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REVIEWS

# Mediterranean diet and breast cancer: A narrative review

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**ABSTRACT**

Breast cancer is the second most common neoplasm and the deadliest among women worldwide. Its incidence varies according to human development and is associated with several risk factors, including age, genetic factors, obesity, and dietary habits. Recent research has revealed a significant influence of dietary habits on the onset and progression of this disease, which is why this review aims to comprehensively analyze the available literature to understand better the role played by the mediterranean diet in the development and management of breast cancer. The mediterranean diet has anti-inflammatory and antioxidant effects, may influence gene regulation, and produce hormonal and intestinal microbiota changes, resulting in improved quality of life for breast cancer patients by alleviating symptoms such as pain, inflammation, and reducing the risk and mortality from this disease. Evidence suggests that greater adherence to the mediterranean diet reduces the risk of breast cancer, as well as an improvement in patients' quality of life and mortality. These findings underscore its potential relevance in the context of dietary patterns associated with breast cancer prevention and management, which could inform considerations for public health policies. Further research is needed to confirm these observations and to understand the underlying mechanisms better.

**KEYWORDS** Breast Cancer, Mediterranean Diet, Breast Cancer Management, healthcare

## INTRODUCTION

Breast cancer ranks as the second most frequently diagnosed neoplasm worldwide and stands out as the most common and lethal cancer among women, with approximately 2.26 million new cases reported in 2020 [1]. Notably, countries with higher levels of human development exhibit higher incidence rates, ranging from under 30 cases per 100 000 in sub-Saharan Africa to over 70 cases per 100 000 in Western Europe and North America [2]. Despite its prevalence in developed regions, most cases are detected in low and middle-income countries, underscoring the significant burden of this disease in these areas [3].

Various established risk factors are associated with breast cancer, with age being the foremost among them [4]. Factors linked to higher development indices, such as early menarche, late menopause, low or null parity, and limited exposure to breastfeeding, also contribute, as evidenced by a reanalysis of 47 epidemiological studies involving 50 302 women with breast cancer and 96 973 controls across 30 countries [5]. Genetic factors, including mutations in genes such as BRCA1 or BRCA2, ATM, BARD1, PALB2, and CHECK2, account for only 20 to 25% of the disease's risk [6], emphasizing the need to explore additional factors associated with this cancer type further.

Obesity and dietary habits are significant contributors to breast cancer risk. Particularly postmenopausal obesity elevates the risk of breast cancer (RR 1.18 (95% CI 1.13 to 1.24) $p < 0.001$), as reported in a 2020 meta-analysis of 197 prospective cohort studies [7]. This study also found that increased consumption of fruits and vegetables acts as a protective factor, reducing the risk of breast cancer (RR 0.87 (95% CI 0.83 to 0.90)), while higher consumption of red meats raises the risk (RR 1.10 (95% CI 1.02 to 1.19)) [8]. Additionally, a 2020 population-based study analyzing the global burden of alcohol-attributable breast cancer found that approximately 4% of all breast cancer cases diagnosed that year were attributable to alcohol, particularly in Europe [9].

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**MAIN MESSAGES**

- Adherence to the mediterranean diet has been linked to a lower risk of breast cancer, thanks to its anti-inflammatory and antioxidant properties. Components like olive oil and polyphenols help reduce oxidative stress and inflammation and influence gene expression, potentially slowing cancer progression.
- For breast cancer patients, following the mediterranean diet improves the quality of life by reducing pain and inflammation. It also promotes better physical and mental well-being, supporting treatment adherence and overall health during cancer care.
- The mediterranean diet may reduce breast cancer mortality by improving treatment response and reducing recurrence risk. Its benefits extend beyond cancer prevention, supporting better long-term health outcomes for survivors.

These findings highlight the connection between dietary habits and breast cancer, emphasizing the need to investigate the role of diet as an etiological factor further. Due to how people consume food, studying dietary patterns can better predict health risks than studying individual foods and components. However, the available evidence remains limited [10].

In this context, the mediterranean diet is a well-established dietary pattern known for its health benefits. It is characterized by an abundant intake of fruits, vegetables, nuts, whole, unrefined grains, and extra virgin olive oil, moderate consumption of fish, dairy, and alcohol, and a low intake of red meat, saturated fats, and added sugars [11].

