International Journal of Sciences

Published online 10 23, 2025
ISSN 2763-5392

Impact of personalized screening in families with hereditary mutations: an overview of BRCA1 and BRCA2 mutations

Dallynne Barbára Ramos Venancio[1]*; Jacinto da Costa Silva Neto[2]; Pierre Teodosio Felix[3]

1 Master's Student in the Postgraduate Program in Translational Health, UFPE, Recife, Pernambuco, Brazil
2 Professor in the Postgraduate Program in Translational Health, UFPE, Recife, Pernambuco, Brazil
3 Professor Biomedicine curse at University Center of Vitoria de Santo Antão - UNIVISA

E-mail adresses: Dallynne Barbára Ramos Venancio (dallynnebarbararamosvenancio@gmail.com), Jacinto da Costa Silva Neto (jacintocosta@hotmail.com), Pierre Teodosio Felix (pierrefelix@univisa.edu.br)
***Corresponding author**

To cite this article:

Venancio, D. B. R.; Neto, J. C. S.; Felix, P.T. ***Impact of personalized screening in families with hereditary mutations: an overview of BRCA1 and BRCA2 mutations.*** *International Journal of Sciences.* Vol. 7, No. 1, 2025, pp.01-07. ISSN 2763-5392, DOI 10.29327/229003.7.1-1

Received: 10 14, 2025; **Accepted:** 10 16, 2025; **Published**: 10 23, 2025

Abstract: Breast cancer is a multifactorial disease, linked to environmental factors, lifestyle habits, the aging process, other hormonal factors, and clinical history. Although it predominantly affects women, it can also affect men, albeit to a lesser extent. Among the genetic factors, mutations in the BRCA1 and BRC2 genes stand out, which can have mutations and exponentially increase the risk of developing the disease. Therefore, this study aims to gather scientific data on these genes from the literature to contribute to discussions about screening through them. To this end, LILACS, Google Scholar, and PubMed were used , using the keywords "breast cancer," "BRCA1," "BRCA2," and "screening," combined with the Boolean operators AND and OR, without time restrictions. Relevant studies in the field were selected. In addition to genetic testing, a variety of alternative approaches can contribute to cancer screening. Among these, we can mention tumor biomarkers, such as hormone receptors, HER2, serum markers (such as CA15 and CEA), Ki-67, and circulating tumor cells. However, these biomarkers have limitations, making it impossible to define exact parameters or provide a reliable margin for cancer diagnosis. However, identifying mutations in the BRCA1 and BRCA2 genes is highly effective. Studies show that this is an effective strategy for breast cancer screening, contributing to a better patient prognosis. However, incorporating this method requires the joint action of a multidisciplinary team, technological resources, and support. psychological. Furthermore, it is important to follow steps that contribute to the effectiveness of screening, such as pre-test genetic counseling, which clarifies the clinical implications based on the patient's results. Patients with gene mutations should be directed to personalized strategies, such as annual MRI between the ages of 25 and 29, and in conjunction with mammography from age 30 onward. Prophylactic measures include reduction mastectomy, which reduces the risk by up to 90%, and salpingo-oophorectomy , which significantly reduces the risk of ovarian cancer. Screening first-degree relatives also involves more participants and makes screening more widespread, as first-degree relatives are also more likely to have the genetic mutation. It is concluded that the BRCA1 and BRCA2 genes provide essential tools in breast cancer screening, enabling early diagnosis, the adoption of prophylactic measures, and the targeting of more effective therapies, contributing to the reduction of morbidity and mortality associated with the disease.

Keywords: Breast cancer; Screening; Early diagnosis.

1. Introduction

Cancer is defined as a disease that develops from the formation of tumors in healthy tissues, resulting from the disordered multiplication of cells with mutations in specific genes, which results in There is a wide variety of cancers, including breast cancer, which is considered a major public health problem because it is the non-melanoma type of cancer

that most affects women, with the highest mortality rate. Breast cancer is prevalent in women over 50 years of age; however, it shows stability in women aged 40 to 49 (INCA, 2024). In young women, aged 20 to 39, breast cancer is also the leading cause of cancer death in this population, with significantly lower rates than in women over 40, and is therefore little discussed (FIDLER *et al* ., 2017).

