Revista Contexto & Saúde
Editora Unijuí
Programa de Pós-Graduação em Atenção Integral à Saúde
ISSN 2176-7114 – v. 23, n. 47, 2023

http://dx.doi.org/10.21527/2176-7114.2023.47.13038

COMO CITAR:
Pereira MML, Silvino VO, Sousa BLSC, Magalhães MT de JFM, de Moura RC, Lima IMOM. et al. Pre- and Post-Chemotherapy nutritional status in women with breast cancer: A systematic review. Rev Contexto & Saúde, 2023;23(47):e13038

Pre- and Post-Chemotherapy Nutritional Status in Women With Breast Cancer:
A Systematic Review

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ABSTRACT

Introduction: Breast cancer (BC) is the malignant neoplasm with highest incidence and mortality among women worldwide. Nutritional status (NS) before and after chemotherapy treatment can be decisive for prognosis and survival of the patient with BC. *Objective:* Systematic review of the NS before and after chemotherapy in women with BC. *Methods*: An extensive search on Pubmed, Web of Science, and Scopus databases was conducted. It was limited to manuscripts published until 2020 using the Boolean method with the following combinations of descriptors: "breast cancer" AND "nutritional status" AND "chemotherapy". *Results*: A total of 12 articles were included in this review. Two studies with patients diagnosed with eutrophic and 10 studies with overweight patients addressed pre-chemotherapy NS. For post-treatment NS, nine studies enrolled overweight patients, two with eutrophic patients and one with patients at nutritional risk. *Conclusion*: Several studies confirm the association of BC and overweight/obesity with increased prevalence of the disease, poor prognosis, and reduced survival after the end of the treatment. Current data support the need for interventions in the patients' lifestyle. Further studies on the association between interventions in BC should be conducted in order to form a larger body of evidence.

Keywords: nutrition; breast neoplasm; chemotherapy.

ESTADO NUTRICIONAL PRÉ E PÓS-QUIMIOTERAPIA EM MULHERES COM CÂNCER DE MAMA: UMA REVISÃO SISTEMÁTICA

RESUMO

Introdução: O Câncer de Mama (CM) é a neoplasia maligna com maior incidência e mortalidade entre as mulheres em todo o mundo. O Estado Nutricional (EN) antes e após o tratamento quimioterápico pode ser decisivo para o prognóstico e sobrevida da paciente com CM. *Objetivo*: Este estudo, portanto, teve como objetivo revisar sistematicamente o EN antes e após a quimioterapia em mulheres com CM. *Métodos*: Uma extensa pesquisa foi realizada nas bases de dados Pubmed, Web of Science e Scopus. A busca limitou-se a manuscritos publicados até 2020 utilizando o método booleano com as seguintes combinações de descritores: "câncer de mama" E "estado nutricional" E "quimioterapia". *Resultados*: Um total de 12 artigos foram incluídos nesta revisão. Em relação ao EN pré-quimioterapia, 2 estudos foram com pacientes com diagnóstico de eutrofia e 10 foram com pacientes com sobrepeso. Em relação ao EN pós-tratamento, 9 estudos foram com pacientes com sobrepeso, 2 com pacientes eutróficos e um com pacientes em risco nutricional. *Conclusão*: Vários estudos confirmam a associação entre CM e sobrepeso/obesidade com aumento da prevalência da doença, pior prognóstico e redução da sobrevida após o término do tratamento. Os dados atuais suportam a necessidade de intervenções no estilo de vida dos pacientes. Novos estudos sobre a associação entre intervenções no CM devem ser realizados a fim de formar um corpo maior de evidências.

Palavras-chave: nutrição; neoplasia mamária; quimioterapia.

Submetido em: 31/1/2022
Aceito em: 28/6/2022

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INTRODUCTION

Cancer has a chronic multicausal origin and is characterized by the uncontrolled propagation and development of cells with altered genetic material, which promotes the formation of neoplastic tumors in organs or tissues of the organism. The World Health Organization (WHO) estimates that in the next 20 years the number of new cases of cancer will increase by approximately 70%, mainly due to smoking, alcohol use, poor quality of food, and physical inactivity[1].

Breast cancer (BC) plays a prominent role in this panorama, representing 25% of the global cases of the disease. It is the malignant neoplasm with the highest mortality rate among women in Brazil and worldwide. The incidence of this neoplasia is higher in developed countries, reaching 89.7 cases per 100 thousand inhabitants. The mortality rate in developing countries is even higher, mostly due to a series of factors, including the difficulty of early detection of cancer[2].

Chemotherapy drugs cause adverse effects during treatment, such as infections related to decrease in white blood cells, fatigue related to decrease in red blood cells, emotional changes, functional loss, and alopecia. In addition, chemotherapy drugs are associated with the development of changes in taste, as mucositis, nausea, and vomiting, which are results of acute toxicity. This contributes for gastrointestinal disorders and anorexia, which are determinants of eating habits quality, nutritional status (NS), and prognosis of cancer patients[3,4].