Several studies demonstrate the protective effects of the mediterranean diet against breast cancer. A 2014 case-control study involving 250 women with breast cancer and 250 controls found that each unit increase in the mediterranean diet score was associated with a 9% decrease in breast cancer risk (OR 0.91 (95% CI 0.86 to 0.97)) [12]. Similar results were reported in a 2014 case-control study in Spain, where adherence to the mediterranean diet in 1017 incident breast cancer cases and 1017 controls was associated with reduced cancer risk (OR 0.56 (95% CI 0.40 to 0.79)) [13]. Furthermore, in another randomized clinical trial, women following the mediterranean diet with extra virgin olive oil supplementation experienced a 62% decrease in the risk of developing malignant breast cancer compared to the control group (HR 0.38 (95% CI 0.16 to 0.87) p = 0.02) [14]. However, some studies report negative effects [15] or no significant effect [16] of the mediterranean diet on breast cancer, creating disparities in results and preventing a clear conclusion regarding its impact.

Therefore, we aim to comprehensively review the available literature to better understand the mediterranean diet's role in breast cancer development and management. Additionally, we seek to identify potential molecular mechanisms involved in this association, providing a more comprehensive understanding of how diet influences breast cancer prevention and treatment. This could lead to more specific and effective dietary orientations for at-risk women.

## METHODS

For this narrative review, key publications focusing on breast cancer and the mediterranean diet were included. The search was performed using PubMed and the Cochrane Library, employing a combination of relevant keywords such as "Dietary Patterns," "Mediterranean diet," "Diet," "Breast Cancer," "Triple-negative Breast Cancer," and "Neoplasms." Two research team members (AK-Z and E-FT) independently screened the titles and abstracts of the identified articles, selecting them for full review only when both agreed. Additionally, the references of these articles were examined to identify further relevant studies. The final selection of articles underwent a comprehensive content review to explore the evidence linking the mediterranean diet to breast cancer.

## UNRAVELING MOLECULAR MECHANISMS: THE MEDITERRANEAN DIET AS A CORNERSTONE IN BREAST CANCER TREATMENT

As research in the field of oncology advances, the fundamental role of diet in the prevention and treatment of cancer has been increasingly recognized [17]. Among the different dietary options that have emerged, the mditerranean diet has captured researchers' attention due to its potential protective effects against this disease [18]. Accumulated evidence suggests that the bioactive components of the mediterranean diet, such as the monounsaturated fatty acids in olive oil and antioxidants found in fruits and vegetables, may exert significant effects in breast cancer prevention and treatment [19]. However, it is still necessary to better understand the mechanisms through which these benefits occur.

One of the possible mechanisms through which this dietary pattern could influence breast cancer is through its anti-inflammatory and antioxidant effects [20]. Critical components of this diet, such as the monounsaturated fatty acids present in extra virgin olive oil [21] and phytochemicals found in fruits and vegetables, have been shown to reduce inflammation and oxidative stress in the body [22]. These processes are known to play a significant role in the development and progression of breast cancer. These potential effects are supported by several studies, for example, a systematic review conducted in 2021 [23], where six observational studies and seven intervention studies reported a significant decrease in the concentration

of proinflammatory biomarkers C-reactive protein, Interleukin-6 (IL-6), Tumor necrosis factor alpha (TNF-α) and oxidative stress (F2-isoprostane, Oxidized low-density lipoprotein (ox-LDL), soluble Nox2-derived peptide (sNOX2-dp) for mediterranean diet groups compared to control groups.

Additionally, the mediterranean diet has been associated with changes in gene expression and the regulation of molecular pathways involved in cell proliferation, apoptosis, and angiogenesis [24]. For example, studies have shown that the polyphenols present in fruits and vegetables can modulate the activity of genes related to cell survival and metastasis [25], suggesting a potentially positive impact on breast cancer treatment [26]. Similarly, tyrosol and hydroxytyrosol present in extra virgin olive oil could have beneficial effects on breast cancer prevention by reducing glutathione levels [13], inhibiting NF-κB transcription factor activation, and cell apoptosis [27], all processes involved in angiogenesis [28].