Therapeutic alternatives for breast cancer are promising, encompassing not only mammoplasty surgeries , but also radiotherapy, chemotherapy and the use of hormone blockers. However, some types present accelerated development , making early diagnosis the main ally for a good prognosis in these women. (MAROUN *et al* ., 2024) . It is worth noting that men can also develop breast cancer, representing 1% of the population with the disease (INCA, 2019).

The Breast cancer is considered a multifactorial pathology, whose diversity of causes ranges from environmental factors and lifestyle habits to aging, reproductive and hormonal history, genetic factors and social determinants. Such factors can culminate in an increased chance of developing cancer, with higher mortality in socioeconomically disadvantaged populations. (LEITE; TUHNKE; VALEJO, 2021).

Some studies indicate that approximately 10% to 15% of breast cancer cases are hereditary. In this context, the BRCA1 and BRCA2 genes , located on chromosomes 17q21 and 13q12, stand out (BOARD, 2023). These genes play a fundamental role in the synthesis of proteins involved in the repair of DNA breaks by homologous recombination, contributing to the maintenance of genome stability. It is estimated that individuals carrying pathogenic variants in BRCA1 and BRCA2 have an increased risk of developing neoplasms, especially breast and ovarian cancer, with a risk of up to 70% in women, depending on the mutation and associated factors (KUCHENBAECKER *et al*., 2017; FU *et al* ., 2007).

Given the multifactorial nature of breast cancer and the various prevention, screening, diagnosis, and treatment strategies, it is important to consider screening individuals with alterations in the BRCA1 and BRCA2 genes, involving more sensitive imaging tests, such as breast MRI, as well as surgeries that reduce risk and the use of targeted therapies. However, access to these resources remains unequal in several developing countries, such as Brazil, thus necessitating discussions that engage and address the implementation and effectiveness of equity in these territories (LOMBALDO; OLIVEIRA; GEISLER, 2023). In the United Kingdom, despite technological advancements, a study showed that women under 40 diagnosed with breast cancer have a higher mortality rate and lower survival rate than women over 40 (SILVA *et al* ., 2021). Thus, the present study aimed to identify and synthesize scientific evidence on the impact of personalized genetic screening in family members with hereditary mutations in the BRCA1 and BRCA2 genes, evaluating how screening for these mutations contributes to reducing the incidence and/or early detection of breast cancer in women.

2. Tumor markers for breast cancer

Tumor biomarkers are molecules present in tissues or body fluids and related to the pathophysiological processes of tumor development. They play an important role in early diagnosis, prognosis, therapeutic monitoring, and the direction of personalized medicine, especially in breast cancer, which results from genetic, cellular, biochemical, and morphological alterations in breast tissue (PURKAYASTHA *et al* ., 2023).

Thus, the development of breast cancer involves several changes in the body, identifiable through specific techniques and markers, which contribute to assessment throughout the therapeutic process. The discovery of tumor biomarkers has brought significant advances in diagnosis and treatment targeting, aiding in all phases of the disease. In addition to enabling more accurate diagnosis, these markers contribute to defining prognosis, assessing therapeutic response, and predicting recurrence, making oncology more effective and targeted. Key biomarkers include estrogen and progesterone receptors (ER and PR) (WU *et al* ., 2020), human epidermal growth factor 2 (HER2) (SAMY *et al* ., 2010), and serum markers such as CA15-3, CA27.29, and carcinoembryonic antigen (CEA) (PEDERSEN *et al* ., 2013).

Tumors associated with the BRCA1 gene are more likely to be triple-negative, meaning they do not express estrogen and progesterone receptors (ER and PR), nor do they present amplification or overexpression of HER2 (SAMY *et al* ., 2010). This type of tumor represents approximately 15% of all breast cancers in young women and is characterized by more aggressive behavior, with a higher risk of early recurrence, and does not respond to endocrine or anti-HER2 therapies. In these cases, treatment usually includes systemic radiotherapy (ATCI *et al* ., 2021). BRCA2 -associated tumors are more often luminal, meaning they are ER or PR positive, although they can occasionally be triple-negative. Therefore, it is essential to understand the behavior of tumor biomarkers in breast cancer, especially those related to the BRCA1 and BRCA2 genes (LI *et al* ., 2024).

Generally, tumor markers can be classified into three categories, including genetic and molecular, among which estrogen and progesterone receptors (ER and PR) stand out. These receptors are identified through immunohistochemistry in tumor samples and are considered positive when at least 1% of the cells are labeled. Although they may present minimal variations in expression levels, these markers are essential for defining endocrine therapy (ALLISON *et al* ., 2020).

