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Prognostic factors in hereditary breast cancer: A review

Ziske Maritska[1*], **Sarmoko**[2]

[1]Department of Medical Biology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
[2]Department of Pharmacy, Faculty of Science, Institut Teknologi Sumatera, South Lampung, Indonesia
[*]Corresponding author: Jalan Dokter Muhammad Ali, Sekip Jaya, Kec. Kemuning, Palembang City, South Sumatera.
Email: ziske_maritska@unsri.ac.id

ABSTRACT

Hereditary breast cancer, primarily driven by BRCA1 and BRCA2 mutations, presents distinct challenges and prognostic factors compared to sporadic breast cancer. BRCA1-associated breast cancer is often triple-negative (TNBC), which has a more aggressive course and poorer prognosis. Despite this, BRCA mutation carriers exhibit higher sensitivity to platinum-based chemotherapy and PARP inhibitors, potentially improving outcomes. However, the risk of developing other malignancies, such as ovarian cancer and melanoma, remains elevated in BRCA mutation carriers. Studies show a significant variation in survival rates, with BRCA mutation carriers having lower overall survival compared to non-carriers. Loss of heterozygosity (LOH) in BRCA1/2 tumors is frequent but does not significantly alter overall survival rates. Identifying the presence of LOH can guide personalized treatment strategies, particularly the use of PARP inhibitors. The response to chemotherapy, especially platinum-based drugs, is influenced by genetic mutations such as TP53 and PTEN, which are common in TNBC. Surgical choices also impact prognosis; mastectomy may lower ipsilateral breast recurrence but does not affect overall survival. Pathologic complete response (pCR) following neoadjuvant chemotherapy is a critical prognostic marker, with higher rates observed in BRCA mutation carriers, particularly those with TNBC. These factors collectively influence the prognosis and guide treatment strategies for hereditary breast cancer.

Keywords: hereditary breast cancer, BRCA1/2 mutations, prognosis, triple-negative breast cancer, pathologic complete response

Introduction

Cancer is a disease characterized by the uncontrolled growth and spread of abnormal cells within the body [1]. These cells can develop in various tissues and organs, beginning with normal cell division followed by uncontrolled proliferation. When cancer cells invade surrounding tissue, they are termed invasive. Metastasis occurs when these cells enter the bloodstream or lymphatic system, spreading to other tissues or organs. Among the various types of cancer, breast cancer is the most prevalent, particularly among females [2].

Breast cancer remains the leading cancer diagnosis in women worldwide. According to the World Health Organization (WHO), there were over 2 million new cases of breast cancer in 2020 [2]. Globally, 7.8 million women have been diagnosed with breast cancer in the past five years, with approximately 685,000 deaths attributed to the disease [2]. The incidence is particularly high in Western countries, where the lifetime risk of developing breast cancer is about 1 in 9. However, increased awareness, early screening and detection, and improved treatment options have contributed to a recent decline in mortality rates [3].

A significant portion of breast cancer cases—10-15%—are hereditary, primarily due to mutations in the *BRCA1* and *BRCA2* genes [3]. These mutations are often associated with a pattern of inheritance that includes early onset, a higher incidence of ovarian cancer, bilateral breast cancers, and male breast cancer [4].

Prognostic factors are pivotal in determining the likely outcomes of diseases such as hereditary

breast cancer. These factors encompass a range of characteristics and conditions that provide information regarding the disease course, treatment responses, and patient survival rates. In the context of hereditary breast cancer, prognostic factors include genetic mutations, tumor characteristics, patient factors, and treatment responses [3]. Understanding these factors is essential for physicians to develop individualized treatment strategies, predict disease progression, and ultimately enhance patient outcomes. This review explores hereditary breast cancer, focusing on the various factors that influence its prognosis.

Types of breast cancer

Familial vs. sporadic breast cancer

Breast cancer is commonly divided into two categories: familial and sporadic. Familial breast cancer is caused by germline mutations, while sporadic breast cancer results from acquired mutations [6]. Familial breast cancer can affect up to 50% of women in a large family and is identified when multiple female relatives have also had the disease. Conversely, those without a family history of breast cancer typically develop sporadic breast cancer. The occurrence of breast cancer is influenced by genetic and environmental factors, varying from predominantly environmental to highly genetic. A notable subtype of familial breast cancer with a significant genetic component is hereditary breast cancer.

