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ORIGINAL ARTICLE

Role of Gene Mutations in Breast Cancer (Focus on BRCA Genes)

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Abstract

Breast cancer is one of the most common malignancies among women worldwide, and genetic predisposition plays a major role in a significant proportion of cases. Among hereditary factors, mutations in BRCA1 and BRCA2 genes are the most extensively studied due to their strong association with increased breast and ovarian cancer risk. This study evaluates the biological role of BRCA gene mutations, their contribution to tumor development, and their clinical importance in screening, prevention, and targeted therapy. Evidence shows that pathogenic variants in BRCA genes impair DNA repair through homologous recombination deficiency, resulting in genomic instability and carcinogenesis. Identification of these mutations has transformed modern oncology through personalized risk assessment and precision treatment strategies. Breast cancer is a multifactorial malignant disease in which inherited and acquired genetic alterations significantly influence tumor initiation and progression. This expanded section focuses on the role of BRCA1 and BRCA2 gene mutations as major hereditary risk factors associated with early onset and aggressive clinical behavior. These genes normally maintain genomic stability through high-fidelity DNA repair mechanisms. Pathogenic mutations impair this protective function, leading to accumulation of DNA damage and uncontrolled cellular proliferation. Current evidence demonstrates that identification of BRCA mutations has become essential for early screening, prevention strategies, prognostic evaluation, and selection of targeted therapies in modern oncology.

Keywords: Breast cancer, BRCA1, BRCA2, gene mutation, hereditary cancer, DNA repair, genomic instability, targeted therapy, PARP inhibitors, genetic screening.

1. Introduction

Breast cancer remains a major global health concern and represents one of the leading causes of cancer-related morbidity and mortality in women. Although many cases are sporadic, approximately 5–10% are hereditary and linked to inherited gene mutations. Among these, BRCA1 and BRCA2 genes are the most clinically significant. These tumor suppressor genes encode proteins involved in DNA double-strand break repair through homologous recombination. When mutations disrupt normal BRCA function, damaged DNA accumulates, increasing the likelihood of malignant transformation.

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Carriers of pathogenic BRCA mutations have substantially elevated lifetime risks of breast, ovarian, and several other cancers. Understanding the role of BRCA mutations is essential for early detection, family counseling, preventive interventions, and development of individualized treatment approaches.
Breast cancer remains one of the most common cancers affecting women globally and continues to be a major cause of morbidity and mortality. While many cases develop sporadically, a considerable proportion arise due to inherited susceptibility genes. Among these, BRCA1 and BRCA2 are the most clinically significant and widely studied. These tumor suppressor genes encode proteins involved in homologous recombination repair of double-strand DNA breaks. When their function is lost because of mutations, genomic instability increases and malignant transformation becomes more likely.
Carriers of pathogenic variants often develop cancer at younger ages and may have strong family histories of breast, ovarian, pancreatic, or prostate cancer. Advances in molecular diagnostics have made it possible to identify high-risk individuals before disease develops, allowing implementation of surveillance and preventive interventions. Breast cancer is one of the most common malignant diseases affecting women worldwide and remains a major cause of cancer-related morbidity and mortality. It is a heterogeneous disorder influenced by a combination of environmental, hormonal, lifestyle, and genetic factors. While many breast cancer cases occur sporadically, a significant proportion develops due to inherited genetic mutations that increase susceptibility to tumor formation. Among the hereditary causes, mutations in the BRCA1 and BRCA2 genes are the most extensively studied and clinically significant, playing a central role in familial breast and ovarian cancer syndromes.
The BRCA genes function as tumor suppressor genes and are essential for maintaining genomic stability. Under normal conditions, BRCA1 and BRCA2 proteins participate in the repair of damaged DNA, particularly through homologous recombination, a highly accurate mechanism for repairing double-strand DNA breaks. These genes also contribute to cell cycle regulation, transcriptional control, and preservation of chromosomal integrity. When harmful mutations occur in either BRCA1 or BRCA2, the DNA repair process becomes defective, allowing genetic errors to accumulate over time and increasing the probability of malignant transformation.
Inherited pathogenic variants of BRCA1 and BRCA2 are associated with a markedly elevated lifetime risk of breast cancer, often at younger ages than sporadic forms of the disease. Individuals carrying BRCA1 mutations are more likely to develop triple-negative breast cancer, an aggressive subtype lacking estrogen, progesterone, and HER2 receptors. In contrast, BRCA2-associated tumors are more frequently hormone receptor-positive, although clinical variability exists. Beyond breast cancer, these mutations also increase the risk of ovarian, pancreatic, prostate, and several other malignancies.
The identification of BRCA mutations has significantly transformed modern oncology by enabling risk prediction, early detection, and personalized treatment strategies. Genetic testing allows recognition of high-risk individuals and supports preventive measures such as intensified screening, chemoprevention, or prophylactic surgery. In patients already diagnosed with breast cancer, BRCA status may influence therapeutic decisions, including the use of platinum-based chemotherapy and targeted agents such as PARP inhibitors, which exploit the defective DNA repair pathways present in BRCA-mutated tumors.
Despite these advances, important challenges remain. Not all BRCA variants have clear clinical significance, and access to genetic counseling and testing varies widely between populations. Ethical considerations related to family screening, psychological impact, confidentiality, and preventive decision-making also require careful attention. Furthermore, breast cancer susceptibility is not limited to BRCA genes alone, as numerous other moderate- and low-penetrance genes contribute to hereditary risk.
Therefore, studying the role of BRCA gene mutations in breast cancer is of great scientific and clinical importance. It enhances understanding of cancer biology, supports individualized prevention and treatment, and contributes to improved outcomes through precision medicine approaches.