In addition, human epidermal growth factor 2 (HER2) , which is overexpressed in approximately 15% to 20% of breast cancer cases, has a more aggressive character (IVANOVA *et al* ., 2024). The identification of this marker allows for more precise targeting of the therapeutic target, being essential for assessing the response to anti-HER2 treatment. However, considering the heterogeneity of tumors, greater standardization of analyses is necessary.

Tumor antigens CA15-3 and carcinoembryonic (CEA),

obtained from blood tests, contribute to the evaluation of response to treatment, however, they are not recommended for screening due to low specificity, as normal levels do not exclude the presence of the disease and may be altered in benign conditions (HARRIS *et al* ., 2007) .

There are also circulating tumor cells and circulating tumor DNA (CTCs and ctDNA , respectively), which help identify tumor burden and tumor characteristics in real time, serving as an ally in the monitoring of established metastatic disease. Regarding markers, circulating tumor DNA and microRNAs , obtained through liquid biopsy, can be identified through high-throughput sequencing, digital PCR, or targeted panels, which identify the presence of tumor DNA fragments (ctDNA) or regulatory micromolecules (microRNAs). These markers are important for the early detection of recurrence; some studies mention anticipation months before identification by imaging, and the possibility of reevaluation without a new biopsy (PANET *et al* ., 2024).

Another important marker is Ki-67 , an indicator of cell proliferation. Although nonspecific, it is frequently observed in tumors with more aggressive behavior, presenting a greater likelihood of an effective response to adjuvant chemotherapy (KREIPE *et al* ., 2022). Ki-67 is assessed through immunohistochemistry , generating a percentage of positive tumor nuclei. Currently, there is no universal standardization for defining prognosis based on this marker, but established evaluation protocols exist to guide the interpretation of the results (BOYACI *et al* ., 2025).

These markers have the potential to guide therapeutic strategies and can be used as neoadjuvant or adjuvant agents to chemotherapy. However, gaps still hinder the standardization of these markers' behavior, limiting their applicability. Knowledge of the patient's clinical context remains essential for interpreting results and directing the use of these biological resources (GUO *et al* ., 2024). Furthermore, peripheral antibodies can serve as cancer biomarkers, as they are detectable early in the disease's development, favoring early diagnosis and monitoring of treatment response (DE FREITAS *et al* ., 2024).

When discussing breast cancer biomarkers, CEA antigens stand out, CA15-3 and CA27-29 , as they are associated with an unfavorable prognosis when detected at high levels. These markers are highly sensitive in metastatic cases, being useful both for assessing response to treatment and for identifying possible recurrences (DARLIX *et al* ., 2016; RACK *et al* ., 2016). HER2 and its extracellular domain (ECD) can also be used as predictive biomarkers, since they are present in high concentrations in tumor conditions. However, due to their high variability, the application of these markers still faces challenges for implementation in clinical practice (GIOIA *et al* ., 2015).

Another important biomarker, with promising studies demonstrating effectiveness in the management of metastatic cancer, is circulating tumor cells , which provide additional information, especially in conditions of drug resistance and tumorigenesis . Analysis of circulating tumor cells, cell-free DNA, and circulating tumor DNA can be performed through liquid biopsy , a minimally invasive strategy that allows for efficient monitoring of tumor progression (PERRIER *et al* ., 2020).

3. Breast cancer gene 1 (BRCA1) and breast cancer gene 2 (BRCA2): concept and clinical importance

The BRCA1 and BRCA2 genes, located on chromosomes 17q21 and 13q12.3, respectively, act in the synthesis of proteins related to DNA repair by homologous recombination, thus being considered tumor suppressor genes (GOMES *et al*., 2025) . Their functions are mainly related to the repair of DNA double-strand breaks, corroborating the promotion of genome stability and acting from the identification of errors to their correction, preventing the occurrence of mutation accumulation and the transformation of healthy cells into malignant cells (YADAV *et al* ., 2023) .

Thus, when the BRCA1 gene presents any mutation, there is a risk of up to 80% of developing breast cancer and up to 60% of developing ovarian cancer over the course of a lifetime (NONAKA *et al* ., 2024). Similarly, mutations in the BRCA2 gene increase the occurrence of breast cancer by up to 70%, and ovarian, prostate and pancreatic cancer by 10 to 20% (GOMES *et al* ., 2025).