Hereditary breast cancer

Hereditary breast cancer is characterized by genetic heterogeneity and is inherited in an autosomal dominant manner. It is clinically distinguishable by dominant inheritance patterns, early onset (affecting two or more generations of women before menopause), or severe disease. Additionally, breast cancer in men and breast cancer in women involving the ovary or fallopian (uterine) tube are classified as hereditary breast cancer [5].

Lynch and Krush identified hereditary breast cancer as a distinct condition, and it has been a significant focus in medical literature since the 19th century. The likelihood of developing breast cancer increases significantly if a close relative has had the disease. The risk further escalates with the number of affected relatives. Immediate family or first-degree relatives of a woman who has had breast cancer are at twice the risk of developing the disease compared to the general population. This highlights the critical role of heredity. According to 38 studies on the history of breast cancer in a first-degree relative, spanning from 1954 to 1996, having a first-degree relative with breast cancer increases a person's risk of developing the disease by 2.1 times [6].

Genetic factors

BRCA1 and BRCA2 mutations

BRCA1-associated breast cancer is frequently triple-negative breast cancer (TNBC). The prognosis for BRCA-associated breast cancers generally mirrors that of sporadic breast cancers. However, meta-analyses yield contradictory results: some indicate lower overall survival, while others show improved survival among TNBC patients. Additionally, individuals with BRCA1/2 mutations face an 8–62% lifetime risk of developing ovarian cancer.

In comparison to non-carriers, who had a five-year disease-free survival rate of 91.1%, BRCA mutation carriers had a significantly lower rate of 73.3%. BRCA mutation status serves as an independent prognostic factor for cancer mortality and recurrence. The poor clinical outcome in BRCA mutation carriers is primarily due to distant metastatic recurrence, rather than new primary breast cancer, although the latter risk is also higher in BRCA mutation carriers. It is suggested that breast cancers in BRCA germline mutation carriers are more aggressive. While earlier investigations have not consistently demonstrated a substantial predictive effect of BRCA mutations on clinical outcomes, a recent comprehensive study revealed that individuals with BRCA1 and BRCA2 mutations had considerably lower breast cancer-specific survival [7].

Other genetic mutations

Li-Fraumeni syndrome accounts for approximately 1% of hereditary breast cancer cases. Carriers of the p53 mutation, associated with this syndrome, have nearly a 100% lifetime cancer incidence and are predisposed to various malignancies. Female mutation carriers have a lifetime breast cancer risk exceeding 50% by age 60, with the average onset around 35 years and rare first diagnoses after age 50 [8].

Cowden syndrome, characterized by multiple hamartomas, involves germline PTEN mutations, which increase the risk of breast, thyroid, endometrial, kidney, and colorectal cancers. In breast cancer, reduced PTEN expression may correlate with poor outcomes [9].

The *PALB2* gene has linked to hereditary breast cancer and is regarded as a moderate to high-risk gene. A family history and environmental factors influence the breast cancer risk associated with PALB2 pathogenic variations [14]. Women with no family history of breast cancer have a cumulative risk of 33%, while those with two or more affected relatives have a 58% cumulative risk. *PALB2* mutation carriers typically develop breast cancers resembling BRCA1/2 tumors: 50% have grade III tumors, 40% have the triple-negative phenotype, 58% lack estrogen receptors, and 93% lack HER2 protein. These patients face a higher breast cancer risk, with a cumulative incidence of about 55% and a mean diagnosis age of 37 years [10].

Prognosis of BRCA1/2 mutation carriers of hereditary breast cancer

BRCA1 and BRCA2 mutations not only increase the risk of breast and ovarian cancers but also elevate the likelihood of developing malignant melanoma, pancreatic cancer, and prostate cancer. The risk of developing these malignancies varies depending on the reporting cohort and the risk assessment techniques used. Results from 24 studies revealed that women have a 46-87% chance of developing breast cancer by age 70 if they carry a BRCA1 mutation, and a 38-84% chance with a BRCA2 mutation [11]. BRCA1 mutations also carry a 1.2% risk of male breast cancer, compared to 8.9% for BRCA2 mutations. Additionally, BRCA1/2 mutation carriers are significantly more likely to develop contralateral breast cancer.

Numerous studies have focused on the prognosis of BRCA1/2 mutation carriers. An association between these mutations and overall survival (OS) was observed in a study on breast cancer patients with BRCA1/2 mutations [11]. Findings from over a hundred multicenter prospective cohort studies in the United Kingdom, involving thousands of breast cancer patients under forty (including 388 BRCA1/2 mutation carriers), indicated no significant association between BRCA1/2 mutations and two, five, or ten-year OS rates [3]. This modest advantage in early survival might be attributed to the higher chemosensitivity of BRCA-mutant breast tumors.