Another notable component of the mediterranean diet is whole grains, as they have a low glycemic index and have been associated with a lower risk of breast cancer [29]. This is because foods with a low glycemic index tend to maintain stable blood glucose and insulin levels. The relationship between insulin levels and breast cancer is relevant, as elevated insulin levels can promote cell proliferation and inflammation, critical factors in the development and progression of this cancer type [30], as demonstrated in a meta-analysis of cohort studies showing a significant association between breast cancer and diabetes (RR 1.6 (95% CI 1.02 to 1.11)) [29].

Intestinal microbiota also plays an essential role in human health and well-being and can be modified by factors such as genetics and diet [31]. In particular, the mediterranean diet, characterized by its high content of complex carbohydrates and foods such as fruits, vegetables, whole grains, fish, and olive oil, has been associated with beneficial changes in intestinal microbiota [32]. Studies have revealed that consumers of this diet show greater microbial diversity and a more favorable proportion of specific bacterial genera, such as *Lactobacillus, Clostridium, Faecalibacterium*, and *Oscillospira*, compared to those following a Western diet [33]. Furthermore, it has been observed that mediterranean diet-modified intestinal microbiota is linked to reduced breast cancer risk and progression [34]. The consumption of foods in this diet, rich in probiotics and prebiotics, can influence inflammation and the genetic stability of mammary cells [35,36], suggesting that modulation of intestinal microbiota could be an essential strategy in breast cancer prevention and treatment.

There is another biologically plausible explanation for the potential beneficial effects of the mediterranean diet on breast cancer. Studies suggest that the mediterranean diet may decrease estrogen levels related to the development of this neoplasm. This was reported in a European clinical trial in 2006, where 115 postmenopausal women were randomly assigned to the mediterranean diet or the control group. After six months of follow-up, a decrease of over 40% in estrogen levels was observed in women in the intervention group compared to those in the control group ($p < 0.02$) [37].

These findings provide a foundation for understanding how this dietary pattern can influence breast cancer progression and treatment. From the modulation of inflammation and oxidative stress to the regulation of gene expression and hormonal regulation, this diet appears to be a promising tool in preventing and treating this devastating disease. However, further studies, primarily controlled clinical trials, must confirm these findings and fully understand the molecular mechanisms underlying these effects (Figure 1).

## THE INTEGRAL ROLE OF THE MEDITERRANEAN DIET IN COMPREHENSIVE BREAST CANCER MANAGEMENT

Breast cancer represents a significant burden of morbidity and mortality in women worldwide. The comprehensive approach in its management spans primary prevention to the ongoing care of diagnosed patients. In this context, the mediterranean diet has emerged as a crucial component in the global strategy for breast cancer management.

