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Obesity in breast cancer patients after oncological treatment. How to conduct a nutritional intervention?

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Obesity in breast cancer patients is a significant predictor of morbidity as well as adverse treatment outcomes. It correlates with poorer response to treatment, particularly affecting survival length and quality of life. This paper aims to describe the relationship between obesity and breast cancer prognosis, highlighting the importance of integrated prehabilitation strategies. Prehabilitation, which includes nutritional counseling, psychological support, and physical activity, is proposed as a proactive approach to prepare patients for the rigors of cancer treatment, such as surgery, chemotherapy, and radiation therapy. The results emphasize the need to maintain optimal weight and body composition through dietary adjustments, particularly high protein intake, and physical rehabilitation. An interdisciplinary approach, including the involvement of oncologists, nutritionists, psychologists, and physiotherapists, is crucial for successful treatment outcomes.

Obesity among patients with breast cancer

Obesity is defined as a pathological increase in adipose tissue in women exceeding 25% of ideal body weight (IBW), which increases the risk of breast cancer by up to 3-fold [CITATION Maz10 \l 1045 \m Are06]. Insulin resistance, hyperglycemia, and hyperinsulinemia are key factors leading, on the one hand, to obesity, and, on the other, to the development of cancer. Therefore, it is not surprising that, despite the disease, 15–45% of the European population's cancer patients are overweight and obese [CITATION Pis08 \l 1045].

Obese women have the pooled relative risk (RR) of breast cancer 1.41, while overweight women have a much lower risk 1.07, according to a Chan et al. study. Another important factor is the timing of

obesity onset: when it occurs before menopause it increases the risk of breast cancer (BC) more than in the postmenopausal period (RR pre-menopause 1.75, post menopause 1.34) [CITATION Cha14 \l 1045]. Increased body weight is not only associated with a more frequent diagnosis of breast cancer but also with an unfavorable treatment outcome. An increase in body weight (by 5 kg/m^2) before diagnosis of BC is associated with a 17% increase in total risk of death, up to 12 months after diagnosis and over this time by 11% and 8% respectively [CITATION Cha14 \l 1045]. Both the time of gaining weight and the intensity of this process are important. Women with obesity in II and III class have a 58% increased risk of breast cancer [CITATION Neu15 \l 1045]. Interestingly, women with a body mass index (BMI) > 35 kg/m^2 had a higher risk of breast cancer with the expression of estrogen (ER) and progesterone receptors (PR). There was no association between weight gain and an increased risk of cancer without the estrogen receptors expression. Additionally, no correlation was found between premenopausal hormone therapy, BMI, and breast cancer [CITATION Neu15 \l 1045].

In the case of patients with a higher BMI, tumors of larger dimensions, less differentiation and more frequent lymph node metastases were diagnosed[CITATION Neu15 \l 1045].

Obesity after oncological treatment

The body composition of female patients undergoing and after oncological treatment undergoes dangerous changes [CITATION Dal08 \l 1045]. Catabolic processes, prolonged periods of weakness or bedrest, increased inflammatory state, loss of appetite, and changes in taste during the disease causes reduction in nutrient intake and an inability to engage in regular physical activity. This leads to unfavorable changes in body composition [CITATION Cru \l 1045 \m Kłę15] such as:

- loss of muscle mass (LBM) and strength,
- decreased physical performance,
- increase in fat tissue content.

These changes are characteristic for sarcopenia or sarcopenic obesity and have a negative impact on treatment course. The International guidelines for the assessment of nutritional status (GLIM) highlight the importance of assessing muscle mass by including its measurement as one of the phenotypic criteria for this assessment on a par with weight loss (>5% within six months, or >10% beyond six months), low BMI (<20 if <70 years, or <22 if >70 years)[CITATION Ced191 \l 1045]. Assessing malnutrition using only BMI is insufficient because loss of lean body mass may be masked by excess fat mass [CITATION Del18 \l 1045]. Therefore, an obese patient according to the GLIM criteria (due to loss of muscle mass) could also be considered a malnourished patient.

The incidence of sarcopenia in breast cancer patients varies, depending on the measurement techniques from 15.9% to 47.8% (dual X-ray absorptiometry scans *vs.* CT scans), event to 58% [CITATION Del18 \m Zha20 \l 1045]. Sarcopenia increases the risk of complications (postoperative complications, chemotherapy toxicity, cardiovascular disease e.g., hypertension – the reduction in muscle mass also reduces the expression of myokines, including irisin, involved in the maintenance of vagal tone and in the parasympathetic modulation of cardiac function) and prolongs rehabilitation. It reduces the percentage of patients responding to treatment, overall survival (OS), progression-free survival PFS), quality of life (Q0L), increases the risk of depression, and overall mortality in breast cancer survivors[CITATION Vil12 \l 1045].

Unintentional loss of body weight, which is often accompanied by loss of muscle tissue, should automatically alert the therapeutic team. Monitoring patients (weight, muscle mass) and promptly addressing any abnormalities in body weight and body composition is crucial to providing optimal care [CITATION Car16 \l 1045]. Adequate nutrient supply, particularly protein, and regular physical activity are crucial during and after treatment, as the adverse effects of chemotherapy and radiotherapy may result in undesirable changes in body composition that have been demonstrated to persist for months or even years [CITATION Yip15 \l 1045].

Prehabilitation as a method of supporting therapy

Prehabilitation is a comprehensive process that prepares patients for surgery and long-term oncological treatment, including chemotherapy, immunotherapy, and radiotherapy. The fundamental premise of this process is to ensure the optimal state of health of patients, enabling successful surgical procedures without complications. Prehabilitation facilitates the implementation of therapy, helps minimize adverse events (AE) and contributes to a faster return to optimal psycho-physical condition [CITATION San15 \m Kłę16 \l 1045]. The effectiveness of this process depends on the cooperation between the interdisciplinary prehabilitation team, which should include: a physician (surgeon, oncologist, anesthesiologist), clinical dietitian, physiotherapist, psychologist, nurse, and the patient. Prehabilitation is based on four inseparable pillars:

- elimination of addictions,
- psychological support,
- nutritional preparation,
- physical activity.

Every single pillar has an individual character and guidelines which are adapted to the patient's current condition and the expected effect [CITATION Mac \l 1045]. Each element of prehabilitation is crucial, but special attention is focused on nutritional and physical preparation for treatment.