Studies on cancer and NS have focused on nutritional deficit and malnutrition due to their negative impact on recovery, treatment, hospitalization, and quality of life[5–7]specifically, nutritional outcome, morbidity, and quality of life. On the other hand, several studies report that obesity can also have a serious negative impact on the treatment, recurrence, prognosis, and survival of cancer patients[8–10].

Morbidity and mortality depend directly on the previous NS as well as on the compromised nutritional profile of patients during treatment. The general condition of the patient is decisive for the achievement of the desired results and reduction of the odds of complications. Thus, this study aims to systematically review the nutritional status before and after chemotherapy in women with breast cancer.

METHODS

Search strategy

This systematic review was conducted based on the Preferred Reporting Item guidelines for Systematic Reviews and Meta-Analyzes (Prisma)[11]. It was registered at the PROSPERO database, number CRD42021261438. A wide bibliographic search of original manuscripts was carried out systematically on Pubmed, Web of Science and Scopus databases. The search was limited to manuscripts published until 2020 using the Boolean method with the following

combinations of descriptors: "breast cancer" AND "nutritional status" AND "chemotherapy".

In this study, the inclusion criteria for the retrieved articles were: (i) no language limitation, (ii) published in peer-reviewed journals, (iii) focused on female patients undergoing chemotherapy and (iv) involving nutritional assessment before and after chemotherapy treatment. In order to assess the methodological quality, only full-text sources were included, while abstracts and conference papers from annual meetings were disregarded. The authors codified the studies according to the selection criteria and eliminated duplicates. Four reviewers assessed independently the relevant articles identified through the search process, examining the titles, abstracts, and full texts in order to decide whether they would be included or excluded from the study.

Eligibility criterion

Studies addressing the nutritional status before and after chemotherapy in women with breast cancer were included. Animal or in vitro studies, duplicates, and review articles were excluded.

Data extraction

The studies were collected between March and May 2020. This collection included sample size, sex, age, method of assessing nutritional status, assessment of nutritional status before and after chemotherapy, and type of treatment. After the data extraction was completed, independent reviewers checked the data to confirm its accuracy.

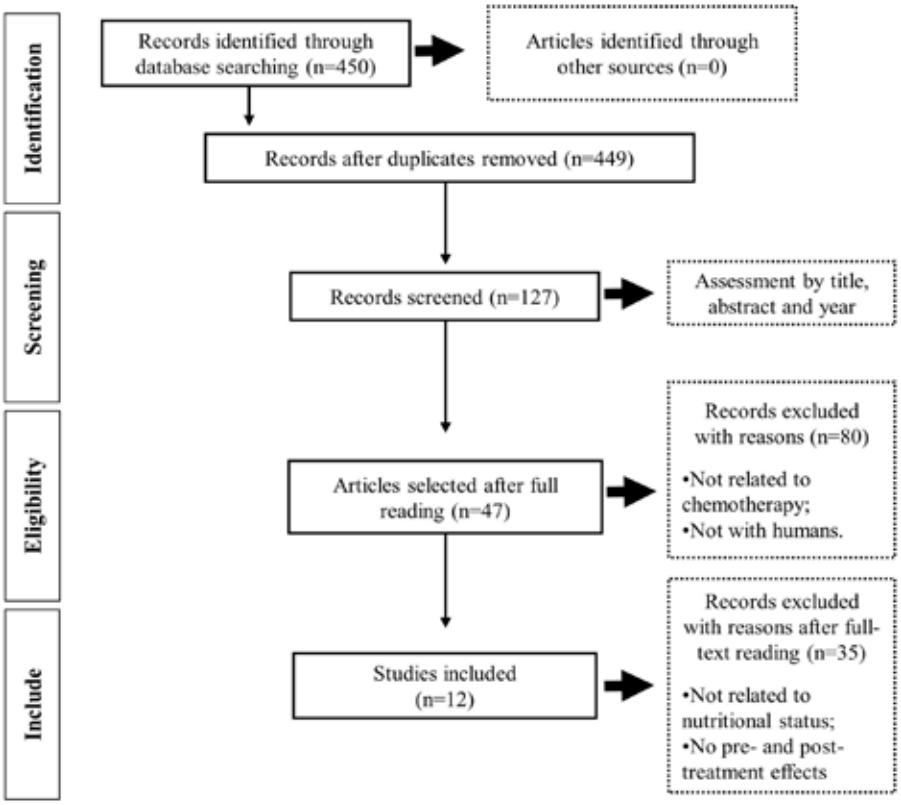
Quality assessment

The quality of the studies included in this review was independently assessed by two evaluators using the tool QualSyst[12]. This 28-items instrument has the following possible scores for each item: Yes: 2; Partial: 1; No: 0; N / A: not applicable. The quality standard adopted in this review was a conservative quality score above 75%.

RESULTS

Initially, four hundred and fifty articles (n=450) were identified. After reading the titles, 322 studies were excluded, for not being associated with the subject of interest. Of the remaining 127 articles, 80 were excluded after reading the abstracts, since they were review or duplicate articles. After reading the full version, another 35 articles were excluded, totaling 12 studies included in this review. They were chosen since they addressed NS before the start of chemotherapy treatment and after its completion in women diagnosed with BC. The details of the selection are shown in Figure 1.