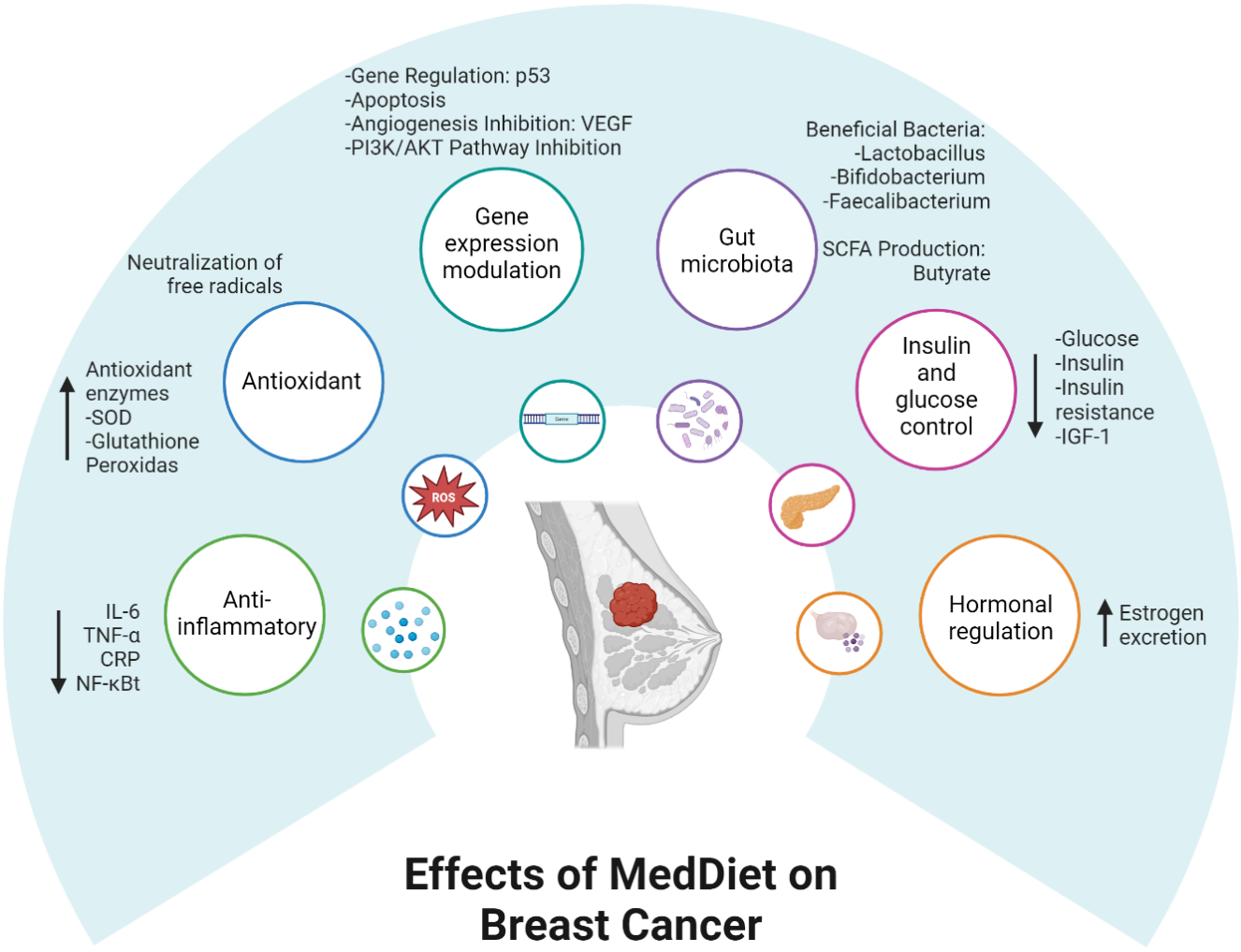
It is known that both the disease and cancer treatment produce a series of unpleasant symptoms, including pain and decreased physical and mental functioning in affected women, potentially reducing treatment adherence and affecting disease prognosis [38]. This dietary pattern, which has been associated with a lower risk of developing breast cancer in various epidemiological studies, has also been shown to improve patients' quality of life [39], enhance prognosis, and even reduce the risk of death [40]. An Italian clinical trial that studied the quality of life of 309 women with breast cancer revealed that higher adherence to the mediterranean diet improved physical functioning ($p = 0.001$), reduced pain ($p = 0.002$), increased overall well-being ($p = 0.05$), and enhanced the quality of life of these patients [41]. Similar results were reported in the multicenter HEAL study, which analyzed the relationship between nutritional status and health-related quality of life in women with breast cancer. This research concluded that dietary patterns similar to the mediterranean diet are associated with better physical and mental health in these oncological patients [42].

Another argument favoring the mediterranean diet, which positions it as an essential pillar in the comprehensive treatment of breast cancer, is its components' anti-inflammatory and antioxidant effects [43]. Nutrients and bioactive compounds such as polyphenols can play a fundamental role in relieving pain and inflammation, which are significant symptoms of this disease that decrease patients' quality of life [44].

Considering the increasing trend in life expectancy among breast cancer survivors, it is essential to emphasize the importance of adopting healthy dietary habits as an integral part of their long-term care [45].

By adopting the mediterranean diet, breast cancer survivors can experience additional benefits in terms of quality of life and overall well-being, such as improvement in insomnia [46] and

**Figure 1.** Effects of mediterranean diet on Breast cancer.




Abbreviations: IL-6 - Interleukin-6; TNF-α - Tumor Necrosis Factor-alpha; CRP - C-Reactive Protein; NF-κB - Nuclear Factor Kappa B; SOD - Superoxide Dismutase; ROS - Reactive Oxygen Species; p53 - Tumor Protein p53; VEGF - Vascular Endothelial Growth Factor; PI3K/AKT - Phosphoinositide 3-Kinase/Protein Kinase B pathway; SCFA - Short-Chain Fatty Acids; IGF-1 - Insulin-like Growth Factor 1.
Source: Created with BioRender.com by the authors.

relief from unpleasant symptoms such as nausea and dyspnea [41].