Nutritional preparation is an extremely important pillar of prehabilitation, although it is often overlooked. The patient's nutrition in the perioperative period, before and during chemotherapy and radiotherapy, has a direct impact on the course and effectiveness of treatment [CITATION Mac \l 1045]. All patients before starting any planned treatment should be under the supervision of a clinical dietitian. The clinical dietitian will determine the patient's nutritional status and individual needs (for macro-, micronutrients and fluids). Particular attention should be paid during this period to patients with low muscle mass (malnourished according to the GLIM criteria [CITATION Ced191 \l 1045] and high body mass which are associated with worse treatment outcomes [CITATION Zha20 \l 1045 \m Vil12 \m EMA \m Pam18]. American studies indicate that if breast cancer patients >50 years of age maintained a BMI <25 kg/m^2, approximately 11-18 thousand deaths could be avoided per year[CITATION Pet021 \l 1045]. Therefore, both during preparation for surgery and other oncological treatments, in the case of obese patients, the goal is to reduce body weight with maintaining or rebuilding muscle mass [CITATION Pet02 \l 1045]. For this purpose, nutritional treatment should focus on an adequate supply of protein and supplementation of omega-3 fatty acids.

The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines on nutrition in cancer patients recommends protein intake above 1 g/kg body weight/day and if possible, up to 1.5 g/kg BW/day [CITATION Mus21 \l 1045]. The synthesis of muscle tissue in oncological patients is extremely difficult due to the inflammation associated with the disease. It is also important to consider that the synthesis of muscle tissue in the geriatric population requires an increased supply of protein per kilogram of body weight compared to younger individuals. This is due to several factors, including disturbed intracellular signalling, impaired circulation of nutrients in the blood, the presence of chronic inflammation, and reduced physical activity. [CITATION Moo15 \l 1045]. In this population, to maximize skeletal muscle protein synthesis, an intake of 25-30 g of high-quality protein per meal is required [CITATION Pad09 \l 1045].

One of the amino acids that is often used in the perioperative period is arginine. This amino acid contributes to the wound healing process at every stage (synthesis of nitric oxide, growth factors,

collagen), and is an essential amino acid for the proliferation and activation of immune system cells. Due to this effect, it is used as a common component of immunonutrition. However, it must be noted that arginine supplementation is not recommended for routine use. Some types of cancer cells are dependent on external arginine sources (arginine auxotrophy) due to the inability of its synthesis to internally. In other words, some type of cancer cells may respond to Arg supplementation with growth. Deficiencies of the key enzymes in the synthesis of arginine (arginine succinate synthetase, ASS1) have been found in some cancer types e.g., hepatocellular, prostate, pancreatic, head and neck carcinoma, malignant melanoma [CITATION Jah18 \l 1045]. Moreover, breast cancer expresses high levels of another enzyme arginase (ARG1), which is associated with polyamine production (growth factors) and inhibition of the NO generation by macrophages. This leads to cancer cell proliferation, Arg deprivation in the tumor microenvironment, inhibition of T-cell proliferation and impairment of their functions. [CITATION Mat21 \l 1045]. Other components of immunomodulatory diets are beta-glucans, or more precisely, the dectin-1 receptor, which are responsible for triggering immunostimulatory effects. Immunonutrition also uses ingredients such as selenium, zinc, and vitamin C, which will regenerate wounds and support the immune system [CITATION Are06 \l 1045].

Supplementation with omega-3 fatty acids (another immunomodulatory component) is recommended in patients with advanced cancer undergoing chemotherapy and at risk of weight loss or malnourished (ESPEN, Clinical Nutrition in cancer, 2021)[CITATION Mus21 \l 1045]. The consumption of omega-3 fatty acids improves appetite, food intake, increases lean body mass and body weight. These fatty acids, on the one hand, reduce synthesis of pro-inflammatory mediators [CITATION Are06 \l 1045], and, on the other, have the ability to increase (even double) the anabolic response in reaction to increased amino acid and insulin concentrations [CITATION McG191 \l 1045]. However, the anabolic effect of omega-3 fatty acids requires long-term intervention. A change in the structure of the myocyte cell membrane and, therefore, a change in their sensitivity to anabolic signals (increased concentration of amino acids in the blood) occurs over a period of 4–6 weeks, with supplementation of 5 g of omega-3/day [CITATION McG191 \l 1045] (fig. 2).

The diet of a prehabilitated patient should, first be individually tailored to the patient's health condition and needs. The frequently used intervention is a modification of the usual diet (often a reduction diet) with high protein content and supplementation with omega-3 acids (1–2 g/d) Doses exceeding 2 g/day of EPA + DHA are generally required to reduce levels of prostaglandin E2. In the treatment of hypertriglyceridemia or inflammatory disorders, the most commonly administered dosage is 3.0 to 3.5 g/day of EPA + DHA. The European Union has established that doses of EPA and DHA up to 5 g per day are safe [CITATION Fab15 \m Sci12 \l 1045]. As long as BC patients consume an adequate amount of protein and follow dietary recommendations, dietary fortification is rarely

required. It is also worth noting that each patient should be educated on the importance of hydration which influence e.g., taste perception, especially during chemotherapy. It is recommended that oncology patients should drink 30–40 ml/kg BW/ day [CITATION Kłę15 \l 1045 \m Kłę19].

According to ESPEN and Enhance Recovery After Surgery Society (ERAS Society) recommendations, providing increased nutritional support (especially protein intake) prior to planned surgery is beneficial in many clinical situations but depends on a number of variables. However, if the patient is malnourished or at risk of malnutrition, surgery can be postponed for 10–14 days. [CITATION Wei \l 1045]. On the day before surgery and 2–3 hours before the procedure, it is recommended that the patient should consume an oral carbohydrate solution. This approach minimizes the body's response to injury, postoperative insulin resistance and hyperglycemia, and has a protective effect on muscle tissue [CITATION Wei \l 1045 \m Tem171].

The fourth pillar of prehabilitation is physical activity. Lack of physical physical strength the sensitivity of muscle cells to anabolic signals such as an increase in amino acid concentration in the blood. Additionally poor physical function is a predictor of adverse events in the perioperative period [CITATION Mor16 \l 1045] and poor outcomes in the long term. Moderate physical activity (3–5 h/week) will influence the effectiveness of treatment, including overall survival (OS), especially in patients with hormone-dependent cancer [CITATION Hol05 \l 1045] and it is a cost-effective procedure [CITATION Tew \l 1045]. Muscle tissue has an important impact on the functioning of the immune system, mediated by myokines. Physically active patients after diagnosis of breast cancer have a higher survival rate than physically inactive patients, and these effects are mediated by regulation of natural killer cells. The breast cancer survivors can also mobilize NK cells to the circulation to the same degree as age-matched healthy controls by exercise [CITATION Hoj181 \l 1045 \m Sev20].