According to a meta-analysis of ovarian cancer patients, those with BRCA1/2 mutations had significantly longer OS and progression-free survival (PFS) than those without the mutations. However, there was no discernible difference in PFS for patients with BRCA1 mutation alone or those with BRCA2 mutation alone [12]. In a large trial without selection bias, 218 patients with BRCA1/2 mutations showed higher three-year short-term survival compared to the mutation-free group. However, reports indicate that this effect on survival is temporary, with no increase in survival rates beyond ten years [11].

Loss of heterozygosity (LOH)

Several studies have hypothesized a relationship between prognosis and the presence or absence of loss of heterozygosity (LOH) in malignancies caused by carriers of hereditary BRCA1/2 mutations. LOH occurs when a locus contains one normal allele and one aberrant allele; the loss of the normal allele results in the absence of normal function at that locus.

In an analysis of 160 tumors with BRCA1/2 mutations, LOH was found in 90% of breast cancer cases with BRCA1 positivity, 54% with

BRCA2 positivity, 93% of ovarian cancer cases with BRCA1 positivity, and 84% with BRCA2 positivity. Despite the high incidence of LOH, OS did not significantly differ depending on the presence of LOH in breast cancer patients. The OS rate was higher in the BRCA1/2-positive group compared to the BRCA-negative group. Patients with BRCA-positive cancer had a considerably higher OS rate, while BRCA1/2-positive groups without LOH had an OS rate similar to BRCA-negative groups. When predicting the outcomes of medications like PARP inhibitors, it is important to consider whether LOH is present in tumors, as this can influence the effectiveness of the treatment [13].

Factor of tumor characteristics

Tumor subtypes: triple-negative breast cancer

Triple-negative breast cancer (TNBC) is characterized by the absence of estrogen (ER), progesterone (PR), and human epidermal growth factor 2 (HER2) receptors, accounting for about 15% to 20% of all breast cancer cases. Compared to non-TNBC breast cancer patients, those with TNBC often have lower OS and PFS. TNBC tends to progress more rapidly than hormone receptor-positive tumors, resulting in worse prognoses and higher relapse rates. The significant incidence of grade 3 tumors, which are highly proliferative upon diagnosis, contributes to the aggressive nature of TNBC. Recurrence rates for TNBC peak between one and three years after diagnosis, with the majority of fatalities occurring within five years of treatment [14].

Attempts to identify specific molecular markers for TNBC have been complicated by the absence of therapeutic targets. Despite the generally poor prognosis, TNBC shows better sensitivity to neoadjuvant treatment. It is crucial to identify targetable modifications in the residual tumor, as chemotherapy frequently alters the tumor's genetic makeup. Studies comparing biopsy samples from patients before and after therapy have identified substantial genetic differences, primarily in cell-cycle regulators and the PI3K/mTOR pathway. These genetic alterations may contribute to resistance to traditional chemotherapies. Discovering novel druggable targets in post-treatment biopsy samples could significantly enhance TNBC prognosis. Thus, post-treatment biopsy samples from TNBC patients who do not achieve pathologic complete response (pCR) following neoadjuvant chemotherapy must undergo molecular analysis [14].

Gene mutations affect TP53 in 65% to 80% of TNBC patients, making it the most commonly altered gene. In one of the largest investigations, TP53 mutations were found in 43% of non-basal and 62% of basal-like TNBC cases. These mutations increase genomic instability, cytogenetic alterations, and the likelihood of losing heterozygosity. Recent studies have shown that TNBC patients with reduced p53 function have lower OS and a higher risk of metastatic disease. Although some research did not support the predictive value of TP53 mutations or p53 expression, the differences between these factors may indicate poor prognosis in TNBC. TP53 mutations are also associated with chemoresistance. The high mutation rate of TP53 in TNBC makes it a desirable target for anticancer treatments. Additionally, PTEN, a critical inhibitor of the PI3K pathway, is often lost in TNBC, leading to rapid tumor cell proliferation and poor prognosis. Loss of PTEN expression is strongly related to ER negativity and a basal-like phenotype [14].

Tumor staging

Several factors impact the OS of breast cancer patients with BRCA mutations. Characteristics that decrease OS include lymph node infiltration in the armpit, larger primary tumors (T3 and T4 stages), older age, and negative steroid receptor status (ER-negative). Specifically, BRCA mutation carriers have a five-year OS rate of 77.3% [15].