Figure 1 – Search strategy flow diagram



More than half of the studies (61.54%) were carried out in America and the remaining studies in Europe, Asia, and Oceania. The period of publication ranged from 2005 to 2020 and the majority of the works were published between 2014 and 2019. Regarding the evaluation of the quality of the articles included, the scores ranged from 72 to 84%. The overall quality of the studies was satisfactory, where most of the articles (n=9) scored above 75%. Only three studies were scored below 75% (Table 1).

Table 1 – Quality index of the studies included

Author/year	Quality index (%)
M. T. M. Lima et al., 2020[13]	72
Oba et al., 2020[14]	72
Custódio et al., 2019[15]	72
Ambrosi et al., 2012[16]	80
Brain et al., 2011[17]	76
Hurria et al., 2006[18]	76
Custódio et al., 2016[19]	84
Georges et al., 2014[20]	76
Cisneros et al., 2014[21]	76
Liz et al., 2018[22]	80
Harvie et al., 2005[23]	72
Boltong et al., 2014[24]	80

The detailed description of the selected studies is shown in Table 2. Of the total number of articles analyzed, 10 used body mass index (BMI) as a method of assessing nutritional status; 5 used waist circumference (WC); 4 used waist-to-hip ratio (WHR); 3 used hip circumference (HC); 2 used lean mass and % of body fat, and 1 used albumin, mini nutritional assessment (MNA), neutrophil-to-lymphocyte ratio (NLR), mid-arm muscle circumference (MAMC), and prognostic nutritional index (PNI). Each study used one or the association of two or more methods as a strategy to diagnose the patients' NS.

Table 2 – Description of the studies included in the review

Author/ year	Type of study	Country	Population	NS assessment	NS before chemotherapy	NS after chemotherapy	Outcome	Treatment/ Medication
M. T. M. Lima et al., 2020[13]	Prospective longitudinal	Brazil	55 women (≥18 years)	WHR and BMI	BMI = 29.8 kg/m^2 when patients ate <4.67 times a day and 25kg/m^2 when patients ate a ≥4.67 times a day. WHR = 0.9 cm when patients ate > 4.67 a day and 0.8 cm with food intake ≥4.67 a day.	BMI = 27.3 kg/m^2 when the patients ate <4.33 times a day and 25.9 kg/m^2 when patients ate ≥4.33 times a day. WHR = 0.9 cm when patients ate > 4.67 a day and 0.8 cm with food intake ≥4.67 a day.	Inverse association between FF and BMI and WHR at TO and T1.	Neoadjuvant or adjuvant treatment with doxorubicin and/or taxane-based chemotherapy.
Oba et al., 2020[14]	Retrospective	Japan	191 women (51 ± years) in NAC	BMI, PNI, Albumin, and NLR.	PNI = 52.6; Albumin = 4.41; NLR = 2.50; BMI = 22.5.	PNI = 46.5 (p = <0.01); Albumin = 4.11 (p = <0.01); NLR = 2.96 (p < 0.01); No significant difference in BMI.	PNI was the most commonly decreased NS variable. The influence of Δ PNI on survival is stronger in advanced stages. NAC has a negative effect on NS. PNI may be the most sensitive parameter to assess NS.	Neoadjuvant treatment; anthracycline, including EC (60 - 75 mg/m^2 of epirubicin and 600 mg/m^2 of cyclophosphamide) or FEC (500 mg/m^2 of fluorouracil, 75-100 mg/m^2 of epirubicin, 500 mg/m^2).
Custódio et al., 2019[15]	Prospective	Brazil	55 women (≥18 years)	WHR, WC, and BMI	BMI after the first cycle = 26.4 kg/m^2. WC after the first cycle = 86.5 cm. WHR after the first cycle = 0.6 cm.	BMI after last cycle = 26.5 kg/m^2 (p = 0.009). WC after the last cycle = 87.0 cm (p = 0.030). WHR after the last cycle = 0.6 cm (p = 0.761).	BW, BMI, and WC differed significantly (p>0.05). WHR and WC showed weak and positive correlations with intestinal inflammatory disease during and after the CT scan.	Adjuvant and neoadjuvant treatment with FAC, CMF, AC-docetaxel, and AC-paclitaxel