Therefore, each patient should have an individually prescribed set of exercises adapted to their health condition and physical predispositions aimed at changing the body mass composition (resistance training), and increasing the patient's aerobic capacity (aerobic training). Most patients preparing for surgery or the entire treatment process, require consultation with a physiotherapist [CITATION Hen11 \l 1045]. Appropriately selected physical exercises performed daily for a minimum 2 week period (optimally 4–6 weeks) will help eliminate the side effects of surgical treatment e.g., the most common respiratory complications. These is why a form of resistance training of the diaphragm, respiratory muscles, and intercostal muscles – inspiratory muscle training should be especially included in the prehabilitation exercise program [CITATION Gil15 \l 1045]. Physical activity

may also be an effective remedy for chronic fatigue frequently reported by BC patients [CITATION McT06 \l 1045].

Treatment methods and effects on body weight

Treatment of breast cancer includes a wide range of interventions as surgical treatment, radiotherapy, and systemic treatment (hormone therapy HT, immunotherapy, chemotherapy CT as neoadjuvant or adjuvant treatment). There are many regimens due to dynamic development of personalized treatment which are based on receptor expression on cancer cells [CITATION Goy22 \l 1045]. Due to such a large variety of therapies and drugs used to treat breast cancer, we can expect various adverse events and, consequently, different effects on body weight.

Weight gain during treatment is most common in HR+ breast cancer treatment, however studies indicate an ambiguous relationship between e.g. TMX therapy and weight gain (tab. I). It is also worth noting that patients with adjuvant chemotherapy (CT) prior to TMX for the first 3 years were more obese than those who had not undergone CT and this may be due to the prolonged effects of chemotherapy [CITATION Lim17 \l 1045].

Other adverse events accompanying oncological treatment which affect nutritional status (body weight and body composition) are vomiting [CITATION EMA \l 1045 \m Hur23 \m Nas12], decreased appetite [CITATION Hur23 \l 1045 \m EMA23 \m Bas12 \m Swa12] anorexia [CITATION Joh19 \l 1045], feeling of fullness [CITATION Mel \l 1045], xerostomia [CITATION Nat23 \l 1045], diarrhea[CITATION EMA \l 1045 \m Hur23 \m EMA23 \m Bas12 \m Mos22], constipation [CITATION Dzi22 \l 1045], loss or change of taste [CITATION Bas12 \l 1045 \m Swa12 \m Rav05], mucositis [CITATION Ela20 \l 1045]. These events, through their negative impact on adequate protein and energy intake affect the results of oncological treatment.

Nutritional guidelines for obese patients during and after completion of therapy

Diet may, on the one hand, be a factor influencing the risk of developing breast cancer and, on the other hand, be a factor influencing the course of oncological treatment (tab. II) [CITATION Woj16 \l 1045]. Weight gain (overweight or obesity) during or after cancer treatment increases the risk of the disease (HR+), is a predictor of poor prognosis, increases recurrence, and reduces the overall survival (OS) [CITATION Hea85 \l 1045]. Moreover, women who survive breast cancer have a 30% higher risk of developing another type of cancer[CITATION McI01 \l 1045]. For this reason, the oncologist should

recommend a reduction diet, with adequate protein intake by a clinical dietitian [CITATION Sch00 \l 1045], and lifestyle changes including physical activity and psychosocial support.

Inadequate protein supply will affect the functioning of the immune system both during treatment (e.g., with checkpoint inhibitors ICI) and after its completion. Lack of sufficient protein delivery leads to atrophy of the thymus, reduction of thymus-dependent areas in lymphatic organs, a decreased number of T lymphocytes, inability to produce responses to T-dependent antigens, cell-mediated responses, activity of macrophage system, complement system (C1, C2, C4, C3)[CITATION Sob13 \l 1045]. Insufficient protein intake not only weakens the immune system, but also contributes to the depletion of muscle tissue. Muscle mass loss is associated with high neutrophil to lymphocyte ratios or proteolytic cascades (increase TNF-α), which promote tumor migration and invasion[CITATION Zha20 \l 1045]. If one considers that muscle tissue has an important impact on the function of the immune system (mediated by myokines), the need to preserve this tissue becomes obvious. Interventions such as adequate protein and energy supply and physical activity ("exercise oncology") are necessary, and it should be perceived as multidisciplinary supportive care during and after treatment[CITATION Tor22 \l 1045].

Maintaining the appropriate energy balance and thus proper body weight is related to improving BC patient prognosis and quality of life [CITATION Fat \m Dem01 \m Lak12 \m Sha12 \m Dęb10 \l 1045]. Consumption of foods rich in dietary fiber, soy, lower consumption of saturated fatty acids and total fats are related to higher survival after BC [CITATION Hea85 \m Fat \l 1045]. A meta-analysis by Xing et al. suggests that following a low-fat diet after a BC diagnosis can improve survival by reducing the risk of disease recurrence by 23% [CITATION Xin14 \l 1045]. Breast cancer survivors whose diet was characterized by the highest dietary quality index had a 23% lower mortality rate compared to women with the lowest dietary quality index category [CITATION Fat \l 1045].

A meta-analysis by Lee, et al. [CITATION Chr151 \l 1045] showed that following the DASH diet and Chinese Pagoda Guidelines can reduce breast cancer-related mortality. This relationship turned out to be particularly important in older people, physically fit and women with cancer call with estrogen (ER+) and human epidermal growth factor 2 receptors expression (HER2+), and without progesterone receptor expression (PR-) [CITATION Chr151 \l 1045]. A diet based on the Mediterranean model was able to improve the body's antioxidant capacity as well as the glycemic profile [CITATION Par091 \l 1045].

The above-mentioned dietary models are based on the consumption of vegetables, fruit, whole grain products, eggs, fish, lean meats, and dairy products, as well as limiting the consumption of salt, fat, sugar, and alcohol. The Pagoda guidelines additionally recommend at least: 150 minutes

of physical activity per week and performing at least 6000 steps a day [CITATION Maz10 \m Dal08 \m Pal16 \l 1045].

