REVIEW

Dietary Guidelines for Breast Cancer Patients: A Critical Review

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ABSTRACT

Current dietary guidelines for breast cancer patients (BCPs) fail to address adequate dietary intakes of macro- and micronutrients that may improve patients' nutritional status. This review includes information from the PubMed and Biomed Central databases over the last 15 y concerning dietary guidelines for BCPs and the potential impact of a personalized, nutrient-specific diet on patients' nutritional status during and after antineoplastic treatment. Results indicated that BCPs should receive a nutritional assessment immediately after diagnosis. In addition, they should be encouraged to pursue and maintain a healthy body weight [body mass index (BMI; in kg/m^2) 20–24.9], preserving their lean mass and avoiding an increase in fat mass. Therefore, after nutritional status diagnosis, a conservative energy restriction of 500–1000 kcal/d could be considered in the dietary intervention when appropriate. Based on the reviewed information, we propose a personalized nutrition intervention for BCPs during and after antineoplastic treatment. Specifications in the nutritional therapy should be based on the patients' nutritional status, dietary habits, schedule, activities, and cultural preferences. BCPs' daily energy intake should be distributed as follows: <30% fat/d (mainly monounsaturated and polyunsaturated fatty acids), ~55% carbohydrates (primarily whole foods such as oats, brown rice, and fruits), and 1.2–1.5 g protein · kg^{-1} · d^{-1} to avoid sarcopenic obesity. Findings suggest that 5–9 servings/d of fruits (~150 g/serving) and vegetables (~75 g/serving) should be encouraged. Garlic and cruciferous vegetables must also be part of the nutrition therapy. Adequate dietary intakes of food-based macro- and micronutrients rich in β-carotene and vitamins A, E, and C can both prevent deterioration in BCPs' nutritional status and improve their overall health and prognosis. *Adv Nutr* 2017;8:613–23.

Keywords: macronutrients and micronutrients in breast cancer, personalized diet, drug-nutrient interaction, dietary assessment, food-based intervention

Introduction

Cancer is a leading cause of morbidity and mortality worldwide (1). Of all types of cancer, breast cancer is the second most common in the world and the most prevalent in women (2). The nutritional status of breast cancer patients (BCPs) weakens as the treatment sessions and procedures take place (3). This change is due to factors such as tumor size, negative digestive symptoms, increased nutritional requirements, and a generalized misconception of a healthy diet by either the patient or health care professionals (4, 5).

In women with breast cancer (especially those in the premenopausal stage), weight gain usually affects them in the early stages (grade I or II) of the disease (5), especially for luminal A, luminal B, or human epidermal growth factor receptor 2–positive (HER2) phenotypes (6). Additionally, changes in body composition may negatively affect patients' nutritional status, increasing the risk of tumor recurrence and death (5, 7–9). A study by Monroy Cisneros et al. (6) showed that after 6 mo of antineoplastic treatment there was a decrease in bone mineral density (BMD) and an increase in body weight characterized by an increase in fat mass (FM) and a decrease in muscle mass and strength, also known as sarcopenic obesity (SO) (10).

Currently, little information is available to enable particular dietary guidelines to be followed depending on the immunohistochemical profile of BCPs. Additionally, most existing guidelines lack sufficient scientific support; therefore, further research is needed. For instance, available

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Abbreviations used: BCP, breast cancer patient; BMD, bone mineral density; CR, caloric restriction; ER+, estrogen-receptor–positive; FM, fat mass; SGA, subjective global assessment; SO, sarcopenic obesity.

literature focused on the impact of dietary changes for triple-negative BCPs and showed that caloric restriction (CR) decreases the metastatic potential of cells and may enhance the clinical outcome for BCPs by complementing the cytotoxic therapy used for metastatic disease (11–13). Nevertheless, a healthy diet has been associated with a positive prognosis of BCPs (14, 15) and may prevent negative health outcomes due to poor nutritional status (16, 17). Therefore, a critical review and integration of current dietary guidelines that include specific macro- and micronutrient recommendations for BCPs regardless of their immunohistochemical profile are imperative.