Ambrosi et al., 2012[16]	Non-randomized clinical trial	Brazil	53 women (52 ± years) in NAC	BMI, WC, HC, and WHR	30.2% were eutrophic, 37.7% were overweight and 32.1% were obese. WC ≥88 cm in 49% of the individuals. WHR ≥ 0.85 in 45.3% of cases. BMI = 28kg/m^2; WC = 89.69 cm; HC = 103,9 cm; WHR = 0.86 cm.	73.6% of the patients gained weight and 56.6% gained ≥2 kg. Significant increases were found in 2.81 kg for BW, 1.08 kg/m^2 for BMI, 1.93 cm for WC and 3.62 for HC. No difference in WHR. BMI = 29.12 kg/m^2 (p = 0.001); WC = 90.63 cm (p = 0.012); HC = 107.5 cm (p = 0.000); WHR = 0.84 (p = 0.207)	Patients gained weight after diagnosis and during adjuvant treatment. BW gain was associated with chemotherapy treatment, alone or in combination with radiotherapy.	*
Brain et al., 2011[17]	Prospective	France	40 women (≥ 70 years)	MNA	34 (85%) had a normal MNA score. 6 (15%) had an MNA score at risk of malnutrition.	23 (62.2%) had normal MNA score; 14 (37.8%) were at risk of malnutrition	No cardiac toxicity and impairment of functional, cognitive, or mental status were observed. Standard anthracycline CT can be used in older adult patients carefully selected with negative tumors related to heart rate.	Adjuvant treatment with 60mg/m^2 liposomal non-pedylated doxorubicin and 600mg/m^2 cyclophosphamide.
Hurria et al., 2006[18]	Prospective longitudinal	USA	49 women (≥ 65 years) in stages I to III BC with adjuvant chemotherapy.	BMI	BMI = 28 kg/m^2	BMI intermediately after = 29 kg/m^2; BMI 6 months after = 28 kg/m^2 (p > 0.9).	Patients maintained their functional status and quality of life 6 months after chemotherapy. Subtle changes in higher order functioning would require assessment with different geriatric methods.	Adjuvant treatment with cyclophosphamide 600 mg/m^2, methotrexate 40 mg/m^2, 5-fluorouracil 600mg/m^2, doxorubicin 60 mg/m^2, cyclophosphamide 600mg/m^2, followed by ACT 175 mg/m^2 or AC followed by ACT 80mg/m^2; and ACT followed by 2mg/kg of trastuzumab.

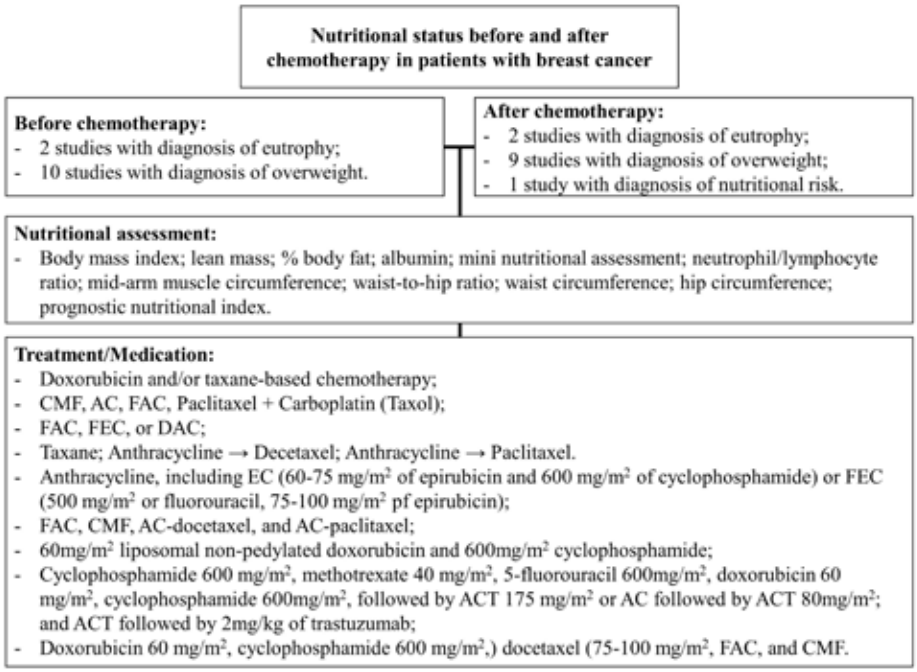
Custódio et al., 2016[19]	Prospective longitudinal	Brazil	55 women (≥ 18 years)	BMI, WC, HC, WHR	BMI = 28.4 kg/m^2; WC = 90.8 cm; HC = 0.9 cm; WHR = 0.6 cm	BMI = 28.7 kg/m^2 (p = 0.009); WC = 91.1 cm (p = 0.03); HC = 0.9 (p > 0,05); WHR = 0.6 (p > 0.05).	Most patients started CT with high weight, aggravated by a statistically significant increase in BMI and WC during CT.	Adjuvant and neoadjuvant treatment with (doxorubicin 60 mg/m^2, iv, cyclophosphamide 600 mg/m^2,) docetaxel (75-100 mg/m^2, FAC, and CMF.
Georges et al., 2014[20]	Retrospective descriptive	Brazil	30 women (34 to 80 years) in adjuvant or NAC.	BMI	BMI = 27.45 kg/m^2; Low weight = 1 patient (3.3%); Eutrophic = 9 patients (30%); Overweight = 10 patients (33.3%); Obese = 10 patients (33.3%).	BMI = 27.53 kg/m^2 (p = 0.75). Low weight = 2 patients (6.7%); Eutrophic = 9 patients (30%); Overweight = 10 patients (33, 3%); Obese = 9 patients (30%). 14 patients (46.7%) gained BW and 16 (53.3%) lost weight during treatment.	There was no significant influence of chemotherapy on weight of the women evaluated	Adjuvant and neoadjuvant treatment with CMF, AC, FAC, Paclitaxel + Carboplatin (Taxol), in combinations of 4, 6, or 8 cycles.
Cisneros et al., 2014[21]	Experimental	Mexico	40 women (32 to 61 years).	BMI, WC, HP, LM, FM	BMI = 29.6 kg/m^2; WC = 97.5 cm; HP = 104 cm; LM = 37.8 kg; FM = 31.7 kg	BMI = 29.8 kg/m^2 (p = 0.233); WC = 99.8 cm (p = 0.008); HP = 104.7 cm (p = 0.369); LM = 37.2 kg (p = 0.032); FM = 32.5 kg (p = 0.102)	Negatively effect on body weight and fat, especially in young women.	Adjuvant and neoadjuvant treatment with FAC, FEC, or DAC.
Liz et al., 2018[22]	Non-randomized clinical trial	Brazil	86 women (68 in the comparison group and 18 in the nutritional intervention group, ≥ 18 years)	BMI and WC	Control: BMI = 27.6 kg/m^2; WC = 88.8 cm. Intervention: BMI = 28.9 kg/m^2; WC = 93.3 cm	Control: BMI = 28.6 kg/m^2 (p; 0.01); WC = 90.7 cm (p = 0.02). Intervention: BMI = 29.2 kg/m^2 (p = 0.28); WC = 93.4 cm (p =0.22)	Control group increased in BMI and WC, while no change was observed in the intervention group.	*