The study, conducted as part of the Nurses' Health Study (NHS; 1980–2010) and NHSII (1991–2011) involved 8,927 women with stage I-III breast cancer, concluded that total fruit and vegetable (green, leafy, and cruciferous vegetables) intake was associated with lower all-cause mortality (ACM) but not with breast cancer-specific mortality. It is worth highlighting that a higher consumption of fruit juices (except orange juice) was associated with worse breast cancer- and non-breast cancer-related survival[CITATION Cha14 \l 1045].

The composition of the microbiota found in the mammary glands seems to be diverse and may influence both the development of BC and the course of treatment. Researchers will confirm the hypothesis that intestinal dysbiosis is the source of the development of breast cancer (BC). Disturbed microbiota activate mast cells in the breast, which will facilitate the spread of cancer cells[CITATION Kon22 \l 1045]. Diets rich in dietary fiber may have a beneficial effect on composition (increased diversity) and functioning of the intestinal microbiota and therefore on the functioning of the immune system [CITATION OhB \m Bie81 \l 1045]. For this reason, the consumption of various sources of fiber is crucial before and after BC treatment.

Better diet quality after cancer diagnosis appears to be associated with lower levels of inflammation measured by the C-reactive protein (CRP), regardless of BMI or physical activity [CITATION Neu15 \m Kon22 \m Par21 \m Fer18 \l 1045]. On the other hand, the high risk of cancer recurrence in obese patients may be caused by pro-inflammatory cytokines e.g., CRP, IL-3, IL-6, IL-8, as well as TNFα [CITATION Mir19 \l 1045].

Conclusions

Increased body weight is not only associated with a more frequent diagnosis of breast cancer but also with an unfavorable treatment outcome (decreased QoL, disease free survival, DFS, and overall survival OS). The time of gaining weight (before or after menopause) and the intensity of this process influences treatment results. Therefore, maintaining the appropriate energy balance and proper body weight and composition of BC patients is crucial. In this area, the support of a clinical dietitian and physiotherapist is necessary. The oncologist should recommend a reduction diet with adequate protein intake (1,2 g/kg body weight/day and if possible up to 1.5 g/kg BW/day) by a clinical dietitian and lifestyle changes including physical activity. Clinical dietitians’ support during and after breast cancer treatment is an essential element that can improve the patient's prognosis.

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Authors contributions

Ewa Stachowska – conceptualization, writing – review and editing.

Nikola Janowska – writing – original draft preparation.

Agata Łyczek – writing – original draft preparation.

Natalia Komorniak - writing – review and editing.

Natalia Jakubiak – visualization.

Karolina Siedlecka-Kaźmierczak – writing – review and editing.

Conflicts of interest

None declared

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References

1. Mazur-Roszak M. et al. Otyłość a rak piersi. *Współ. Onkol.* 2010, 14 (4): 270–275; DOI: 10.5114/wo.2010.14436.

2. Arends J et al. ESPEN guidelines on enteral nutrition: non-surgical oncology. *Clin. Nutr.* 2006, Apr;25(2):245-59. doi: 10.1016/j.clnu.2006.01.020.

3. Pischon T et al. Obesity and cancer. *Proc Nutr Soc.* 2008, May;67(2):128-45. doi: 10.1017/S0029665108006976.

4. Chan DS et al. Body mass index and survival in women with breast cancer – systematic literature review and meta-analysis of 82 follow-up studies. *Ann Oncol.* 2014, Oct;25(10):1901-1914. doi: 10.1093/annonc/mdu042.

5. Neuhouser ML et al. Overweight, obesity, and postmenopausal invasive breast cancer risk: a secondary analysis of the Women's Health Initiative randomized clinical trials. *JAMA Oncol.* 2015, Aug;1(5):611-21. doi: 10.1001/jamaoncol.2015.1546.

6. Dal Maso L et al. Prospective analysis of case-control studien on environmental factors and health (PACE) study group. Effect of obesity and other lifestyle factors on mortality in women with breast cancer. *Int. J. Cancer.* 2008, Nov 1;123(9):2188-94. doi: 10.1002/ijc.23747.

7. Cruz-Jentoft AJ et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing*. 2010, 39:412–423. doi: 10.1093/ageing/afq034.

8. Kłęk S et al. Standardy leczenia żywieniowego w onkologii. *Nowotw. J. Oncol.* 2015, 65(4):320–337 DOI: 10.5603/NJO.2015.0062.

9. Cederholm T et al. GLIM criteria for the diagnosis of malnutrition - A consensus report from the global clinical nutrition community. *J Cachexia Sarcopenia Muscle.* 2019, Feb;10(1):207-217. doi: 10.1002/jcsm.12383.

10. Deluche E et al. Impact of body composition on outcome in patients with early breast cancer. *Support Care Cancer.* 2018, Mar;26(3):861-868. doi: 10.1007/s00520-017-3902-6.

11. Zhang X-M et al. Sarcopenia as a predictor of mortality in women with breast cancer: a meta-analysis and systematic review. *BMC Cancer.* 2020, 20:172; DOI.org/10.1186/s12885-020-6645-6.

12. Villaseñor A et al. Prevalence and prognostic effect of sarcopenia in breast cancer survivors: the HEAL Study. *J Cancer Surviv* . 2012, 6, 398–406 (2012). https://doi.org/10.1007/s11764-012-0234-x.

13. Carneiro IP et al. Clinical implications of sarcopenic obesity in cancer. *Current oncology reports*. 2016, Oct;18(10):62. doi: 10.1007/s11912-016-0546-5. .

14. Yip C. et al. Imaging body composition in cancer patients: visceral obesity, sarcopenia and sarcopenic obesity may impact on clinical outcome. *Insights into imaging*. 2015, Aug;6(4):489-97. doi: 10.1007/s13244-015-0414-0.

15. Santa Mina D et al. Optimization of surgical outcomes with prehabilitation. *Appl Physiol Nutr Metab*. 2015, Sep;40(9):966-9. doi: 10.1139/apnm-2015-0084.

16. Kłęk S et al. Protokół ERAS – sposoby odżywiania i leczenia żywieniowego pacjentów oddziału chirurgicznego. Protokół ERAS dla poprawy wyników leczenia. Sposoby odżywiania i leczenia żywieniowego pacjentów oddziału chirurgicznego. *Medycyna Praktyczna*. [Online] 01 04 2016. https://www.mp.pl/eras/wytyczne/show.html?id=132020.