Individuals with lymph node metastases (N+) exhibited a 3.0 times increased risk of mortality and have substantially worse five-year OS compared to patients without lymph node involvement. Tumor size is also related to five-year OS: 90% for T1, 84% for T2, and 63% for T3-T4. Advanced T3-T4 stages of the illness have the highest mortality risk, varying according to disease stage.

Patients with ER+ tumors have a negligibly better five-year OS compared to those with ER- tumors. Additionally, younger patients (under 40 years old) have a marginally higher OS. Lymph node metastases and ER- status are poor prognostic indicators in BRCA mutation carriers. Conversely, TNBC appears to be a positive predictive factor in this group [15].

Patient-related factors

Carrier status

Individuals with BRCA mutations had significantly lower survival rates compared to non-carriers. The ten-year OS rate for all examined groups was 78.0%, with BRCA mutation carriers having a survival rate of 65.9% and non-carriers having a rate of 81.1%. Similarly, the five-year OS rate was 86.2% across all groups, with BRCA mutation carriers at 77.3% and non-carriers at 88.1% [15].

BRCA mutation carriers exhibited a substantially increased risk of death compared to non-carriers. After adjusting for other prognostic variables, the difference in survival between carriers and non-carriers remained significant. Lower OS among BRCA mutation carriers was significantly correlated with higher tumor grade (T3–4), lymph node metastases (N+), and histological grade G3. In contrast, superior OS was associated with estrogen receptor-positive (ER+) status and younger age (under 40 years), although these factors did not have a major impact on survival outcomes [15].

Pathologic complete response (pCR)

Pathologic complete response (pCR) is a critical factor in determining the prognosis and survival of patients with breast cancer who have undergone neoadjuvant chemotherapy. Studies have shown that achieving a pCR is associated with improved outcomes [16,17]. The definition of pCR varies slightly across studies, but it generally refers to the absence of cancer in both the breast and armpit, indicating a significant regression of the neoplasia [18].

Studies have shown that pCR rates are higher in patients with BRCA1/2 mutations compared to those without mutations. The highest pCR rates were observed in BRCA1/2 mutation carriers with TNBC who received platinum-based treatment, although BRCA1/2 status did not significantly impact pCR rates in patients treated with anthracyclines versus those receiving carboplatin. Another study found that pCR positively influenced prognosis regardless of BRCA1/2 mutation status, showing a strong correlation between pCR and a three-year disease-free survival rate of 96.1% for patients with wild-type mutations and 95.5% for patients with BRCA1/2 mutations [19].

Understanding the relationship between pCR and prognosis across different patient subgroups is crucial for applying neoadjuvant research results to adjuvant settings. While a clear link between pCR and prognosis exists in patients with TNBC and HER2-positive breast cancer, this effect is less pronounced in those with hormone receptor-positive breast cancer [20]. As genetic testing becomes more integrated into clinical practice and neoadjuvant PARP inhibitor trials continue, knowledge of BRCA1/2 status will be increasingly important [19].

In conclusion, BRCA1/2 mutations carriers achieve higher pCR rates following neoadjuvant chemotherapy than non-carriers. The prognostic benefits of pCR in BRCA1/2 mutation carriers are comparable to those observed in individuals with wild-type genotypes. High pCR rates in mutation carriers with TNBC, particularly after platinum-based chemotherapy, support the use of these regimens in this patient population [19].

Treatment factors

Surgical intervention

BRCA1/2 mutation carriers undergoing breast cancer surgery have a higher risk of ipsilateral breast recurrence, which refers to the recurrence of cancer in the same breast where the initial tumor was treated, compared to those who undergo mastectomy. However, studies indicate no significant difference in OS, breast cancer

mortality, or distant recurrence between these surgical options. Data from a meta-analysis suggest that adjuvant chemotherapy and oophorectomy can lower the incidence of ipsilateral breast recurrence in BRCA1/2 mutation carriers who have had breast cancer surgery [21].

Breast cancer surgery can be a safe and appropriate choice for BRCA1/2 mutations carriers, but each case must be reviewed individually. Factors to consider include patient's ability to undergo necessary breast surveillance and their understanding of the increased risk for a new primary breast cancer in the ipsilateral breast, along with potential emotional effects. According to international guidelines, individuals with early-stage breast cancer who have mutations in moderate penetrance breast cancer susceptibility genes should be offered breast cancer surgery if appropriate. Patients with TP53 germline mutations should avoid breast conservation surgery and radiation due to a significant risk of acquiring radiation-induced cancers, such as angiosarcoma [7].