Harvie et al., 2005[23]	Experimental	England	19 women (55 ± years)	BW, % FFM, % FM, and MAMC	BW = 73.6 kg; FFM = 45.7 kg; % FM = 37.3; MAMC = 28 cm	Weight = -0.3 (p > 0.05); FFM = -1.9 kg (p = 0.074); % FM = + 2.1% (p < 0.05); MAMC = -1 cm (p > 0.05)	No change in overall BW, but they tended to gain FM and lose FFM. The ability to meet or exceed energy needs led to gains in body fat, but did not prevent the loss of FFM.	*
Boltong et al., 2014[24]	Prospective and cohort	Australia	52 women (≥ 18 years) undergoing adjuvant chemotherapy	BMI	BMI = 26.9kg/m^2	Significant association between reduced appetite and the decline in final BMI cycle compared to the baseline (r = 0.42; p <0.0005).	The reduction in appetite had a moderate association with BMI and a small association with worsening NS. Taste is negatively affected by chemotherapy.	Adjuvant treatment with taxane; Anthracycline → Docetaxel; Anthracycline → Paclitaxel.

Symbols and abbreviations: AC, adriblastine and cyclophosphamide; ACT, Paclitaxel; BMI, body mass index; BW, body weight; CMF, cyclophosphamide, methotrexate, and fluorouracil; DAC, docetaxel, adriamycin, and cyclophosphamide; EC, epirubicin and cyclophosphamide; FAC, 5-Fluorouracil, Adriamycin, Cyclophosphamide; FEC, 5-fluorouracil, epirubicin, and cyclophosphamide; FF, food frequency; FFM, free fat mass; FM, fat mass; HC, hip circumference; LM, lean mass; MAMC, mid-arm muscle circumference; MNA, mini nutritional assessment; NAC: neoadjuvant chemotherapy; NLR, neutrophil to lymphocyte ratio; PNI, prognostic nutritional index; WC, waist circumference; WHR, waist-to-hip ratio; *, information not available.

All patients underwent adjuvant or neoadjuvant chemotherapy treatment, and their NS was assessed before the start of the treatment and after its completion. One study associated NS with food frequency whereas another study compared the NS between an intervention group, (where nutritional education interventions were carried out) and a comparison group. Regarding pre-chemotherapy NS, two studies involved eutrophic patients before treatment and 10 studies were conducted with overweight women. The NS after chemotherapy was classified as overweight in nine studies, eutrophic in two studies, and nutritional risk in one study. The most commonly used chemotherapeutic drugs in adjuvant and neoadjuvant therapies were 5-fluorouracil, doxorubicin, taxane, cyclophosphamide, and anthracycline. Of the 12 articles included, 6 are longitudinal prospective, 2 are clinical trials, 2 are experimental, 1 is a retrospective study, and 1 is a prospective cohort study. A summary of the main findings of this systematic review are presented in Figure 2.

Figure 2 – Main nutritional assessment methods and treatments or medications reported in the studies included in this systematic review



Symbols and abbreviations: AC, adriblastine and cyclophosphamide; ACT, Paclitaxel; CMF, cyclophosphamide, methotrexate, and fluorouracil; DAC, docetaxel, adriamycin, and cyclophosphamide; EC, epirubicin and cyclophosphamide; FAC 5-fluorouracil, adriamycin, and cyclophosphamide; FEC, 5-fluorouracil, epirubicin, and cyclophosphamide.