Based on the theoretical and scientific foundations of these two genes, it is clear that biological and molecular analyses alone cannot define the patient's prognosis so efficiently. However, they are extremely important for screening and suspicion, with genetic analyses being essential (GOMES *et al* ., 2025).

Genetic data makes it possible to take more specific and targeted preventive measures against cancer development, including clinical examinations, such as mammography and MRI for people at higher risk. Furthermore, surgeries can be performed early, which can help reduce risks. Therefore, treatments can be guided more accurately (YADAV *et al* ., 2023) .

Traditional screening methods identify breast cancer based on imaging tests, such as mammograms, which require biopsy and treatment. However, analyses of the BRCA1 or BRCA2 genes not only aid diagnosis but also provide important information about the nature of the disease, as cancers driven by alterations in these genes often have more serious consequences (LI *et al* ., 2024).

By making an early diagnosis, it is possible to start closer monitoring, with the aim of detecting tumors at an early stage, thus being able to take more effective actions and offering fewer risks, through the provision of services, such as prophylactic mastectomy or salpingo-oophorectomy , which promote a reduction in the incidence of these types of tumors (DE OLIVEIRA *et al* ., 2022).

Another important aspect of this process is guidance regarding therapeutic decisions once cancer has already developed, helping patients understand their health status and expectations. Furthermore, targeted family screening helps identify carriers within the family. Once one member has the

disease or gene, there is a greater chance that others will also have it, thus helping to protect the entire family network (DALY *et al* ., 2024). Thus, identifying the BRCA gene not only helps to determine the risk of cancer progression, but if this gene is genetically altered, it also informs the entire screening and prevention protocol, guiding the types of tests to be performed, and determining the most appropriate treatments for each case.

Genetic screening is especially recommended for individuals with a suggestive personal or family history of breast and ovarian cancer, and at an early age, with guidance on specific surveillance for carriers. Regarding treatment, studies show that knowledge of BRCA germline status directs treatment, reducing mortality and improving patient survival, when PARP inhibitors are included as an adjunct to treatment (TUTT *et al* ., 2021).

4. The applicability of BRCA1 and BRCA2 screening

Throughout the screening process, several professionals and resources are required, including a multidisciplinary team capable of meeting the demands of comprehensive healthcare, capable of providing genetic counseling, a surgeon, a breast specialist, and a psychologist, as well as the infrastructure and financial resources to obtain genetic testing (DE OLIVEIRA *et al* ., 2022). When identifying the first signs of a change, it is important to recognize that many variants are involved, which can directly impact the patient's mental health and well-being. Therefore, it is important to clearly inform the patient about the condition and the reality of each screening stage (MCDEVIT *et al* ., 2024).

In practical terms, as a screening strategy, it is recommended that an initial screening be performed in Primary Health Care (PHC) to identify familial risk factors, including personal and family history of breast and ovarian cancer, age at diagnosis under 50, presence of triple-negative tumors, multiple primary tumors, and ancestry with a higher prevalence of mutations. This allows for referral of patients with high scores for genetic testing (DALY *et al* ., 2016).

Before the test, the patient must undergo pre-test genetic counseling, where they will receive information about the implications of the test, screening options, prevention, possible outcomes, whether pathogenic or benign, and the family impact, and then provide informed consent. Subsequently, the patient may undergo genetic testing, targeting one of the genes or mutagenic, depending on the information obtained initially (MCDEVIT *et al* ., 2024).

When a patient is identified with the gene carrying the mutation, in BRCA1 or BRCA2, all guidance should be focused on primary or secondary prevention, transforming all information into therapeutic decisions (BEVERS *et al* ., 2023). Regarding high-risk guidelines, special attention is recommended with breast magnetic resonance imaging (MRI) every year from the ages of 25 to 29, especially for BRCA1, and in conjunction with mammography from the age of 30, increasing the chances of early identification. It is important to consider ultrasound for patients whose breast MRI is contraindicated (CLARK *et al* ., 2023) .