Determining the best surgical care for high-risk patients, including those with BRCA1/2 germline mutations who are diagnosed at a young age, remains an individual and often controversial decision. The increased risk of developing primary or contralateral breast cancer in BRCA1/2 mutation carriers often necessitates more aggressive surgical treatments for therapeutic and risk-reduction purposes. Skin-sparing mastectomies, with or without nipple-areolar complex preservation, have been shown to be safe and to produce better cosmetic results than breast-conserving surgery. When planning the appropriate surgical strategy, considerations should include the patient's genetic risk, family history, prior breast cancer characteristics, and personal preferences [22].

Chemotherapy response

Tumor cells with BRCA mutations may respond differently to various chemotherapy drugs. For example, they tend to be more sensitive to platinum-based therapies while showing resistance to taxanes [23,24]. A study found that BRCA1-associated patients had a significantly lower RR (23% vs 38%) and shorter median PFS (2.2 vs 4.9 months) compared to sporadic patients. In hormone receptor (HR)-negative patients, BRCA1-associated cases showed even poorer outcomes. Conversely, BRCA2-associated patients, mostly HR-positive, exhibited higher RR (89% vs 38%) but similar PFS compared to sporadic cases. These results suggest that BRCA1-associated, HR-negative metastatic breast cancers are less responsive to taxane chemotherapy, whereas BRCA2-associated cancers remain highly sensitive [25].

The optimal treatment for BRCA mutation carriers requires further prospective research. Determining the BRCA mutation status before starting cancer treatment is essential, as it can predict the effectiveness of adding PARP inhibitors to the treatment regimen for breast cancers associated with BRCA mutations. Additionally, research identified individuals with TP53 and PMS2 protein-truncating mutations, which are high-penetrance cancer-predisposing genes, indicating an increased risk for various malignancies [12].

Platinum-based drugs treatment

Platinum-based drugs, including cisplatin, carboplatin, and oxaliplatin, are essential in cancer treatment. They have demonstrated substantial effectiveness in addressing BRCA1/2-related cancers, attributed to defects in homologous recombination [26]. The effectiveness of platinum-based drugs in BRCA1/2 mutation carriers is largely attributed to the concept of synthetic lethality, where the inhibition of two pathway leads to cell death. In particular, platinum-based drugs and PARP inhibitors are theoretically effective for patients with loss-of-function mutations in BRCA1/2, such as those with BRCA2 p.I3169M fs*48 mutations, as seen in pancreatic cancer [27]. In another case, platinum-based therapy followed by a PARP inhibitor led to near-complete remission in a patient with hereditary breast and ovarian cancer syndrome [28]. This suggests that platinum-based drugs could be a significant factor affecting the prognosis of hereditary breast

cancer, potentially improving outcomes for patients with BRCA mutations. However, resistance to platinum-based therapies has developed in some cases. Factors affecting the prognosis of hereditary breast cancer, such as response to platinum-based drugs, can be influenced by biomarkers like ATP7A and ATP7B, which are involved in drug resistance mechanisms [29].

PARP inhibitors

The introduction of PARP inhibitors has significantly enhanced treatment options for BRCA1/2-related breast cancer, contributing to improved survival rates. PARP inhibitors, including olaparib, talazoparib, niraparib, and rucaparib, have received regulatory approval for various indications. For example, olaparib approved for maintenance treatment of ovarian cancer and for BRCA-mutated metastatic breast cancer. Veliparib remains under evaluation in clinical trials and has not yet received FDA approvals [30]. The efficacy of PARP inhibitors in patients with BRCA-mutated advanced breast cancer significantly improves both PFS and OS. The study found a HR of 0.64 for PFS and 0.86 for OS, indicating a substantial benefit in survival outcomes for germline BRCA-mutated breast cancer patients treated with PARP inhibitors [31]. Research is ongoing into combinatorial approaches using PARP inhibitors with chemotherapy or immunotherapy. These combination strategies are showing promise for future and long-term management of BRCA1/2-related breast cancer [22].