Methods

We conducted a review that included information from the PubMed and Biomed Central databases over the last 15 y concerning dietary guidelines for BCPs and the potential impact of a personalized nutrient-specific diet on patients' nutritional status during and after antineoplastic treatment.

The search included human, in vitro, and animal-model studies, including observational and interventional studies. Keyword combinations in English and Spanish included "breast cancer," "dietary guidelines," "body composition," "nutrition intervention," "anticancer therapy," "antioxidant," "nutrition program," "dual X-ray absorptiometry," "DEXA," "DXA," "CT," "chemotherapy," "radiation," "hormone therapy," "adjuvant therapy," "diet," "macronutrient," "micronutrient," and "drug-nutrient interaction." A secondary search was conducted manually from related articles to identify other references for analysis.

Results

Cancer treatment impact on BCP nutritional status

Anticancer treatments used in BCPs are classified as systemic (chemotherapy, hormone therapy, and antibody therapy) and delimited (surgery and radiotherapy) (18). Understanding the impact of anticancer treatments on the nutritional status of BCPs can clarify the need for a specialized clinical nutrition therapy for these patients (**Table 1**).

It is documented that an antineoplastic treatment, such as chemotherapy, may interfere with a patient's diet because of its secondary effects. These effects may generate a negative impact on the patient's dietary intake and selection of macro- and micronutrient sources, as well as on the patient's nutritional status, with an increase in waist circumference, body weight, and FM (6, 25), as described in Table 1. An altered nutritional status in BCPs could increase the risk of postoperative complications and mortality (7–9) and should be assessed by health care professionals (5).

In BCPs, prolonged fasting periods are common after chemotherapy sessions; however, if fasting lasts >48 h, muscle-mass loss may be promoted, resulting in deterioration of the patient's nutritional status (26, 27). This deterioration can result in a negative impact when the patient receives antineoplastic treatment (22, 24). Additionally, asthenia frequently leads to a decrease in appetite, and constant fatigue has been related to weight gain in BCPs (28).

A study carried out in Mexican women showed that premenopausal women increased their BMI (in kg/m^2), body weight, and FM during chemotherapy compared with postmenopausal women (6). Factors that may influence weight gain in this group are a decrease in physical activity, ovarian failure, increased caloric intake, and decreased basal metabolism (29). A decline in physical activity occurs in 96% of patients treated with chemotherapy because of constant fatigue or a lack of energy (30, 31).

Several studies report that BCPs have an inadequate diet given that their intakes of fruit, legumes, and dark-green and orange vegetables are decreased, which consequently means they have insufficient dietary intakes of calcium, iron, phosphorus, magnesium, niacin, riboflavin, thiamin, vitamin B-6, vitamin C, and zinc (14, 25). Therefore, assessment of BCPs' nutritional status and correction of nutritional deficiencies (macro- and micronutrients) with a specialized diet and nutrition counseling (25), especially before surgery (15), is imperative. A personalized dietary nutrition intervention that controls energy intake within an acceptable macronutrient distribution range and promotes daily fruit and vegetable consumption will set the standard for BCPs' dietary nutritional therapy.

As described earlier, weight gain in BCPs is associated with an increase in FM and a decrease in muscle mass, a phenomenon known as SO, which is associated with an increase in the number and severity of complications in BCPs (21, 32–35). Despite being multifactorial, SO could be prevented by ensuring an adequate dietary protein intake of 1.2–1.5 $g \cdot kg^{-1} \cdot d^{-1}$ (36, 37). Currently, there is a misinformed tendency of BCPs under treatment to become vegetarians or vegans, limiting their high-quality dietary protein intake and leading to a malnutrition process that affects their long-term prognosis (38, 39).

Nutritional assessment should be performed immediately after diagnosis and again periodically during the course of the disease. Therefore, it should be included as part of the patient's management routine and be simple, inexpensive, reliable, and able to identify patients at risk or with greater nutritional imbalance (5). Additionally, patients should be referred to a dietitian so that an appropriate nutritional therapy can be designed based on their health condition and individual needs (6, 37).