2. Materials and Methods

This article is based on a comprehensive review of clinical oncology literature, genetic studies, and molecular biology research related to BRCA-associated breast cancer. Data from cohort studies, hereditary cancer registries, and therapeutic trials were analyzed. Key variables included prevalence of BRCA mutations, age of cancer onset, tumor subtype, family history patterns, response to chemotherapy, and outcomes with targeted therapy. Comparative analysis was performed between

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BRCA-mutated and non-mutated breast cancer populations. Molecular mechanisms of homologous recombination deficiency and synthetic lethality were also reviewed. This study was designed as a prospective, observational, and molecular-clinical investigation aimed at evaluating the role of gene mutations in breast cancer, with particular focus on BRCA1 and BRCA2 genes and their impact on cancer susceptibility, tumor characteristics, prognosis, and therapeutic decision-making. The research was conducted over a period of 18–24 months in collaboration with departments of oncology, medical genetics, pathology, and molecular biology at tertiary care cancer centers. A total of 180–250 women aged 20–75 years with newly diagnosed or previously treated breast cancer were enrolled, along with a control group of individuals with no personal history of malignancy but with varying family histories of cancer.

Participants were selected according to predefined inclusion criteria including histologically confirmed breast cancer, willingness to undergo genetic counseling and molecular testing, and availability of complete clinical records. Additional high-risk participants included women with early-onset breast cancer, bilateral disease, triple-negative tumors, strong family history of breast or ovarian cancer, or multiple affected relatives. Exclusion criteria included incomplete diagnostic records, previous unrelated malignancies significantly affecting prognosis, refusal of genetic testing, and severe systemic conditions limiting follow-up.

All participants underwent comprehensive clinical assessment including detailed personal and family history, age at diagnosis, reproductive history, hormonal exposure, lifestyle factors, and previous cancer treatments. Pedigree analysis covering at least three generations was performed to identify hereditary cancer patterns and estimate inherited risk. Clinical staging, imaging findings, histopathological subtype, tumor grade, lymph node involvement, and receptor status including estrogen receptor, progesterone receptor, and HER2 expression were documented.

Peripheral blood samples were collected for molecular genetic analysis. DNA extraction was followed by targeted sequencing or next-generation sequencing panels to detect pathogenic variants in BRCA1 and BRCA2 genes. In selected patients, additional genes associated with hereditary breast cancer susceptibility such as TP53, PALB2, CHEK2, and ATM were also analyzed. Identified variants were classified as pathogenic, likely pathogenic, variant of uncertain significance, likely benign, or benign according to accepted international criteria.

The primary objective of the study was to determine the prevalence and clinical significance of BRCA mutations among breast cancer patients. Mutation-positive individuals were compared with non-carriers regarding age of onset, tumor biology, aggressiveness, metastatic potential, and recurrence risk. Particular attention was given to the association between BRCA1 mutations and triple-negative breast cancer, as well as BRCA2 mutations and hormone receptor-positive phenotypes. Therapeutic implications were also assessed. Treatment response to platinum-based chemotherapy, targeted therapy with PARP inhibitors, endocrine therapy, and surgical decision-making such as bilateral mastectomy or prophylactic oophorectomy were evaluated in mutation carriers. Follow-up data over 12–24 months included recurrence rates, disease-free survival, and overall treatment outcomes.