DISCUSSION

Pre-chemotherapy nutritional status of patients with breast cancer

In this review, most patients were overweight in the BC diagnosis before starting treatment, representing over 83% of the studies included. These patients tend to be overweight or obese at the time of diagnosis and obesity is associated with an increase in general and disease-specific mortality[25].

Obese individuals are 1.5 to 3.5 times more likely to develop cancer when compared to eutrophic individuals[26]. A study evaluated women aged between 34 and 80 years before the start of treatment and observed that almost 70% were overweight and obese [20]and met the demand of the service. A questionnaire was used to obtain personal identification data, social-demographic data, and anthropometric data as well as general health status. For the 30 study participants body mass index (BMI. In fact, studies carried out in Europe attribute between 15 to 45% of cancers cases to overweight and obesity. In addition, a recent literature review[27] showed that obesity is also a risk factor for other types of cancers, such as pancreas, endometrium, colon, kidneys, malignant esophageal adenomas, gastric cardia, pancreas, liver, and gallbladder cancer. It is estimated that about 20% of the types of cancers mentioned are related to overweight.

A study identified the association between BMI and the occurrence of BC in patients with menopause and post-menopause in Salvador, Brazil. The average BMI of the patients was 27.5 kg/m^2 for the cases and 26.1 kg/m^2 for the controls. The proportion of normal, overweight, and obese patients was 33.8, 38.2, and 27.9% among cases, respectively and 43.4, 43.4, and 13.1% among controls, respectively. Therefore, there were more obese among cases than among controls in menopausal and post-menopausal patients with BC.

Cisneros *et al.*[21] assessed women with BC and found that they had a mean BMI of 29.6 kg/m^2 and mean WC of 97.5 cm. Similarly, another study also observed the prevalence of pre-obesity and general obesity in women with BC[28]. The authors detected a mean BMI of 29kg/m^2, where 38% of the patients had BMI ≥ 30kg/m^2 and 9.2% of the patients had WC ≥80cm, which indicates the high incidence of central obesity.

A cohort study confirmed that the development of BC is more prevalent in women with a BMI >35.0 kg/m^2, in addition to contributing to the growth of the tumor and worsening of the prognosis[29]. Likewise, the study by Neuhouser *et al.*[30] also reinforced the multiplied risk of developing breast cancer in obese and postmenopausal women. Therefore, the relationship between previous obesity and BC is evident, especially in women in the post-menopausal period, which poses as a risk factor for the onset of the disease.

Post-chemotherapy nutritional status of patients with breast cancer

Women diagnosed with BC have lower risk of weight loss, so it is important to carry out detailed anti-cancer monitoring, as the disease itself poses as a nutritional risk factor. Overweight or obesity during chemotherapy can negatively impact BC prognosis and overall survival, since it can influence other medical

conditions, such as diabetes, heart disease, hypertension, and hypercholesterolemia[31,32]. A study observed a significant difference between BMI before and after chemotherapy[15], which corroborates that, in women undergoing chemotherapy, the prevalence of overweight reaches about 40%, especially in patients with breast, intestine, and uterus tumor[33].

Breast cancer patients have a progressive tendency to gain weight during the recovery phase[34]. The explanation for this increase in weight is not clear, as it may be associated with food intake, reduced physical activity, changes in the basal metabolic rate, or menopause[35]bioelectrical impedance, total body potassium.

A clinical trial evaluated the effect of nutritional intervention in women with BC during chemotherapy[22]. The authors observed that the control showed an increase in BMI and WC, while no changes were observed in the intervention group. This demonstrates that the nutritional intervention contributed positively to the maintenance of body weight during chemotherapy treatment. This result is in line with another investigation involving overweight patients with BC. The authors concluded that the prevalence of excess weight is due to dietary inadequacy, demonstrating that individualized nutritional guidance and monitoring can improve prognosis as well as the quality of life of the patients[36].

Weight gain is the most common side effect in women during chemotherapy and is associated with a negative effect on quality of life and survival25. A study reported weight gain in 73.6% of BC patients after chemotherapy treatment, of which 56.6% increased about 2 kg or more16. This evidence is in accordance with a study that showed that the increase in body weight after chemotherapy usually varies from 1 to 5 kg, which may be associated with the increase in fat mass and decrease of muscle mass31.

It is well established that weight gain usually occurs when energy intake exceeds energy expenditure. A recent study investigated the association between weight gain after chemotherapy and food frequency. The authors observed that the BMI was higher (27.3 kg/m^2) when patients ate <4.33 times a day and lower (25.9 kg/m^2) when patients ate ≥4.33 times a day[13]diet quality and nutritional status of fifty-five women with breast cancer (BC. However, it is worth mentioning that patients with BC during chemotherapy diminishes calory intake during the first year after diagnosis[37]adiposity, dietary factors, supplement use, and quality of life (QOL. Thus, weight gain may not result from overeating, but it may be related to less physical activity and reduced resting metabolic rate. Therefore, maintaining a correct and individualized diet, as well as improving eating habits, is essential for a good nutritional prognosis during chemotherapy treatment[37,38]adiposity, dietary factors, supplement use, and quality of life (QOL.