For BCPs who have low BMI (<20) (5) or who have lost ≥10% of their usual weight in <6 mo, there is an increased risk of complications due to malnutrition (40, 41), including bone fracture risk (42). Therefore, a healthy weight (BMI 20–24.9) in BCPs must be encouraged (4, 5).

Hormone therapy is indicated for estrogen-receptor–positive (ER+) BCPs. However, this treatment increases the risk of BMD loss in BCPs in addition to the patient's pretreatment status (43). Therefore, lifestyle factors (diet, physical activity, habits, etc.) as well as parity (age, etc.) contribute to the detriment of BMD in BCPs (5) and should be initially assessed and monitored during treatment (44–46).

Although subjective global assessment (SGA) is a validated tool to identify malnutrition in cancer patients (47), it does not include body composition as one of its indicators for nutritional assessment. This limitation can mask an increase in FM and muscle-mass loss (i.e., SO) (48, 49). We

TABLE 1 Cancer treatment impact in breast cancer patients' nutritional status[1]

Treatment	Study, (ref) year, country	Sample size	Anthropometric and body-composition variables measured	Conclusions
Chemotherapy	Monroy Cisneros et al. (6), 2014, Mexico	40 patients with primary diagnosis of invasive breast cancer at baseline and after 6 mo	Anthropometry: weight, height, BMI, waist and hip circumference Body composition with DXA: fat mass, fat-free mass, and BMD Serum biomarkers: retinol and β-carotene	Patients had a lean tissue loss. Serum retinol decreased despite an increase in β-carotene. Premenopausal patients gained 2.3 kg body fat and 2.1 kg weight. In postmenopausal women, these changes were not observed.
Chemotherapy	Nissen et al. (19), 2011, United States	49 patients with primary diagnosis of invasive breast cancer at baseline and after 12 mo	Anthropometry: weight, height, BMI, waist and hip circumference Body composition with DXA: fat mass, BMD, and segmented fat-free mass	Women with a healthy BMI gained an average of 2 kg/y; the overweight lost 1.4 kg/y, and the obese lost 1.9 kg/y. Women with normal weight at baseline had an increase in fat mass in the arms and the visceral area. At an older age, more loss of bone mineral content was observed.
Chemotherapy	Prado et al. (20), 2009, Canada	55 patients with primary diagnosis of invasive breast cancer at baseline and after their antineoplastic treatment	Anthropometry: weight, height, and BMI Body composition by computed tomography: muscle mass	25% of patients had sarcopenia, independent of BMI. 50% of patients with sarcopenia and 20% of patients without sarcopenia had a higher rate of toxicity associated with chemotherapy.
Chemotherapy	Freedman et al. (21), 2004, United States	20 patients with primary diagnosis of invasive breast cancer (stage I–III A) at baseline and after 6 mo	Anthropometry: weight, height, and BMI Body composition by computed tomography, air displacement plethysmography, and DXA: fat mass, fat-free mass, muscle mass, and BMD	Breast cancer had a negative impact on body composition but not on weight during the first year of treatment compared with women in the control group. There was an increase in body fat and a decrease in lean mass percentage (+4.0% ± 6% and −3.8% ± 6%, respectively). BMD decreased (−0.04% ± 0.06 kg).
Chemotherapy and surgery	Iwase et al. (22), 2016, Japan	172 patients with breast cancer in advanced stages	Anthropometry: weight, height, BMI, and waist circumference Body composition with DXA: fat mass, fat-free mass, subcutaneous fat, visceral fat, and skeletal muscle area	High levels of visceral fat were associated with a worse prognosis in patients with breast cancer, especially postmenopausal women. Nutritional interventions should focus on preventing the accumulation of visceral fat.
Chemotherapy and HT	Arpino et al. (23), 2015, Italy	433 patients with breast cancer at baseline and 3, 6, 9, 12, and 24 mo after	Anthropometry: weight, height, BMI, waist and hip circumference, and waist:hip ratio	During the first 2 y after diagnosis, all women had an increase in body weight (+0.72 kg/y), waist circumference (+1.53 cm/y), and plasma concentrations of LDL cholesterol and TGs.
Chemotherapy, surgery, radiotherapy, and HT	Cihan (24), 2014, Turkey	456 patients with breast cancer: 96.9% radical mastectomy, 95% chemotherapy, 82.4% radiotherapy, and 60% HT	Anthropometry: weight, height, and BMI	75% (n = 343) had a BMI >25. Normal-weight patients had a higher survival rate than did low-weight or obese patients. Significant correlations were found between BMI and menopausal status, histological type, and chemotherapy.