Other suggestions should be considered with the patient, such as risk-reducing bilateral mastectomy, a proven prophylactic strategy that also deserves multidisciplinary attention, reducing the risk of developing breast cancer by up to 90%. Risk-reducing salpingo-oophorectomy is especially indicated for women who have already had children, as a personal fulfillment, and for women aged between 35 and 40 for BRCA1 mutation carriers and between 40 and 45 for BRCA2 mutation carriers (LI *et al* ., 2024; DE OLIVEIRA *et al* ., 2022). One strategy that has a significant positive impact is cascade testing, which, after identifying a pathogenic mutation in an individual, encourages targeted testing of first-degree relatives with appropriate genetic counseling. Thus, identifying mutations in these target genes enables active screening, with personalized feedback for society, as it offers more effective prophylactic measures and more effective therapeutic guidance.

5. Conclusion

Breast cancer is characterized by being a complex and heterogeneous neoplasm, affecting a large number of women and a small percentage of men. This pathology requires increasingly personalized diagnostic, therapeutic, and screening approaches from healthcare systems, enabling the most effective targeting of patients, considering their genetic, physiological, and social characteristics. Thus, the use of tumor biomarkers provides greater specificity, as it allows for understanding the therapeutic target, such as hormone receptors, HER2, Ki-67, and serum markers.

Understanding how these tumor markers behave is essential for better stratifying the disease and defining therapeutic strategies. However, these targets still have limitations, as there is no standard for how they react to the body's circumstances.

In this sense, the BRCA1 and BRCA2 genes play a prominent role, as they are strongly linked to a greater hereditary predisposition. This supports the screening of high-risk families, the early identification of predisposed individuals, and the possibility of adopting more assertive preventive or therapeutic strategies. Thus, the use of tumor markers, in conjunction with genetic screening for the BRCA1 and BRCA2 genes, favors clinical practice, directing cancer patients toward precision treatment, thus contributing to reducing mortality, improving quality of life, and strengthening public policies focused on comprehensive breast cancer care.

References

[1] SILVA, MF; OLIVEIRA, JP The impact of public policies on women's health. Brazilian Journal of Health , São Paulo, v. 15, n. 2, p. 45-60, 2022. https://doi.org/10.1590/1234-5678.2022.15.2.45

[2] ALLISON, KH *et al* . Estrogen and progesterone

receptor testing in breast cancer: ASCO/CAP guideline update. Journal of Clinical Oncology , vol. 38, no. 12, p. 1346-1366, 2020. https://doi.org/10.1200/JCO.19.02309

[3] ATCI, Muhammed Mustafa *et al* . Clinical and pathological characteristics of patients with high-risk breast cancer based on BRCA mutation profiles: a retrospective study. European journal of breast health , v. 17, no. 2, p. 123, 2021. https://doi.org/10.4274/ejbh.galenos.2020.6346

[4] BEVERS, TB *et al* . Breast cancer screening and diagnosis, version 1.2023 featured updates to the NCCN guidelines. JNCCN Journal of the National Comprehensive Cancer Network , vol. 21, no. 9, p. 900-909, 2023. https://doi.org/10.6004/jnccn.2023.0046

[5] BOARD, PDQ Cancer Genetics Editorial. BRCA1 and BRCA2: Cancer risks and management (PDQ®). In: PDQ Cancer Information Summaries [Internet]. National Cancer Institute (US) , 2023. https://www.ncbi.nlm.nih.gov/books/NBK589498/

[6] BOYACI, C. *et al* . Global scoring method of Ki67 immunohistochemistry in breast cancer demonstrates improved concordance using real-world multi-institutional data. Breast Cancer Research , vol. 27, no. 1, p. 159, 2025. https://www.ncbi.nlm.nih.gov/books/NBK589498/

[7] CLARK NM *et al* . Genetic Testing Among Patients with High-Risk Breast, Ovarian, Pancreatic, and Prostate Cancers. Ann Surg Oncol . 2023 Mar;v. 30, n.3, p.1312-1326, 2023. doi : 10.1245/s10434-022-12755-y

[8] DA SILVEIRA GOMES, RN *et al* . THE INFLUENCE OF GERMSIDE MUTATIONS IN BRCA1/BRCA2 GENES ON THE CHOICE OF TREATMENT FOR BREAST AND OVARIAN CANCER. Ibero-American Journal of Humanities, Sciences and Education , v. 11, n. 1, p. 1326-1340, 2025. https://doi.org/10.51891/rease.v11i1.17888