Methods of nutritional status evaluation

The most popular methods for NS evaluation used in the studies included in this review were BMI, WC, and WHR (83.3%, 41.6% and 33.3%, respectively). This is probably due to the fact that they are non-invasive, low-cost methods and have good applicability in the nutritional diagnosis and prognosis of oncological diseases[39].

A systematic literature review and meta-analysis with 82 studies, including 213,075 BC survivors and 41,477 deaths (23,182 deaths attributed to BC), showed a correlation between BMI and BC survival. In particular, the authors observed an increased risk of 17%, 11%, and 8% for general mortality and 18%, 14%, and 29% for specific BC mortality for every increment of 5 kg/m^2 in BMI (i) before breast cancer diagnosis, (ii) less than 12 months after diagnosis, and (iii) 12 or more months after diagnosis, respectively[39]. In addition to BMI, a study has also reported a significant positive association between WHR and WC in BC mortality in postmenopausal women[40].

A cohort study evaluated the impact of chemotherapy on the nutritional status in 55 women with BC using BMI, WC, and WHR as a diagnostic strategy[19]which may interfere with adequate diet and nutritional status of women with BC. It compared the patients before and after the completion of the cancer treatment. The authors observed that BMI and WC significantly increased after treatment, while there was no change in WHR. This confirms the acceptance of these NS evaluation methods, as well as negative influence of chemotherapy on NS in patients with BC.

Similarly, other study also used BMI as a diagnostic strategy and found a prevalence of overweight among cancer patients[41,42]. However, Borges *et al.*[43] highlighted that BMI is a restricted parameter in cancer patients, due to the increase in the concentration of inflammatory mediators, such as cytokines, which can cause both protein degradation and an increase in extracellular fluid. This causes water retention, making it difficult to determine the actual nutritional status of the patients.

Felden and Figueiredo[44] also observed that abdominal fat estimated by WC is a risk factor for developing BC. They found that women with WC> 88 cm showed greater odds of developing breast disease than those with WC between 80-87 cm. Similar results were also observed by Mobarakeh *et al.*[45] Where 81.1% of the participants diagnosed with BC had WC greater than or equal to 80 cm.

It has been reported that BMI can predict the risk of BC better than WC. In fact, BMI has a predictive capacity for BC risk in pre-and post-menopausal women, but the predictive capacity observed for WC has been achieved at a significant degree only in pre-menopausal women[46].

Chemotherapy side effects

The choice of systemic therapy, including chemotherapy, is recommended based on the cancer subtype and risk of recurrence. It is characterized by the use of a combination of drugs, orally or intravenously, which attack and kill cancer cells and normal fast-growing cells. Adjuvant chemotherapy aims to combat or inhibit clinically undetectable micrometastasis after the surgical approach, whereas the neoadjuvant is a treatment strategy for locally advanced tumors favoring a more conservative loco regional approach, or even surgery[47,48].

Generally, two or more therapeutic approaches are associated during the treatment of BC. Chemotherapy regimens last about 3 to 6 months and among the most common are CMF (cyclophosphamide, methotrexate, 5-fluorouracil)

and anthracyclines (epirubicin or doxorubicin), which have been reported to reduce mortality by 35%[49]. However, despite the higher odds of success, side effects that contribute to a decline in the normal functioning of patients' physiological systems are more likely to occur[48,50]. These side effects include nausea, vomit, loss of appetite, dry mouth, and changes in the perception of taste or smell, which contribute for gastrointestinal tract[51] dysfunction.

A recent study evaluated the effect of neoadjuvant chemotherapy (NAC) on nutritional status, using two different NAC regimens, one of which based on anthracycline (AC) and the other on taxane-based regimen, including either DOC (docetaxel) or PTX (paclitaxel). The authors noted that the PNI values decreased significantly, which indicates that a decrease in PNI may be a marker for predicting poor prognosis after NAC in patients with BC[14].

In contrast, weight gain is the most common side effect that occurs in women during chemotherapy, which is associated with a negative effect on quality of life and survival. As reported in Women's Healthy Eating and Living (WHEL) study, women treated with cytotoxic therapies are 65% more likely to gain weight during treatment, compared to women receiving other types of treatment, such as radiation therapy or hormone therapy (tamoxifen or aromatase inhibitors)[52].

Several chemotherapeutic agents, such as anthracyclines (doxorubicin, daunorubicin, epirubicin, idarubicin), trastuzumab, cyclophosphamide, antimetabolite agents (capecitabine, fluorouracil), antimicrocyte agents (paclitaxel, docetaxel), quinine, tyrosine inhibitors sunitinib), monoclonal antibodies (bevacizumab), vinca alkaloids (vincristine, vinorelbine), and angiogenesis inhibitors are associated with an increased risk of mortality and morbidity[53–55].