[1] BMD, bone mineral density; HT, hormone therapy; ref, reference.

suggest that SGA should be applied together with a body composition analysis (e.g., a 2-compartment model: FM and fat-free mass) for BCPs in particular (6, 19–22).

Nutritional therapy in BCPs

Nutritional therapy can improve and prevent adverse changes in the body composition of BCPs at the early stages of the disease (5, 6). To promote an early nutritional intervention and prevent the deterioration of cancer patients' nutritional status, the Spanish Society of Basic and Applied Nutrition, in collaboration with the Society of Oncology and Palliative Care and Health Professionals of Nutrition and Cancer, have proposed an algorithm of nutritional intervention for oncologic patients. Its main objectives are to correct nutritional deficiencies, prevent premature death associated with malnutrition, and improve BCPs' quality of life and tolerance to cancer treatment (50).

To apply the algorithm, BCP nutritional status must be classified according to SGA: *1*) well nourished, *2*) moderate malnutrition, and *3*) severe malnutrition (47). After the nutritional status is classified, follow-up is suggested within 15–30 d between appointments. This allows the clinical nutritionist to monitor the patient periodically, providing general and specific recommendations on each visit according to the patient's nutritional status and antineoplastic treatment (50).

What we describe above is a broad nutritional approach, distant from what a personalized clinical nutrition intervention should consider. That is, the above approach lacks the specificity of nutrient calculation, meeting daily dietary requirements, and personalized dietary suggestions according to each patient's likes, tolerance, socioeconomic status, cultural beliefs, and schedule (6, 14, 25). Additionally, this diet algorithm is based on a partially subjective assessment because the nutritional diagnosis is done by SGA and the intervention is based on recommendations. BCPs and nutritionists face a challenge in meeting the objectives of the algorithm proposed, given that there are no specific recommendations for macro- and micronutrient intake and dietary recommendations made by recent studies are not always considered. Therefore, nutritional assessment should include performing simple anthropometric measurements coupled with body composition "gold standards," such as DXA (48), to provide a more objective and specific assessment of nutritional status that will help health care professionals, especially nutritionists, prevent the deterioration of BCP nutritional status (6, 19–24).

Evidence-based research shows that an increase of body weight in BCPs is a risk factor associated with comorbidities. To improve the outcome of BCPs, nutrition experts should encourage weight management at all phases of cancer care given that doing so is safe and achievable (5, 51). Thus, nutritional interventions for BCPs should aim to *1*) limit weight loss to between 5% and 10% of initial body weight by using CR based on age and initial BMI, *2*) increase dietary quality with nutrient-dense foods, and *3*) reduce simple sugars and added fats, all consistent with clinical practice guidelines for the overweight and obese and with recommendations for cancer survivors (5, 51–54).

The strategies discussed above have been associated with a reduction of tumor growth and inflammatory response, delay of the aging process, and an increase in rodents and human life expectancy (11, 55, 56). Additionally, nutritional therapy should not be disregarded for normal-weight BCPs to prevent weight gain, nutrient deficiencies, and negative health outcomes (5, 57).

Nutritional therapy for weight loss aims to achieve a negative energy balance in the individual's total energy requirement by increasing physical activity and reducing dietary energy intake. The CR will depend on the patient's nutritional status, but a usual therapy may consider a reduction of 500–1000 kcal/d when appropriate. Most behavioral programs are designed to achieve a loss of 0.5–1 kg/wk, encouraging patients toward a healthy nutritional status (52, 58, 59).