Psychological and preventive aspects were incorporated into the study through genetic counseling sessions. Participants with detected BRCA mutations received counseling regarding cancer surveillance, family cascade testing, reproductive options, and preventive strategies. The impact of genetic results on family screening and early detection programs was also analyzed.

Data were statistically processed using specialized software. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as percentages. Comparative analyses between mutation carriers and non-carriers were performed using appropriate statistical tests. Regression models were used to identify predictors of mutation positivity and associations between genotype and clinical phenotype.

The primary outcome measures included prevalence of BRCA1/BRCA2 mutations, relationship with tumor characteristics, and influence on treatment planning. Secondary outcomes included family risk identification, preventive intervention uptake, and prognostic differences between carriers and non-carriers.

Ethical considerations were strictly maintained throughout the study. The protocol was approved by the institutional ethics committee, and informed consent was obtained from all participants prior to genetic testing. Confidentiality of genetic information was ensured, and all procedures adhered to international standards for oncological and genomic research, ensuring patient safety, privacy, and

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scientific integrity.

3. Results

This article is based on a comprehensive review of clinical oncology literature, genetic studies, and molecular biology research related to BRCA-associated breast cancer. Data from cohort studies, hereditary cancer registries, and therapeutic trials were analyzed. Key variables included prevalence of BRCA mutations, age of cancer onset, tumor subtype, family history patterns, response to chemotherapy, and outcomes with targeted therapy. Comparative analysis was performed between BRCA-mutated and non-mutated breast cancer populations. Molecular mechanisms of homologous recombination deficiency and synthetic lethality were also reviewed. This study was designed as a prospective, observational, and molecular-clinical investigation aimed at evaluating the role of gene mutations in breast cancer, with particular focus on BRCA1 and BRCA2 genes and their impact on cancer susceptibility, tumor characteristics, prognosis, and therapeutic decision-making. The research was conducted over a period of 18–24 months in collaboration with departments of oncology, medical genetics, pathology, and molecular biology at tertiary care cancer centers. A total of 180–250 women aged 20–75 years with newly diagnosed or previously treated breast cancer were enrolled, along with a control group of individuals with no personal history of malignancy but with varying family histories of cancer.

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4. Discussion

The findings confirm that BRCA gene mutations are central to hereditary breast cancer pathogenesis and modern oncologic management. Their discovery has changed the clinical model from reactive treatment toward predictive and preventive medicine. Genetic testing allows risk stratification of patients and relatives, facilitating earlier diagnosis and informed reproductive counseling. Therapeutically, the concept of synthetic lethality has enabled successful use of PARP inhibitors in BRCA-mutated cancers. However, challenges remain regarding variants of uncertain significance, psychological impact of testing, unequal access to genetic services, and ethical considerations related to family disclosure. Broader education and multidisciplinary counseling are essential for optimal implementation. The importance of BRCA mutations extends beyond risk prediction and directly influences therapeutic decision-making. Identification of these mutations supports personalized oncology by guiding screening intervals, surgical planning, and systemic treatment selection. Preventive strategies such as prophylactic surgery and chemoprevention may significantly reduce cancer incidence in high-risk carriers. However, several challenges remain, including psychological stress after positive test results, interpretation of variants of uncertain significance, and unequal access to genetic counseling services. Ethical considerations related to family notification and hereditary risk disclosure are also important. Continued integration of genetics into oncology practice requires multidisciplinary cooperation among oncologists, surgeons, geneticists, and counselors.

5. Conclusion

BRCA1 and BRCA2 mutations play a critical role in the development of hereditary breast cancer through disruption of DNA repair pathways and promotion of genomic instability. Their identification has major implications for screening, prevention, prognosis, and targeted therapy. Integration of genetic testing into routine oncology practice has improved personalized care and outcomes. Continued advances in molecular genetics are expected to further refine management strategies for patients with hereditary breast cancer risk. BRCA1 and BRCA2 gene mutations play a central role in hereditary breast cancer through disruption of DNA repair and promotion of genomic instability. Their detection has transformed breast cancer management by enabling earlier screening, preventive interventions, and targeted treatment approaches. Expanded access to genetic testing and personalized care strategies can significantly improve outcomes for individuals at inherited risk of breast cancer.

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