17. Macmillan Cancer Support et al. Macmillan Cancer Support, NIHR Cancer and Nutrition CPrehabilitation for people with cancer: Principles and guidance for prehabilitation within the management and support of people with cancer . [Online] 2019. www.macmillan.org.uk/assets/prehabilitationguidance-for-people-with-cancer.pdf.

18. Durrand J et al . Prehabilitation. *Clin Med (Lond)*. 2019, Nov;19(6):458-464. doi: 10.7861/clinmed.2019-0257.

19. EMA. Sumary of product characteristics - Tecentriq. 2023 updata, EMEA/H/C/004143; https://www.ema.europa.eu/en/medicines/human/EPAR/tecentriq .

20. Pamoukdjian F et al. Prevalence and predictive value of pre-therapeutic sarcopenia in cancer patients: A systematic review. *Clinical Nutrition*. 2018, 37:1101–1113; https://doi.org/10.1016/j.clnu.2017.07.010.

21. Petrelli JM et al. Body mass index, height, and postmenopausal breast cancer mortality in a prospective cohort of US women. *Cancer Causes Control*. 2002, May;13(4):325-32. doi: 10.1023/a:1015288615472.

22. —. Body mass index, height, and postmenopausal breast cancer mortality in a prospective cohort of US women. *Cancer Causes Control*. . 2002, May;13(4):325-32. doi: 10.1023/a:1015288615472.

23. Muscaritoli M et al. ESPEN practical guideline: Clinical Nutrition in cancer. *Clin Nutr*. . 2021, May;40(5):2898-2913. doi: 10.1016/j.clnu.2021.02.005.

24. Moore DR et al. Protein ingestion to stimulate myofibrillar protein synthesis requires greater relative protein intakes in healthy older ver sus younger men. *J Gerontol A Biol Sci Med Sci*. 2015, Jan;70(1):57-62. doi: 10.1093/gerona/glu103.

25. Paddon-Jones D et al. Dietary protein recommendations and the prevention of sarcopenia. . *Curr Opin Clin Nutr Metab Care*. . 2009 , Jan;12(1):86-90. doi: 10.1097/MCO.0b013e32831cef8b.

26. Jahani M et al. Arginine: Challenges and opportunities of this two-faced molecule in cancer therapy;. *Biomedicine & Pharmacotherapy.* 102, 2018, 594–601; doi.org/10.1016/j.biopha.2018.02.109.

27. Matos A et al. Arginine and Arginases Modulate Metabolism, Tumor Microenvironment and Prostate Cancer Progression. *Nutrients*. 2021, Dec 16;13(12):4503. doi: 10.3390/nu13124503.

28. McGlory C et al. The Influence of Omega-3 Fatty Acids on Skeletal Muscle Protein Turnover in Health, Disuse, and Disease. *Front Nutr.* 2019, Sep 6;6:144. doi: 10.3389/fnut.2019.00144.

29. Fabian CJ et al. Omega-3 fatty acids for breast cancer prevention and survivorship. *Breast Cancer Res.* . 2015, May 4;17(1):62. doi: 10.1186/s13058-015-0571-6.

30. EFSA Panel on Dietetic Products Nutrition and Allergies (NDA). Scientific Opinion on the Tolerable Upper Intake Level of eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA) and docosapentaenoic acid (DPA). *EFSA Journal.* 2012, 10(7):2815; https://doi.org/10.2903/j.efsa.2012.2815.

31. Kłęk S. (red) et al. *Standardy Żywienia Dojelitowego i pozajelitowego.* Kraków : Scietifica sp. z o.o., 2019.

32. Weimann A et al. ESPEN practical guideline: Clinical nutrition in surgery. *2021.* Jul;40(7):4745-4761. https://doi.org/10.1016/j.clnu.2021.03.031.

33. al Temple-Oberle et. Consensus Review of Optimal Perioperative Care in Breast Reconstruction: Enhanced Recovery after Surgery (ERAS) Society Recommendations. *Plast Reconstr Surg*. . 2017, May;139(5):1056e-1071e. doi: 10.1097/PRS.0000000000003242. .

34. Moran J et al. The preoperative use of field tests of exercise tolerance to predict postoperative outcome in intra-abdominal surgery: a systematic review. *J Clin Anesth.* 2016, Dec;35:446-455. doi: 10.1016/j.jclinane.2016.09.019.

35. Holmes MD et al. Physical activity and survival after breast cancer diagnosis. *JAMA*. 2005, May 25;293(20):2479-86. doi: 10.1001/jama.293.20.2479.

36. Tew GA et al. Randomized feasibility trial of high-intensity interval training before elective abdominal aortic aneurysm repair. *Br J Surg*. 2017 Dec;104(13):1791-1801. doi: 10.1002/bjs.10669.

37. Hojman P et al. Molecular Mechanisms Linking Exercise to Cancer Prevention and Treatment. *Cell Metabolism.* 2018, January 9, 2018; https://doi.org/10.1016/j.cmet.2017.09.015.

38. Severinsen MCK et al. Muscle-Organ Crosstalk: The Emerging Roles of Myokines. *Endocr Rev.* . 2020 , Aug 1;41(4):594–609. doi: 10.1210/endrev/bnaa016.

39. Hennis PJ. et al. Hennis PJ.Cardiopulmonary exercise testing for the evaluation of perioperative risk in non-cardiopulmonary surgery. *Postgrad Med J.* 2011, 87:550–7. doi: 10.1136/pgmj.2010.107185.

40. Gillis C et al. Promoting perioperative metabolic and nutritional care. *Anesthesiol.* 2015, Dec;123(6):1455-72. doi: 10.1097/ALN.0000000000000795.

41. Kincaid AE et al. Cancer Prevention and Management Through Exercise and Weight Control. *Physical Therapy*, . 2006, Volume 87, Issue 5, 1 May 2007, Page 615, https://doi.org/10.2522/ptj.2007.87.5.615.

42. Goyal A et al. Weight Gain after Hormone Receptor-Positive Breast Cancer. *Curr Oncol.* . 2022, Jun 6;29(6):4090-4103. doi: 10.3390/curroncol29060326. .

43. Lima MTM et al. Temporal influence of endocrine therapy with tamoxifen and chemotherapy on nutritional risk and obesity in breast cancer patients. *BMC Cancer.* 2017, Aug 29;17(1):578. doi: 10.1186/s12885-017-3559-z. .