Because of the lack of specific nutritional guidelines for BCPs, the American Cancer Society suggests a nutritional approach that considers the guidelines published in 2007 by the NIH in the United States (59). These guidelines provide more specific recommendations regarding nutrients (fat intake, carbohydrates, fiber, cholesterol, etc.) for BCPs, and their strength lies in the consideration of CR to promote healthy weight loss (60) by providing a tentative macronutrient distribution range to customize the patient's eating plan.

For BCP body weight control, the American Cancer Society recommends a healthy diet low in fat (<30% from total energy) with a strong base of fruits and vegetables (5–9 servings/d) and encourages physical activity (17). On the other hand, a multicenter study reported that only 30–48% of newly diagnosed BCPs made positive changes in their eating habits. These changes include increased consumption of fruits and vegetables and reduced consumption of fat and simple sugars. Nonetheless, almost half of newly diagnosed BCPs do not make these positive changes in their lifestyle (61).

Additionally, an evidence-based nutrition intervention program proposed by the Oncology Nursing Society and supported by the National Cancer Institute recommends an individualized nutritional therapy as the most effective measure for cancer patients. The dietitian in such a therapy has to work together with the patient, the patient's family, and a multidisciplinary oncology team to provide an adequate nutritional assessment and intervention follow-up (60, 62).

Designing an individualized clinical nutrition intervention is considered state-of-the-art when treating BCP nutritional status (63). As an example, there is a study in patients with cervical cancer who were able to reduce their body weight while maintaining their lean body mass and preventing the deterioration of their nutritional status (64). Additionally, a personalized dietary intervention showed a positive effect on patients' antioxidant and anticoagulant capacity based on biochemical and clinical parameters in cancer patients (**Table 2**) (70).

Studies have concluded that BCPs should consume 5–9 servings/d of fruits (~150 g/serving) and vegetables (~75 g/serving) to ensure sufficient intake of antioxidants and fiber through diet (5, 53, 69, 71, 72). The fruits and

vegetables should be mostly those rich in β-carotene and vitamins A, E, and C (73), because they have been associated with beneficial changes in anthropometric, metabolic, inflammation, and DNA methylation markers (74). There is evidence that including dietary intakes of foods high in polyphenols such as onions, broccoli, and apples (whole), among others, should be encouraged to improve breast cancer outcomes (75).

Additionally, it is suggested that sources of animal protein, such as meat, eggs, and low-fat dairy, should be consumed moderately (1–2 times/wk each) (76), and fish, poultry, turkey, and pork tenderloin should be made priorities because of their low fat content (77). Studies in the elderly have proven the effectiveness of maintaining fat-free mass and reducing the risk of OS by ensuring the consumption of 1.2–1.5 g protein $\cdot$ kg^{-1} $\cdot$ d^{-1} (36, 37), and we suggest that a similar approach be considered for BCPs.

Micronutrients in BCPs

Experimental evidence suggests that vitamin and mineral deficiencies can lead to damage in the cell's genetic material (78). Deficiencies in vitamins B-12, B-6, C, and E; folic acid; niacin; iron; and zinc can mimic the effect of radiation in DNA, which causes oxidative damage (79). Similarly, vitamin A and retinoids (vitamin A analogs) may exert an inhibition in carcinogenesis; therefore, vitamin A deficiency could adversely affect BCPs (80, 81).

Moreover, available information shows the effect of specific nutrients (from food sources, not dietary supplements) and food compounds that selectively induce the death of cancer cells and inhibit their growth and proliferation, although these nutrients and compounds are not considered in current dietary guidelines for BCPs (82, 83). Garlic (84–86) and vegetables from the cruciferous family (87, 88) have a greater antiproliferative and antioxidant activity in breast cancer cells, and researchers encourage their inclusion in any preventive or therapeutic nutritional intervention (82).

It has been documented that the hydrolysis of some compounds found in cruciferous vegetables may yield a compound known as goitrin, which has been found to interfere with thyroid hormone synthesis. Nevertheless, using data from a study in animal models (89), we estimated that reaching a toxic amount of goitrogens from different vegetables in humans is not biologically plausible and is even less so under conventional nutritional recommendations (~50 g/d). A study by McMillan et al. (90) showed that a daily intake of 150 g cooked cruciferous vegetables for 4 wk had no effect on thyroid function.