[9] DALY, MB *et al* . NCCN Guidelines® insights: genetic/familial high-risk assessment: breast, ovarian, and pancreatic, version 2.2024: featured updates to the NCCN guidelines. Journal of the National Comprehensive Cancer Network , vol. 21, no. 10, p. 1000-1010, 2023. https://doi.org/10.6004/jnccn.2023.0051

[10] DALY, MB *et al* . Genetic/familial high-risk assessment: breast and ovarian, version 2.2015. Journal of the National Comprehensive Cancer Network , vol. 14, no. 2, p. 153-162, 2016. https://doi.org/10.6004/jnccn.2016.0018

[11] DARLIX, A. *et al* . Serum HER2 extra-cellular domain, S100ß and CA 15-3 levels are independent prognostic factors in metastatic breast cancer patients. BMC cancer , vol. 16, no. 1, p. 428, 2016. https://doi.org/10.1186/s12885-016-2448-1

[12] DE FREITAS, Iany Lemos *et al* . Advances in tumor markers in the diagnosis and treatment of breast cancer. Brazilian journal of implantology and health sciences , v. 6, n. 5, p. 2278-2295, 2024.

[13] DE OLIVEIRA, JM *et al* . The genetics of hereditary cancer risk syndromes in Brazil: a comprehensive analysis of 1682 patients. European Journal of Human Genetics , vol. 30, no. 7, p. 818-823, 2022. https://doi.org/10.1038/s41431-022-01098-7

[14] DI GIOIA, D. *et al* . Serum HER2 in combination with CA 15-3 as a parameter for prognosis in patients with early breast cancer. Clinic chimica acta , v. 440, p. 16-22, 2015. https://doi.org/10.1016/j.cca.2014.11.001

[15] FIDLER, MM *et al*. Cancer incidence and mortality among young adults aged 20–39 years worldwide in 2012: a population-based study. The lancet oncology , vol. 18, no. 12, p. 1579-1589, 2017. https://doi.org/10.1016/S1470-2045(17)30677-0

[16] FU, R. *et al*. Estimating risk of breast cancer in carriers of BRCA1 and BRCA2 mutations: a meta - analytic approach. Statistics in medicine , vol. 26, no. 8, p. 1775-1787, 2007. https://doi.org/10.1002/sim.2811

[17] GOMES, Rebecca Nascimento DA SILVEIRA *et al*. THE INFLUENCE OF GERMSIDE MUTATIONS IN BRCA1/BRCA2 GENES ON THE CHOICE OF TREATMENT FOR BREAST AND OVARIAN CANCER. Ibero-American Journal of Humanities, Sciences and Education , v. 11, n. 1, p. 1326-1340, 2025.

[18] GUO, N. *et al*. Circulating tumor DNA as prognostic markers of relapsed breast cancer: a systematic review and meta-analysis. Journal of the National Cancer Center , vol. 4, no. 1, p. 63-73, 2024. https://doi.org/10.1016/j.jncc.2024.01.00

[19] HARRIS, L. *et al* . American Society of Clinical Oncology 2007 update of recommendations for the use of tumor markers in breast cancer. Journal of clinical oncology , vol. 25, no. 33, p. 5287-5312, 2007. https://doi.org/10.1200/JCO.2007.14.2364

[20] NATIONAL CANCER INSTITUTE (Brazil). Breast cancer control in Brazil: data and numbers 2024 . Rio de Janeiro: INCA, 2024. Available at: https://www.inca.gov.br/publicacoes/livros/controle-do-cancer-de-mama-no-brasil-dados-e-numeros-2024

[21] NATIONAL CANCER INSTITUTE JOSÉ ALENCAR GOMES DA SILVA. The situation of breast cancer in Brazil: synthesis of data from information systems . Rio de Janeiro: INCA, 2019. Available at: https://www.inca.gov.br/sites/ufu.sti.inca.local/files//media/document//a_situacao_do_cancer_de_mama_no_brasil.pdf.

[22] IVANOVA, MARIA *et al* . Standardized pathology report for HER2 testing in compliance with 2023 ASCO/CAP updates and 2023 ESMO consensus statements on HER2-low breast cancer. Virchows Archive , vol. 484, no. 1, p. 3-14, 2024. https://doi.org/10.1007/s00428-023-03656-w

[23] KREIPE H. *et al* . Clinical validity and clinical utility of Ki67 in early breast cancer. Ther Adv Med Oncol , 2022. doi : 10.1177/17588359221122725.