44. Hurvitz SA et al. Trastuzumab deruxtecan versus trastuzumab emtansine in patients with HER2-positive metastatic breast cancer: updated results from DESTINY-Breast03, a randomised, open-label, phase 3 trial;. *Lancet.* 2023, 401: 105–17; https://doi.org/10.1016/S0140-6736(22)02420-5.

45. B Nasiłowska-Adamska. Profilaktyka i leczenie zaburzeń przewodu pokarmowego towarzyszących chemioterapii i radioterapii. *Gastroenterologia Kliniczna. Postępy i Standardy.* 2012, https://journals.viamedica.pl/gastroenterologia_kliniczna/article/view/29264.

46. EMA. Sumary of product characteristics - KEYTRUDA. 2023, EMEA/H/C/003820; https://www.ema.europa.eu/en/medicines/human/EPAR/keytruda#product-information-section.

47. Baselga J et al. Everolimus in Postmenopausal Hormone-Receptor–Positive Advanced Breast Cancer. *N Engl J Med.* 2012, 366:520-9; DOI:10.1056/NEJMoa1109653.

48. Swain SM et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA): end-of-study results from a double-blind, randomised, placebo-controlled, phase 3 study. *Lancet Oncol.* 2020, Apr;21(4):519-530. doi: 10.1016/S1470-2045(19)30863-0.

49. Johannes CM et al. Anorexia and the Cancer Patient. *Vet Clin North Am Small Anim Pract.* 2019, Sep;49(5):837-854. doi: 10.1016/j.cvsm.2019.04.008.

50. Mello AT et al. Effect of oral nutritional supplements with or without nutritional counselling on mortality, treatment tolerance and quality of life in head-and-neck cancer patients receiving (chemo)radiotherapy: a systematic review and meta-analysis. *British Journal of Nutrition*. . 2021, 125(5):530-547. doi:10.1017/S0007114520002329.

51. Nathan CO et al. Current management of xerostomia in head and neck cancer patients. *Am J Otolaryngol*. 2023, Jul-Aug;44(4):103867. doi: 10.1016/j.amjoto.2023.103867.

52. Moschen AR et al. The Underestimated and Overlooked Burden of Diarrhea and Constipation in Cancer Patients. 2022, Jul;24(7):861-874. doi: 10.1007/s11912-022-01267-3.

53. Dzierżanowski T Mercadante S. Constipation in Cancer Patients - an Update of Clinical Evidence. *Curr Treat Options Oncol*. . 2022, Jul;23(7):936-950. doi: 10.1007/s11864-022-00976-y.

54. P Ravasco. Aspects of taste and compliance in patients with cancer. *Eur J Oncol Nurs*. 2005, 9 Suppl 2:S84-91. doi: 10.1016/j.ejon.2005.09.003.

55. Elad S et al. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. *Cancer*. 2020, Oct 1;126(19):4423-4431. doi: 10.1002/cncr.33100.

56. Nyrop KA et al. Weight gain during adjuvant endocrine treatment for early-stage breast cancer: What is the evidence? *Breast Cancer Res Treat*. Jul;158(2):203-17, 2016, doi: 10.1007/s10549-016-3874-0.

57. Raghavendra A et al. Determinants of Weight Gain During Adjuvant Endocrine Therapy and Association of Such Weight Gain With Recurrence in Long-term Breast Cancer Survivors. *Clin Breast Cancer*. 2018, Feb;18(1):e7-e13. doi: 10.1016/j.clbc.2017.11.006.

58. Cortes J et al. Pembrolizumab plus Chemotherapy in Advanced Triple-Negative Breast Cancer. *N Engl J Med*. 2022, 2022;387:217-26; DOI: 10.1056/NEJMoa2202809.

59. Wojciechowska U et al. Nowotwory złośliwe w Polsce w 2014 roku. *Centrum Onkologii — Instytut*. 2016.

60. Heasman KZ et al. Weight gain during adjuvant chemotherapy for breast cancer. *Breast Cancer Research and Treatment*. 1985, 5(2):195-200. doi: 10.1007/BF01805994. .

61. McInnes JA et al. Weight Gain and Quality of Life in Women Treated With Adjuvant Chemotherapy for Early-Stage Breast Cancer. *Oncology Nursing Forum*. 2001, May;28(4):675-84. PMID: 11383182.

62. Schwartz AL. Exercise and Weight Gain in Breast Cancer Patients Receiving Chemotherapy. *Cancer Practice*. 2000, Sep-Oct;8(5):231-7. doi: 10.1046/j.1523-5394.2000.85007.x.

63. Sobotka L et al. *Podstawy żywienia klinicznego. Edycja Czwarta. Wydanie Polskie.* Prague : Krakowskie Wydawnictwo Scientifica Sp. z o.o., 2013.

64. Torregrosa C et al. Physical Activity as the Best Supportive Care in Cancer: The Clinician's and the Researcher's Perspectives. *Cancers (Basel).* 2022, Nov 2;14(21):5402. doi: 10.3390/cancers14215402.

65. Kumar N et al. Fatigue, Weight Gain, Lethargy and Amenorrhea in Breast Cancer Patients on Chemotherapy: Is Subclinical Hypothyroidism the Culprit? *Breast Cancer Research and Treatment.* 2004, Jan;83(2):149-59. doi: 10.1023/B:BREA.0000010708.99455.e1.

66. Demark-Wahnefried W et al. Changes in Weight, Body Composition, and Factors Influencing Energy Balance Among Premenopausal Breast Cancer Patients Receiving Adjuvant Chemotherapy. *Journal of Clinical Oncology.* 2001, May 1;19(9):2381-9. doi: 10.1200/JCO.2001.19.9.2381.

67. Lakhani S et al. *WHO classification of tumours of the breast. 4th ed. IARC Press.* Lyon : brak nazwiska, 2012. ISBN-13, 978-92-832-2433-4.

68. Shao M et al. Targeting the insulin growth factor and the vascular endothelial growth factor pathways in ovarian cancer. *Mol Cancer Ther.* 2012, 11(7): 1576–1586, doi: 10.1158/1535-7163.MCT-11-0961.

69. Dębska S et al. Leczenia hormonalne chorych na raka piersi z nadekspresją receptora HER2. *Onkol Prak Klin.* 2010, 6: 301–310.

70. Xing MY et al. Effect of low-fat diet on breast cancer survival: a meta-analysis. *Asian Pac J Cancer Prev.* 2014, 15(3):1141-4. doi: 10.7314/apjcp.2014.15.3.1141. .