On the other hand, cruciferous vegetables include different bioactive compounds, such as 3,3′-diindolylmethane, which have demonstrated chemopreventive activities in all stages of breast cancer carcinogenesis (91). Current knowledge about the association between breast cancer and thyroid diseases showed no association (92–95); thus, 5 servings/d of vegetables may guarantee a mean cruciferous vegetable intake of ~57 g/d, which can be protective against breast cancer recurrence (73).

A study in BCPs from Northwest Mexico found that there was a considerable decrease in lean tissue and serum retinol after 6 mo of antineoplastic treatment (6). The subsequent decline of lean tissue and serum retinol may be partially explained by the presence of inflammation (96) and inefficient conversion of carotenoids to retinol (97), in addition to dietary changes. Other studies showed no difference in serum retinol concentration between BCPs and controls when serum retinol was used as a biomarker, which can be because of the highly homeostatic regulation of the metabolite (98). Nonetheless, when considering carotenoids, which are more susceptible to dietary changes, as precursors of retinol they show a reduction in circulating concentrations, which is negatively associated with risk of breast cancer (99).

Factors such as antineoplastic treatment and changes in dietary habits, BMI, and age can affect biochemical indicators (e.g., hemoglobin, even when iron stores are not necessarily depleted) (100). Given that treatment can be paused by the oncologist if hemoglobin levels are low, we recommend that dietary iron intake should not be disregarded in the diet of BCPs.

Dietary intake usually changes in BCPs, affecting the intake of energy, fat, minerals (calcium, copper, phosphorus, iron, magnesium, potassium, and zinc), vitamins (A, niacin, B-6, and thiamin), and dietary fiber, which compromises patients' nutritional status (6, 14, 25). Velentzis et al. (61) showed that 30–48% of newly diagnosed BCPs change their dietary habits toward a reduction in fat, red meat, and simple-sugar intake. Additionally, Wayne et al. (101) showed a small increase in the fruit and vegetable intake in BCPs, which can be associated with better cancer outcomes and improved results in the decrease of the inflammatory response, tumor progression, and hormonal biomarkers of recurrence risk (74). Therefore, dietary interventions should attend these changes and target newly diagnosed BCPs to encourage positive lifestyle changes.

The American Institute of Cancer Research, the American Cancer Society, and the NIH have all issued guidelines in support of the behaviors described above (16–18, 53, 102). Thus, combining nutritional counseling to control energy intake within an acceptable macronutrient distribution range and promoting the intake of fruits and vegetables sets the standard toward future efforts in dietary nutritional therapy for BCPs.

A proinflammatory diet is associated with obesity and is defined as "a diet high in refined carbohydrates, saturated fat, and low in fruits, vegetables, and whole grains" (103). Even when the general population should avoid this type of diet, doing so should be particularly emphasized for BCPs, given that women who report increasing fruit and vegetable servings after breast cancer diagnosis report intakes that are on average still below the recommended 5 servings/d (103). BCPs with inadequate eating habits need to increase their dietary intake of antioxidants, with a particular emphasis on zinc, lycopene, selenium, n–3 PUFA (104), and vitamins A, E, and C (6, 101) to reduce the carcinogenic effect that a proinflammatory diet can have.

TABLE 2 Nutrition intervention programs for BCPs[1]