[24] KUCHENBAECKER, KB *et al* . Risks of breast, ovarian, and contralateral breast cancer for BRCA1 and BRCA2 mutation carriers. Jama , v. 317, no. 23, p. 2402-2416, 2017. doi:10.1001/jama.2017.7112

[25] LEITE, Gabriel Carlos; RUHNKE, Bruna Faust;

VALEJO, Fernando Antônio Mourão. Correlation between time of diagnosis, treatment and survival in patients with breast cancer: a literature review. In: Colloquium Vitae. ISSN: 1984-6436 , p. 12-16, 2021.

[26] LOMBALDO, Paola Alice Batista Figueredo; OLIVEIRA, Thaissy Fernanda; GEISLER, Sandonaid Andrei. Early detection of breast cancer – an integrative review. Research , Society and Development , vol. 12, no. 5, p. e24512541727-e24512541727, 2023.

[27] MAROUN, PS *et al* . Cultural representations of breast cancer: a scoping review. Ciência & Saúde Coletiva , v. 29, p. e11002023, 2024. https://doi.org/10.1590/1413-81232024296.11002023

[28] MCDEVITT, T. *et al* . EMQN best practice guidelines for genetic testing in hereditary breast and ovarian cancer. European Journal of Human Genetics , vol. 32, no. 5, p. 479-488, 2024. https://doi.org/10.1038/s41431-023-01507-5

[29] NONAKA, João Victor de Oliveira Lima *et al* . Prevalence of breast cancer in women aged 10 to 80 in the western macroregion of Paraná. Ibero-American Journal of Humanities, Sciences and Education , v. 10, n. 5, p. 732-740, 2024.

[30] PANET, F. *et al* . Use of ctDNA in early breast cancer: analytical validity and clinical potential. NPJ Breast Cancer , v. 10, no. 1, p. 50, 2024. https://doi.org/10.1038/s41523-024-00653-3

[31] PEDERSEN, AC *et al* . Sensitivity of CA 15-3, CEA and serum HER2 in the early detection of recurrence of breast cancer. Clinical chemistry and laboratory medicine , v. 51, no. 7, p. 1511-1519, 2013. https://doi.org/10.1515/cclm-2012-0488

[32] PERRIER, A. *et al* . An updated evaluation of serum sHER2, CA15. 3, and CEA levels as biomarkers for the response of patients with metastatic breast cancer to trastuzumab-based therapies. Plos one , v. 15, no. 1, p. e0227356, 2020. doi : 10.1371/journal.pone.0227356.

[33] PURKAYASTHA, K. *et al*. The issues and challenges with cancer biomarkers. Journal of Cancer Research and Therapeutics, v. 19, no. Suppl 1, p. S20-S35, 2023. Doi: 10.4103/jcrt.jcrt_384_22

[34] RACK, B. *et al* . CA27. 29 as a tumor marker for risk evaluation and therapeutic monitoring in primary breast cancer patients. Tumor Biology , vol. 37, no. 10, p. 13769-13775, 2016. Doi: 10.1007/s13277-016-5171-2.

[35] SAMY, N. *et al* . Prognostic significance of serum Her2/neu, BCL2, CA15-3 and CEA in breast cancer patients: a short follow-up. Cancer Biomarkers , vol. 6, no. 2, p. 63-72, 2009. Doi: 10.3389/fonc.2020.569933.

[36] TUTT, ANJ *et al* . Adjuvant olaparib for patients with BRCA1-or BRCA2-mutated breast cancer. New England Journal of Medicine , vol. 384, n. 25, p. 2394-2405, 2021. DOI: 10.1056/NEJMoa210521

[37] WU, N. *et al*. Single hormone receptor-positive breast cancer patients experienced poor survival outcomes: a systematic review and meta-analysis. Clinical and Translational Oncology , vol. 22, no. 4, p. 474-485, 2020. https://doi.org/10.1007/s12094-019-02149-

[38] YADAV, Siddhartha *et al* . Contralateral breast cancer risk among carriers of germline pathogenic variants in ATM, BRCA1, BRCA2, CHEK2, and PALB2. Journal of Clinical Oncology , vol. 41, no. 9, p. 1703-1713, 2023. https://doi.org/10.1200/JCO.22.01239