Promoting adherence to a mediterranean diet among cancer survivors can be a valuable strategy to improve long-term health and quality of life in this vulnerable population. Integrating this diet into managing this disease involves a comprehensive approach beyond mere dietary prescription. Educating patients about the specific benefits of the mediterranean diet, providing personalized nutritional guidance, and encouraging sustainable lifestyle changes are crucial steps in providing holistic treatment that addresses both medical and general well-being aspects. By offering continuous support and personalized care, we can help patients adopt and maintain healthy dietary habits that promote recovery and long-term quality of life.

## EXPLORING THE NEXUS BETWEEN MEDITERRANEAN DIET AND BREAST CANCER OUTCOMES

This research has led us to explore the relationship between the mediterranean diet and breast cancer outcomes. Through numerous epidemiological investigations and clinical trials, the beneficial effects of this dietary pattern on the prevention, quality of life, and mortality of breast cancer patients have been consistently observed [47] (Table 1).

Several studies have evaluated the impact of the mediterranean diet on the prevention and progression of breast cancer, demonstrating a correlation between adherence to this pattern and a reduction in breast cancer incidence. For instance, the Spanish multicenter trial PREDIMED, conducted between 2003 and 2011, reported a 68% reduction in breast cancer risk in

**Table 1.** Overview of the mediterranean diet and breast cancer.

| Key aspect | Findings |
|---|---|
| Breast cancer overview | Most common and lethal cancer among women worldwide.<br>Risk factors include age, genetics, obesity, diet, and hormonal factors. |
| Role of diet | Obesity and unhealthy diets increase breast cancer risk.<br>High fruit/vegetable intake and low red meat/alcohol consumption reduce risk. |
| Mediterranean diet components | High intake: fruits, vegetables, nuts, whole grains, olive oil.<br>Moderate intake: fish, dairy, alcohol.<br>Low intake: red meat, saturated fats, added sugars. |
| Molecular mechanisms | Anti-inflammatory and antioxidant effects.<br>Regulates gene expression (cell proliferation, apoptosis, angiogenesis).<br>Modifies gut microbiota and estrogen levels. |
| Impact on quality of life | Improves physical/mental well-being, reduces pain, and enhances overall quality of life in breast cancer patients (clinical trials). |
| Mortality reduction | Higher adherence is associated with lower breast cancer mortality and overall mortality (25% reduction in one study). |
| Challenges and limitations | Variability in study designs, adherence measurements, and population differences.<br>Discrepancies in results across studies. |
| Clinical implications | Suggested as part of dietary guidelines for prevention and management.<br>Education/support programs needed for better adoption by patients and survivors. |

Source: Prepared by the authors.

the group that intervened with the mediterranean diet and extra virgin olive oil compared to the control group [14]. These findings are consistent with those reported by other epidemiological studies indicating a potential relationship between the mediterranean diet and a reduction in breast cancer risk [10]. Similar results were also reported in various observational studies, such as a cohort study conducted in the Netherlands, which included 2573 women aged 55 to 69. This study followed breast cancer incidence for 20 years. It concluded that there is an inverse relationship between adherence to the mediterranean dietary pattern and the risk of breast cancer, specifically the estrogen-negative subtype (risk index: 0.60, 95% CI 0.39 to 0.93, $p = 0.032$) [15]. Although these results seem promising, other studies do not report an association between adherence to the mediterranean diet and a reduction in the overall risk of breast cancer or for specific tumor subtypes [48].

Finally, the mediterranean diet may also influence breast cancer mortality. Prospective studies have found an inverse association between adherence to this dietary pattern and breast cancer mortality, suggesting that higher adherence may reduce the risk of death in patients diagnosed with this disease [46]. The underlying mechanisms of this effect may include the prevention of recurrences, improvement in treatment response, and beneficial effects on cardiovascular health and other aspects of overall health [45]. A Greek prospective cohort study, which included 28 572 subjects, reported that a two-point increase in adherence to the traditional mediterranean diet was associated with a 25% reduction in overall mortality [$p < 0.001$). Although some studies do not find a clear association, most support the idea that this dietary pattern may positively influence the course of cancer [49]. These findings underscore the importance of considering diet as a critical factor in breast cancer prevention and treatment strategies.