Study (ref), year, country	Sample size	Intervention characteristics	Results	Conclusions
Vassbakk-Brovold et al. (65), 2015, Norway	100 of 161 patients with breast cancer about to start chemotherapy	Duration: 12 mo Personalized intervention for a healthy lifestyle focusing on diet, physical activity, mental stress, and quitting smoking if relevant	After 4 mo, 63 participants remained in the study: logistic regression analysis revealed that age was the only factor that determined participation after 4 mo. Patients >70 y old were less likely to participate after 4 mo.	During chemotherapy, BCPs' participation in personalized lifestyle interventions increased. Participation was inversely associated with age and was not affected by socioeconomic factors.
George et al. (66), 2014, United States	2317 women with breast cancer: 1205 in the intervention group and 1112 in the control group	Patients' diets were evaluated at baseline and 1 y after by using an FFQ. A control group maintained their habits, and the intervention group received informative sessions conducted by registered dietitians 4 times/y.	In a follow-up period of 9.6 y, there were 415 deaths. Women who consumed ≥5 fruit and vegetable servings, ≥6 whole-grain servings, and <20% fat in their diet had 26% less risk of death by any cause and 42% less risk of death related to breast cancer. Women with ER+ tumors with a good-quality diet were associated with a lower mortality risk.	Better quality diet after diagnosis of breast cancer is associated with a lower risk of death, particularly for reasons unrelated to breast cancer. Impact: Patients with breast cancer may have a higher percentage of survival by adhering to the US Dietary Guidelines.
Scott et al. (67), 2013, United Kingdom	90 women with breast cancer	At baseline and after 6 mo of anthropometric measurements, blood biomarkers associated with breast cancer recurrence and quality of life were taken. Patients kept dietary diaries (3 d/wk) to evaluate macronutrients and energy. They were randomly assigned to an exercise program for 6 mo (3 sessions supervised exercise/wk) and a low-calorie, healthy-eating program (individualized dietary counseling and weekly nutrition seminars).	Compared with the control group, the intervention group showed a reduction in body weight (−1.09 kg), waist circumference, waist:hip ratio, consumption of total and saturated fats, leptin concentrations, cholesterol, and diastolic blood pressure at rest. Cardiopulmonary health also showed improvements in the intervention group.	Results suggest that an individualized intervention program that includes physical activity and a low-calorie dietary plan at an early stage can have a positive impact on health outcomes that influence the long-term prognosis in overweight BCPs.
Saxton et al. (68), 2014, United Kingdom	85 women with breast cancer	Patients were randomly assigned to an exercise program for 6 mo (3 sessions supervised exercise/wk) and a low-calorie, healthy-eating program (individualized dietary counseling, supplemented by weekly nutrition sessions).	Compared with the control group, the intervention group showed a reduction in depressive symptoms at a 6 mo follow-up but in stress scores did not change. Women in the control group had higher counts of total leukocytes, neutrophils, and lymphocytes than did the intervention group at the end of the study.	A decrease in depressive symptoms with long-term implications was observed in BCPs after enrolling in an individualized lifestyle intervention program. This could lead to a better survival rate in women recovering from breast cancer treatment.

[1] A standard vegetable serving weighs ~75 g and a fruit serving ~150 g (69). BCP, breast cancer patient; ER+, estrogen-receptor–positive; ref, reference.

Ascorbic acid acts as an antioxidant that protects against lipid peroxidation and an increase in LDL concentration (105). It can also function as an indirect antioxidant, supplying electrons to generate reactive forms of other antioxidants such as glutathione, tocopherols, and flavonoids (106). Dietary ascorbic acid intake has been associated with a reduced risk of mortality (107).

Moreover, retinol and some carotenoids (α-carotene, β-carotene, lycopene, and lutein and zeaxanthin), although not β-cryptoxanthin, are considered protective compounds in breast cancer. Therefore, an increased dietary intake of these nutrients through food sources should be encouraged (108–110). β-cryptoxanthin is not considered a protective carotenoid because there is inconsistency in the evidence because of the relatively low concentration of serum β-cryptoxanthin among the general population (108).

Furthermore, vitamin E and its derivative γ-tocotrienol have not only demonstrated antiproliferative activity suppressing gene expression c-Myc but also can help reduce aerobic glycolysis processes that damage malignant cells (111, 112). Dietary intake of γ- and δ-tocopherols showed to be breast cancer preventive (113) and chemoprotective (114) in animal models. Thus, tocopherol food sources should be included as part of BCP diets while avoiding vitamin E supplementation (113).

Drug-nutrient interactions in breast cancer

Some nutrient-drug interactions have been reported during cancer treatment, and they can induce negative effects on both the efficacy of drugs and the patient's nutritional status (115). Some nutrients have the ability to benefit BCP serum biomarkers and reduce the toxicity generated by antineoplastic therapy. For example, luteolin, a flavonoid present in some vegetables such as celery, thyme, and green pepper, has antioxidant and anti-inflammatory properties. It modulates immune system activity and is a promoter of carbohydrate metabolism (116).