Current research and future directions

New genetic markers and their prognostic significance

A recent study on hereditary breast cancer in the Tunisian population identified eleven novel BRCA mutations among 354 patients, revealing significant insights into the genetic landscape and its prognostic implications. Key findings include an early age of onset for BRCA mutation carriers, a higher prevalence of TNBC in BRCA1 carriers, and a notable incidence of contralateral breast cancer and ovarian cancer in BRCA1 mutation carriers. Several novel mutations, such as BRCA1_c.915T>A and BRCA2_c.249delG, were identified, contributing to the understanding of the mutation spectrum in Tunisia. The study emphasizes the importance of targeted genetic testing and personalized treatment strategies, highlighting the genetic heterogeneity of hereditary breast cancer and the critical role of novel genetic markers in improving prognostic assessments and therapeutic approaches [32].

Panel gene testing for hereditary breast cancer

Commercial multigene panel testing allows for the identification of patients with harmful mutations beyond the well-known *BRCA* genes. These tests can detect mutations in genes associated with highly penetrant disorders, such as Li-Fraumeni syndrome and Cowden syndrome, with individuals carrying these mutations having a lifetime breast cancer risk exceeding 50% [33,34].

The availability of affordable gene sequencing has enabled the extensive use of panel testing, which assesses multiple cancer-related genes simultaneously. Through next-generation sequencing (NGS) based multi-gene panel testing, the study discovered a wider range of pathogenic variants (PVs) beyond *BRCA1/2*, including genes like *ATM, CHEK2, PALB2, PTEN*, and *TP53*. The findings indicated that 37.4% of BBC patients possessed germline PVs in these high- and intermediate-penetrance breast cancer susceptibility genes. These results highlight the importance of comprehensive genetic testing for all bilateral breast cancer patients, regardless of their personal or family cancer history, as limited gene testing could overlook a substantial number of PVs [35].

Another study investigates the prevalence of pathogenic and likely pathogenic mutations in non-BRCA1/BRCA2 genes among Turkish breast cancer patients who tested negative for BRCA1/BRCA2 mutations. Utilizing Qiagen's hereditary cancer panels and Illumina MiSeq sequencing, the research identified pathogenic variants in genes such as ATM, NBN, PTEN, and RAD51C, as well

as a likely pathogenic variant in MUTYH among 8.5% and 1.4% of patients, respectively. Notably, a novel RAD51C variant was reported [36].

Using a comprehensive 127-gene hereditary cancer panel, 26 pathogenic and 6 likely pathogenic variants were found in *BRCA1, BRCA2, CHEK2, PALB2*, and *NBN* genes, present in 58% of the patients. Notably, certain variants like BRCA1 p.Trp1815Ter appeared in multiple unrelated patients, suggesting possible founder mutations. The study highlighted that testing only BRCA1/2 genes would have missed 18% of patients with pathogenic variants [37], demonstrating the importance of comprehensive genetic testing in identifying a broader spectrum of hereditary cancer risk genes.

Conclusion

People with hereditary breast cancer due to BRCA1/2 mutations are more likely to have lower overall survival since they are also at a higher chance to develop another cancer in their life. The factors that affect the prognosis of hereditary breast cancer such as type of gene mutation. Different gene mutations will have different types of breast cancer and other cancer that are more likely to develop. These mutations may respond differently to various chemotherapy drugs. High penetrance cancer predisposing genes would considerably increase the risk for various malignancies. The stage of cancer found in every individual will result in different overall survival rates. Neoadjuvant treatment in patients with hereditary breast cancer had a greater pathological complete response. The molecular type of breast cancer is affecting the prognosis too, TNBC often has lower OS and PFS. Further studies investigating the possible contributing factors to its prognosis would benefit in increasing the survival rate of the patients.

Individuals with hereditary breast cancer due to BRCA1/2 mutations are at a higher risk for lower OS, as they are more likely to develop additional cancers throughout their lives. Prognostic factors for hereditary breast cancer include the type of gene mutation, which can influence the specific type of breast cancer and the likelihood of developing other malignancies. Different gene mutations respond differently to various chemotherapy drugs, with high-penetrance cancer-predisposing genes significantly increasing the risk for multiple cancers. The cancer stage at diagnosis also impacts overall survival rates. Patients with hereditary breast cancer who undergo neoadjuvant treatment often achieve a greater pathological complete response. The molecular subtype of breast cancer, such as TNBC, also affects prognosis, with TNBC patients generally having lower OS and PFS. Further research into the factors influencing prognosis could improve survival rates for patients with hereditary breast cancer.

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Authors Contributions

Conceptualization, Methodology, Writing – Original Draft, S: Data curation, Writing – Review & Editing, provided critical revisions to enhance the intellectual content of the review.

Declaration of interest

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