It is understood that side effects, when not properly evaluated and managed, imply in decrease of the functional capacity and quality of life of the patients[56]. A study carried out with women with uterine cancer undergoing chemotherapy with carboplatin and paclitaxel identified nausea and vomiting (83.2%), constipation and diarrhea (38%), and mucositis (20.2%) as the most prevalent gastrointestinal symptoms[57]. Therefore, it is highlighted the importance of nutritional assessment and diagnosis, in addition to follow-up and clinical intervention of women undergoing chemotherapy treatment for BC, in order to avoid a poor prognosis and decrease the prevalence of morbidity and mortality.

Energy expenditure in the oncological context

The majority of healthy adults have a resting energy expenditure (mREE) within 10% of the predicted resting energy expenditure (pREE). However, cancer patients may have a REE beyond this range, which may lead to a state of hypo or hypermetabolism. The recommendations are not specific to individual nutritional needs nor are they evidence-based. Therefore, without an accurate understanding of energy needs, caloric intake can be insufficient or excessive, leading to energy imbalance, abnormal body composition, and poor nutritional status in the oncological context [58].

The presence of a tumor can lead to abnormal REE, since tumors undergo high rates of glycolysis and lactate production. Excess lactate is converted back to glucose in the liver (process known as Cori cycle), leading to a net consumption of adenosine triphosphate. This results in significantly increased REE and muscle catabolism in cancer patients [59,60].

Friesen, Baracos and Tuszynski[61] measured the energy demands of a tumor through mathematical models. They considered the level of anaerobic glucose production in a tumor load of up to 3 kg using two available datasets that measured REE, glucose turnover, glucose recycling, and oxygen consumption in cancer patients. The results showed additional energy expenditure that ranged from 100 to 1400 kcal/day associated with the tumor carrier status. Thus, the energy demand of a tumor has the potential to substantially impact energy expenditure in some patients.

In addition, it has been reported that there is a positive relationship between the increase in REE and tumor size, location, and response rate to chemotherapy[58]. In a study with patients with lung cancer, the volunteers had a higher REE compared to matched controls (up to an average of 173 ± 65 additional kcal/day) and up to 68% of patients had REE 110% above predicted values[62].

Similarly, a study with 714 cancer patients reported that the cancer group had a higher mREE/pREE ratio when compared to the control group, consisted of 642 volunteers (108.3 ± 14.1% vs 102.5% ± 12.6%, respectively)[63]. This same study also revealed that, depending on the type and location of the tumor, participants showed hypermetabolism at different degrees: esophagus (109.4 ± 13.2%), stomach (108.7 ± 13.6%), pancreas (112 ± 13 .4%), and lungs (108.8 ± 14.2%)[63]. Aggressive and advancement of the disease are associated with higher energy expenditure. It has been reported that the tumor stage and poorly differentiated histology individually account for 25% of REE values[64].

In addition to the increased energy demand caused by tumor-related variables, various metabolic disorders can also occur. These metabolic changes can be similar to the processes of infection or injury, characteristic of an activated immune system, which triggers the release of inflammatory mediators such as cytokines and eicosanoids. The inflammation process is associated with changes in the hypothalamic-pituitary axis, dysautonomia, oxidative stress, decreased muscle protein synthesis, increased muscle proteolysis (through the upregulated ubiquitin-proteasome pathway), and hypermetabolism[65].

The link between energy expenditure and inflammation may be partially due to melanocortins, which are a group of peptide hormones derived from pro-opiomelanocortin neurons in the pituitary gland. This process occurs when pro-inflammatory cytokines upregulate melanocortin signaling through the activation of pro-opiomelanocortin neurons and inhibition of orexigenic neuropeptides; generating increased REE and/or decreased appetite by upregulating the activation of type 4 melanocortin receptors[66]. Many findings report an association between inflammation and REE and weight loss, although this is not always the case. Although the impact of inflammation on REE cannot be quantified, current evidence suggests that inflammation is often associated with hypermetabolism[67].

CONCLUSION

This review allowed to conclude that patients with BC usually present overweight or obesity at the time of diagnosis, and tend to gain weight and body fat post treatment. Thus, excessive weight is associated with an expanded risk of developing BC, in addition to favoring an increase in general and specific mortality due to the disease. Furthermore, women with BC are also affected by adverse changes in body composition, such as fat gain, with augmented WC, WHR, % of body fat, and reduced fat-free mass, which represent an important risk factor for the development of comorbidities affecting the prognosis and long-term survival.

Moreover, it is evident that the quality of life of the patient with BC is negatively impacted by the toxicity related to the chemotherapy treatment. The side effects limit overall nutritional factors, associated with eating habits and the proper functioning of the digestive system. However, toxicity often remains an underestimated issue in the management of cancer patients.

Despite the small number of studies included, this review contributed to strengthen the discussions about the nutritional status before and after BC treatment, and how NS is a determining factor in this context. Therefore, patients with BC should be encouraged to improve their lifestyle and eating habits before, during, and after chemotherapy treatment, for better survival chances and quality of life.

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