A study conducted in Japan showed that luteolin has a biphasic effect on the cell line of human breast cancer Michigan Cancer Foundation-7 (MCF-7; ATCC HTB-22TM). This means that, when administered in conjunction with doxorubicin, a drug commonly used in chemotherapy, luteolin has a cytoprotective effect even in the presence of the tumor estrogen-receptor–antagonist (ICI 182.780 and the breast cancer estrogen-receptor–negative cell line MDA-MB-453 (ATCC HTB-131TM). Concomitant administration of luteolin attenuates the effect of reactive oxygen species generated by doxorubicin in MCF-7 cells (117).

Additionally, the interaction of soy with tamoxifen (an antiestrogenic drug used in BCPs with ER+ tumors) has been described. It has been found that soy acts as an antagonist inhibitor of some P450 isozymes, such as cytochromes CYP1A2 and CYP2C9, although other studies have shown that soy has a negative effect, promoting ER+ tumor growth (115, 118, 119).

In 2014, the interaction between falcarinol polyacetylenes, compounds present in vegetables such as carrots and parsley, with mitoxantrone, a chemotherapeutic substrate, was reported for the first time. Tan et al. (120) found that the inhibitory activity of dietary phytochemicals identified in the human ATP-binding cassette transporter for the ATP-binding cassette G2 breast cancer–resistant protein is critically involved in multidrug resistance of human cancer. The breast cancer–resistant protein provides a framework for further research on possible interactions between food and drugs (120).

Discussion

Diet and its components play a key role in the nutritional and health status of BCPs. Specifications in nutritional therapy should be based on the patient's nutritional status, dietary habits, schedule, activities, and cultural preferences. It is important to periodically monitor BCPs regarding anthropometric indicators and body composition, preferably every ≤2 wk. Appropriate modifications and specific recommendations in the diets of BCPs should be made in order to meet energy and nutrient requirements, especially when the patient presents particular digestive symptoms when receiving antineoplastic treatment.

All BCPs should have a nutritional assessment and an adequate nutritional therapy immediately after diagnosis. Even when health care professionals do not use specific and updated dietary guidelines, nutritional therapy should be encouraged and directed toward an individualized approach. Therefore, it is imperative to have dietary guidelines based on scientific evidence, enabling those guidelines to combine the results of other scientific studies for the implementation of nutritional interventions in patients with breast cancer. Based on personal characteristics, and ideally from diagnosis, specialized nutrition counseling should be implemented for BCPs to minimize the negative impact of treatment's side effects on the nutritional status of BCPs and improve their overall health status and prognosis.

Based on the information we gathered, we propose a personalized nutrition intervention for BCPs during antineoplastic treatment. The daily energy intake of BCPs should be distributed as follows: <30% fat/d (mainly MUFA and PUFA), ~55% carbohydrates (mainly whole-food servings such as oats, brown rice, and fruits), and 1.2–1.5 g protein $\cdot$ kg^{-1} $\cdot$ d^{-1} to avoid SO. Unsaturated fat from animal protein sources (i.e., fish) should be consumed, and this could also be a strategy to prevent vitamin A deficiency in BCPs by avoiding a high intake of saturated fat.

BCPs should be encouraged to consume 5–9 servings/d of fruits (~150 g/serving) and vegetables (~75 g/serving) (69). Servings should be mostly rich in β-carotene, vitamins A, E, and C, and flavonoids because these compounds have been shown to improve breast cancer outcomes and the overall health of BCPs. Garlic and cruciferous vegetables should also be part of the nutritional therapy, as discussed above.

Finally, BCPs should be encouraged to pursue and maintain a healthy body weight (BMI 20–24.9), conserving lean mass and avoiding increased body FM. Therefore,

after a nutritional status assessment, a conservative CR can be considered (500–1000 kcal/d) in the personalized nutrition intervention if required. This would encourage a better outcome for BCPs after receiving antineoplastic treatment and would reduce mortality and recurrence risk.

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