## CONCLUSIONS

The present narrative review of the available literature has found several studies suggesting that greater adherence to the Mediterranean Diet reduces the risk of breast cancer. This suggests that following this dietary pattern may protect against this disease, although some studies do not find a clear association. Specific components of this diet, such as monounsaturated fatty acids from olive oil, antioxidants present in fruits and vegetables, polyphenols, and other phytochemicals, may influence breast cancer prevention and treatment due to their anti-inflammatory, antioxidant actions and their ability to modulate gene expression related to cell proliferation and apoptosis.

The present narrative review of the available literature has found several studies suggesting that greater adherence to the mediterranean diet reduces the risk of breast cancer. This suggests that following this dietary pattern may protect against this disease, although some studies do not find a clear association. Specific components of this diet, such as monounsaturated fatty acids from olive oil, antioxidants present in fruits and vegetables, polyphenols, and other phytochemicals, may influence breast cancer prevention and treatment due to their anti-inflammatory, antioxidant actions and their ability to modulate gene expression related to cell proliferation and apoptosis.

Furthermore, adherence to the mediterranean dietary pattern is not only associated with a lower risk of breast cancer but also with a better quality of life in diagnosed patients and a reduction in mortality from this neoplasm. Although most studies support the idea that the mediterranean diet may positively influence the course of the disease, some studies have discrepancies in results.

Some limitations may be causing variability in the findings. Firstly, some studies addressing the topic had a cross-sectional design, which precludes inference about causality and is subject to confounding biases. Other factors include the methodological quality of prospective and intervention studies, which ranged from low to moderate, differences in the measurement scales of dietary adherence, and the geographical and environmental factors of the populations included in the studies, which can significantly influence the reported associations. It is also worth noting that many studies were conducted in populations outside the Mediterranean region, which hinders adherence to this dietary pattern.

In terms of clinical implications, the results suggest that including the mediterranean diet in dietary recommendations for women at risk of breast cancer or diagnosed patients could reduce the risk of the disease and improve quality of life. Additionally, the mediterranean diet can be considered an integral component in breast cancer management, alongside other medical interventions and therapies. Education and support programs are needed to promote the adoption of this diet among patients and survivors.

There are also implications for public health. Educating the public about the benefits of the mediterranean diet in breast cancer prevention and treatment is essential. This could be achieved through awareness campaigns and public health programs. Furthermore, further research, mainly controlled clinical trials, is needed to confirm the findings and fully understand the underlying mechanisms of the effects of this dietary pattern on breast cancer. This would help further support these dietary orientations to develop related public health policies.

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# Dieta mediterránea y cáncer de mama: una revisión narrativa

**RESUMEN**

El cáncer de mama es la segunda neoplasia más común y la más mortal entre las mujeres a nivel mundial. Su incidencia varía según el desarrollo humano y está asociada con varios factores de riesgo, como la edad, factores genéticos, obesidad y hábitos alimentarios. Investigaciones recientes han revelado una influencia significativa de los hábitos alimentarios en el inicio y la progresión de esta enfermedad, por lo que esta revisión tiene como objetivo analizar exhaustivamente la literatura disponible para comprender mejor el papel de la dieta mediterránea en el desarrollo y manejo del cáncer de mama. La dieta mediterránea tiene efectos antiinflamatorios y antioxidantes, puede influir en la regulación génica y producir cambios hormonales y en la microbiota intestinal, lo que resulta en una mejora de la calidad de vida de las pacientes con cáncer de mama al aliviar síntomas como el dolor y la inflamación, así como reducir el riesgo y la mortalidad por esta enfermedad. La evidencia sugiere que una mayor adherencia a la dieta mediterránea reduce el riesgo de cáncer de mama, así como una mejora en la calidad de vida y la mortalidad de los pacientes. Estos hallazgos destacan su posible relevancia en el contexto de patrones dietéticos asociados con la prevención y el manejo del cáncer de mama, lo que podría ser tomado en cuenta en las políticas de salud pública. Se necesita más investigación para confirmar estas observaciones y comprender mejor los mecanismos subyacentes.