71. Ferlay J et al. *Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11.* [GLOBOCAN 2012 v1.0] Lyon : International Agency for Research on Cancer, 2013.

72. Nowotworów Krajowy Rejestr. Czym jest rak piersi? [Online] 2021. https://onkologia.org.pl/pl/nowotwor-piersi-u-kobiet-czym-jest#page-main-image.

73. O'Brien J et al. Macrophages are crucial for epithelial cell death and adipocyte repopulation during mammary gland involution. *Development.* 2012, 139(2): 269–275, doi: 10.1242/dev.071696.

74. Demark-Wahnefried W et al. Why women gain weight with adjuvant chemotherapy for breast cancer. *J Clin Oncol. .* 1993, Jul;11(7):1418-29. doi: 10.1200/JCO.1993.11.7.1418. PMID: 8315439.

75. Christopoulos PF et al. The role of the insulin-like growth factor-1 system in breast cancer. *Mol Cancer.* 2015, 14: 43, doi: 10.1186/s12943-015-0291-7.

76. Parl FF et al. Estrogen exposure, metabolism, and enzyme variants in a model for breast cancer risk prediction. *Cancer Inform*. 2009, May 5;7:109-21. doi: 10.4137/cin.s2262.

77. Paluch-Shimon S et al. Prevention and screening in BRCA mutation carriers and other breast/ ovarian hereditary cancer syndromes: ESMO Clinical Practice Guidelines for cancer prevention and screening. *Annals of Oncology.* 2016, Sep;27(suppl 5):v103-v110. doi: 10.1093/annonc/mdw327.

78. Konarska I. Zaskakujący związek pomiędzy zdrowiem jelit a rakiem piersi. *Gastroenterologia.* 2022, DOI: 10.1158/2326-6066.CIR-21-1120.

79. Oh B et al. Emerging Evidence of the Gut Microbiome in Chemotherapy. *A Clinical Review. Front Oncol*. 2021, Sep 16;11:706331. doi: 10.3389/fonc.2021.706331.

80. Biela A et al. Nowotwory hormonozależne u kobiet. Mikrobiota a rak piersi. *Nowa Medycyna*. [Online] 2012, nr 4, s. 76-81. www.czytelniamedyczna.pl/4296,nowotwory-hormonozalezne-u-kobiet.html.

81. Parida S et al. A pro-carcinogenic colon microbe promotes breast tumorigenesis and metastatic progression and concomitantly activates notch and βcatenin axes. *Cancer Discovery.* 2021, Doi: 10.1158/2159-8290.CD-20-0537.

82. Fernández MF et al. Breast cancer and its relationship with the microbiota. *Int J Environ Res Public Health*. 2018, 15 (8), s. 1747 [online], doi:10.3390/ijerph15081747.

83. *Probiotyki w onkologii.* Gałęcka Mirosława. Szczecin : Konferencja Mikrobiota, 2019.

84. Shachar S.S. et al. Prognostic value of sarcopenia in adults with solid tumours: A meta-analysis and systematic review. *European Journal of Cancer,*. 2016, vol. 56, DOI: 10.1016/j.ejca.2015.12.030.

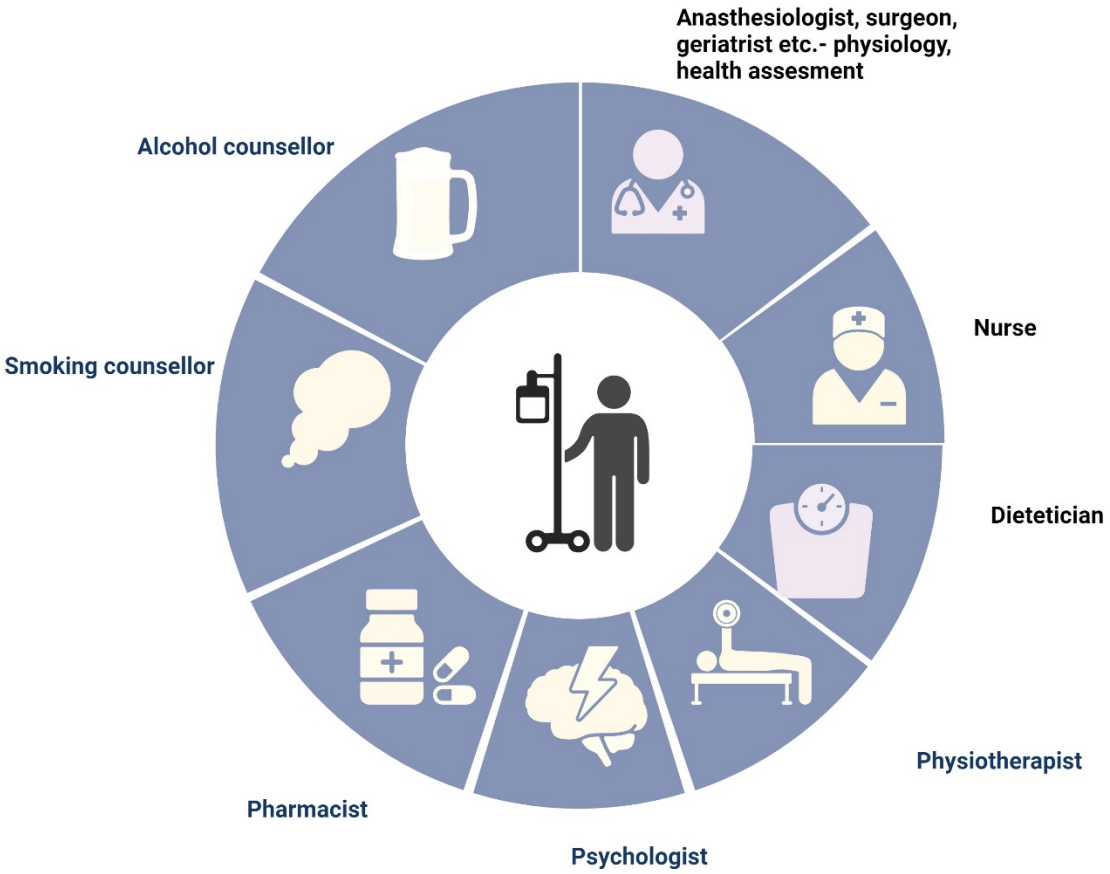
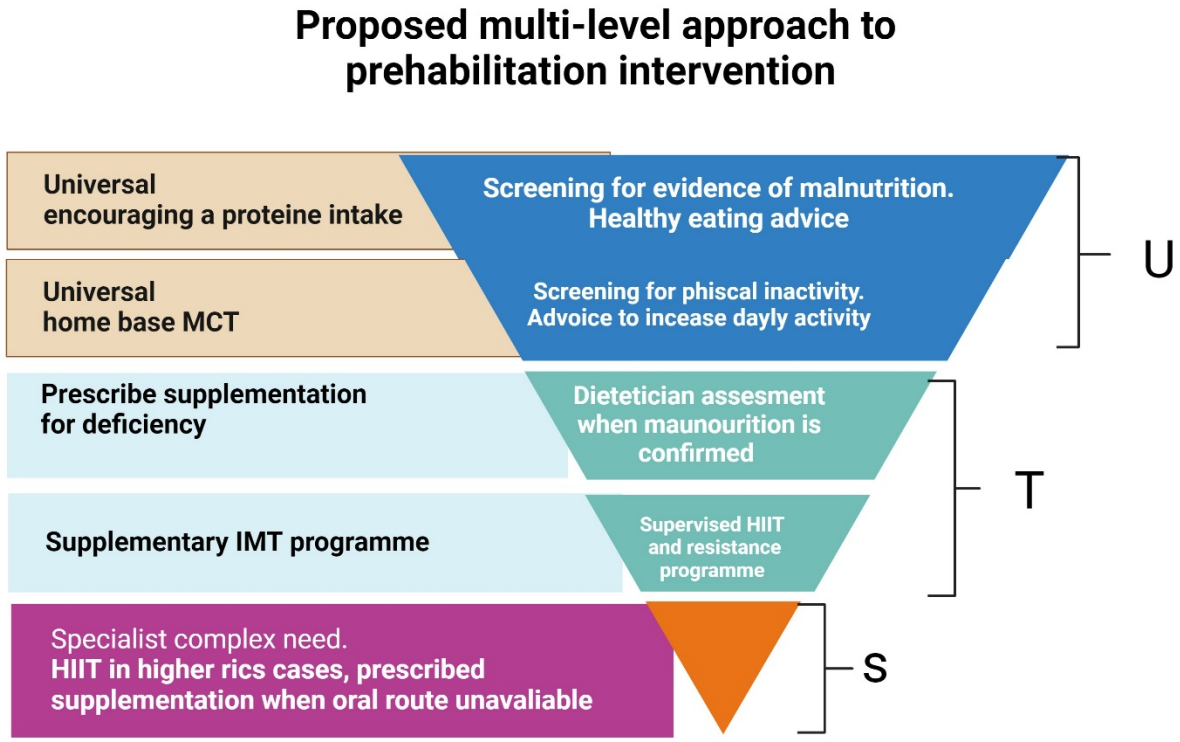


