, and polyphenols may confer antioxidant, anti-inflammatory, and antiproliferative benefits [37], and may also neutralize free radicals and prevent DNA damage [21]. BC survivors are at increased risk for low bone mineral density, loss of muscle mass, coupled with increased fat mass and increased metabolic syndrome rates, due in part to the treatments received [38]. Therefore, the high presence of minerals in health plant-based foods is important for BC survivors. Dietary calcium intake has an important impact on bone metabolism and bone health. Chronic calcium deficiency, resulting from inadequate intakes plays a role in reduced bone mass and osteoporosis [39]. In addition, a calcium-only intervention could have a marginal protective effect against cancer [40]. Magnesium is required for protein synthesis and essential for the regulation of muscular contraction [41]. Potassium intake lowers blood pressure and may impact muscle function, overall muscle health, and potentially contribute to the prevention of falls [42].

On the other hand, an unhealthy plant-based diet would have a higher glycemic index and glycemic load, reduced fiber which may lead to decreased satiety and increased hunger signals [22, 29]. This could adversely affect the pathways mentioned earlier, contributing to potential negative health outcomes. A diet that includes mainly animal foods and unhealthy plant foods like refined grains, potatoes, desserts and SSBs, tends to be richer in energy, in sodium, sugar, SFA, fast-release carbohydrates, and poorer in fiber, vitamin, minerals, antioxidants, flavonoids, and other beneficial phytocomponents [22, 31]. Moderate increases in usual glycemic index and glycemic load, starch, refined grains, added sugar, and starchy vegetables have been associated with more concurrent weight gain throughout midlife, particularly among individuals who are already obese or overweight [32]. Excessive consumption of carbohydrates from low-quality food sources (refined cereals, sweets and SSB), leads to fat storage and, over time, promotes insulin resistance [22]. Insulin resistance, in turn, contributes to additional fat storage and accumulation in the liver, further aggravating insulin resistance [18]. Moreover, a high intake of SFA from animal foods activates pro-inflammatory pathways, increasing oxidative stress and systemic inflammation, which perpetuates obesity [18]. High intake of SSBs, which are rich in added sugar, provides a significant amount of rapidly absorbable energy [43]. Consuming these liquid calories is associated with less satiety and an incomplete compensatory reduction in energy intake at subsequent meals, leading to overconsumption of total daily calories and potentially promote weight gain, contributing to an increased risk of general and abdominal obesity, type 2 diabetes, fatty liver disease, and metabolic syndrome [31, 43].

Implications

Investigating the relationship between weight control and dietary choices in BC survivors could have significant implications for public health, especially considering the substantial increase in overweight and obesity rates in more developed countries [44]. Preventing weight gain in BC survivors is crucial, not only for preventing the comorbidities associated with excess weight but also for enhancing patient quality of life and prognosis, while reducing the risks

of recurrence and mortality [45, 46]. Chief among obesity determinants is diet that can be utilized for timely and sustainable interventions among individuals and populations. Healthful plant-based diets have been associated with lower BMI in women with BC, thereby increasing the potential for population-wide positive impact on survival. Adopting a healthful plant-based diet to improve body weight does not require a total elimination of animal foods, but instead a moderate decrease in the latter while avoiding unhealthy plant foods and increasing healthy plant-based food.

According to the American Cancer Society guidelines for cancer survivors, those who have finished the acute phase of treatment are encouraged to maintain a healthy weight, engage in regular physical activity, and adopt healthier dietary patterns [11]. High quality dietary patterns are generally characterized by a predominance of plant-based foods, including whole grains, vegetables, and fruits, and de-emphasize red, processed meat intake and refined grains [1]. These align with the recommendations for BC survivors, CVD prevention and health promotion. For BC, especially if diagnosed at an early stage, CVD is more common as a cause of death than cancer [47]. Following a healthful plant-based diet is also expected to help reduce the risk of other non-communicable diseases, such as diabetes and osteoporosis [11]. Additionally, plant-based diets are considered beneficial for planetary health [48]. Dietary recommendations focus on promoting moderate adherence to a healthful plant-based diet, along with the encouragement of consuming a variety of minimally processed, possibly locally produced, plant-based foods. This approach contributes to environmental sustainability and may have a lower environmental impact since plant-based food systems generally use fewer resources compared to those heavily reliant on animal foods [19, 21]. By adopting plant-based dietary patterns, individuals can improve not only their own health but also contribute to reducing the environmental impact of food production and consumption [48].

Adopting a plant-based diet without completely eliminating animal foods is preferable, as this approach allows for flexibility and enables individuals to make gradual adjustments to their eating habits. This also preserves "cultural traditions" that involve the moderate consumption of animal foods as in the Mediterranean diet. Moreover, excluding all animal foods may not be suitable for every demographic, as

moderate intakes of animal products like fish, poultry, and fermented dairy have been associated with certain health benefits [49]. In contrast, exclusively plant-based diets may lead to deficiencies in essential nutrients, such as vitamin B12 and calcium [50]. From this standpoint, a healthy plant-based diet encourages a progressive shift towards a healthy vegetarian diet without the necessity of entirely removing a specific food group.

CONCLUSION

In conclusion, it is important to consider the quality of plant-based diets, as some may include vegetarian foods with a low nutritional profile which may negatively impact on body weight. Increased adherence to a healthful plant-based diet, which emphasized intake of high-quality plant foods such as whole grains, vegetables, fruits, and nuts, could be associated with lower BMI and an overall better quality of diet in women with BC. The findings suggest that the observed beneficial effects are attributed to the consumption of healthy plant-based foods while reducing the intake of unhealthy plant-based options and the balance with animal food sources. The international guidelines for BC survivors and the recent updated meta-analysis of international data emphasize the importance of body weight control and dietary fiber intake after BC diagnosis to reduce total mortality [1, 2, 3]. Increasing dietary fiber intakes translates into higher plant-based food consumption; however, increasing adherence to a plant-based diet requires knowledge to avoid the unhealthy vegetarian versions, which may be detrimental to body weight control, cardiometabolic risk, and BC prognosis. There is a need to educate the public on the quality of plant-based diets and the public food courts in governmental buildings, commercial centers, and schools. Additional research involving women with BC will be crucial for a better comprehension of the relationship between BMI and the distinction between healthy and unhealthy plant-based diets. Taking into consideration the quality of plant-based foods may be crucial in preventing weight gain, a risk factor for a poor BC prognosis and reduced survival.

Figure 1. Characteristics of the plant-based diet indices (PDI, uPDI, hPDI).

	Plant-based diet index (PDI)	Healthy plant-based diet index (hPDI)	Unhealthy plant-based diet index (uPDI)
Healthy plant foods — Whole grains, legumes, nuts, vegetables, fruits, vegetables oils, tea, coffee	↑	↑	↓
Less healthy plant foods — Refined grains, potatoes, fruit juices, sweets and desserts, sugar-sweetened beverages	↑	↓	↑
Animal foods — Animal fats, fish/seafood, eggs, dairy, meat	↓	↓	↓

PDI, hPDI, and uPDI are indices derived from the listed food groups. Each food group's consumption is assigned a positive (↑) or negative (↓) score based on the index of interest.

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