Figure 1. Multidisciplinary team, Durrand J. et al., 2019 [CITATION Dur19 \l 1045]



U – universal; T – targeted; S – specialist

Figure 2. Proposed multi-level approach to prehabilitation intervention (nutritional support and exercise used as examples). Durrand J. et al., 2019 [CITATION Dur19 \l 1045]

Table I. Adverse events affecting body weight in distinct therapeutic regimens

Breast cancer type	**Author**	**Therapy**	**AE affecting body weight**	
HR+	Nyrop KA, et al, 2016[CITATION Nyr16 \l 1045]	TMX	weight gain	• 18-52% of patients in 1st year • 7-55% of patients in the 5th year
	Raghavendra A et al, 2018[CITATIO			• in pre-menopausal patients weight gain >5% is 1.4 times higher than post-

	N Rag18 \l 1045]			menopausal
HR+ recurrence	Baselga J et al, 2012[CITATION N Bas12 \l 1045]	steroidal aromatase inhibitor (SAI) + mTOR inhibitor (everolimus)	weight loss	• 19% of patients in everolimus + exemestane • 5% of patients in placebo + exemestane
			other AE	• stomatitis • decreased appetite • diarrhea • dysgeusia
HER+ advanced, metastatic	Swain SM, et al., 2020[CITATION N Swa12 \l 1045]	pertuzumab + transtuzumab + docetaxel	diarrhea	• 68.4% of patients: mild to moderate • patients >65 years of age > probability of diarrhea
			other AE	in pertuzumab arm: • nausea • stomatitis • loss or change of taste • decreased appetite
unresectable HER+ or HER2–low (IHC1+ OR IHC 2+/ISH–)	Hurvitz SA, et al, 2023[CITATION N Hur23 \l 1045]	second line: T-Dxd (conjugated deruxtecan with trantuzumab)	weight loss	• 23% of patients in group T–Dxd • 9% transtuzumab–emtansine
			other AE	• nausea 77% • vomiting 52% • diarrhea 32% • lack of appetite 30%
TNBC	Cortes J, et al, 2022 [CITATION Cor22 \l 1045]	ICI: pembrolizumab (neoadjuvant or adjuvant [CITATION Cor22 \l 1045]) atezolizumab with nab-	other AE	pembrolizumab: • nausea • abdominal pain • diarrhea • decreased appetite [CITATION EMA23 \l 1045] atezolizumab: • decreased appetite

		paclitaxel		• nausea • diarrhea • vomiting [CITATION EMA \l 1045]

HR+ – hormone receptor (HR)-positive; HER+ – human epidermal growth factor receptor positive; TMX – tamoxifen; IHC1+ or 2+ – immunohistochemistry evaluation of the degree of protein expression; ISH – *in situ* hybridization; TNBC – triple negative breast cancer; ICI – immune checkpoint inhibitors

Table II. Differences between diet with preventive effects, lowering BC recurrence, cancer-related mortality

Diet with preventive effects and lowering breast cancer recurrence, breast cancer-related mortality [CITATION Fer13 \m Kra21 \m OBr12 \l 1045]	**Diet increasing breast cancer risk (pro-inflammatory), elevating risk of cancer recurrence [CITATION Fer13 \m Kra21 \m Dem \l 1045]**
Diet rich in: • fresh vegetables (green-leafy, cruciferous), • fruit, • nuts, • fish (EPA, DHA), • dietary fiber, • soy, • whole grain products, • eggs, • lean meats.	Diet rich in: • highly processed foods (with salt and sugar), • high glycemic index, including fruit juice, • red and processed meat, • alcohol, • saturated fatty acids, • total fat.