Breast Cancer

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Introduction

Breast cancer is one of the most common malignancies worldwide and remains a major cause of cancer-related morbidity and mortality among women. Its complex biological and molecular characteristics contribute to differences in tumor behavior, prognosis, and response to treatment. Understanding the molecular mechanisms underlying breast cancer is therefore essential for improving early diagnosis, treatment selection, and patient outcomes.[1]

Pathogenesis

Breast cancer develops through the accumulation of genetic and molecular alterations that disrupt normal mammary epithelial cell growth, differentiation, and survival. These changes can lead to uncontrolled proliferation and the progression from premalignant lesions to invasive and, in some cases, metastatic disease. The tumor microenvironment also plays an important role in breast cancer initiation and progression. Stromal cells, immune cells, macrophages, and extracellular signaling molecules can influence tumor growth, invasion, angiogenesis, and metastasis.[2]

Risk Factors

Genetic Risk Factors

Hereditary factors account for approximately 5–10% of breast cancer cases. The risk is particularly increased in individuals with a strong family history, especially when a first-degree relative is affected. *BRCA1* and *BRCA2* are among the most important high-risk genes and play key roles in homologous recombination-mediated DNA repair. Other high-penetrance genes associated with breast cancer include *TP53, PTEN, CDH1,* and *STK11*, while moderate-risk genes include *CHEK2, ATM, PALB2,* and *BRIP1*.[1]

Hormonal Risk Factors

Hormonal exposure is an important factor in breast cancer development. Estrogen promotes the growth and proliferation of breast epithelial cells through estrogen receptor signaling. Prolonged or increased exposure to estrogen, whether due to endogenous hormonal factors or exogenous hormone use, may therefore contribute to breast cancer risk.[2]

Diet and Lifestyle

Dietary patterns and lifestyle factors may also influence breast cancer risk. Diets rich in fruits, vegetables, legumes, whole grains, and olive oil, such as the Mediterranean diet, have been associated with a lower risk of breast cancer. In contrast, diets characterized by high energy intake and greater consumption of processed foods may contribute to obesity and other metabolic factors associated with cancer risk. Alcohol consumption is also associated with an increased risk of breast cancer, even at relatively low levels of intake.[2]

Treatment

Surgery

Breast-conserving surgery (BCS) followed by radiotherapy and mastectomy are established local treatment options for early-stage breast cancer. BCS is generally preferred when complete tumor removal with acceptable cosmetic outcomes can be achieved and radiotherapy is appropriate. Mastectomy may be considered in patients with extensive or multicentric disease, diffuse suspicious microcalcifications, inability to obtain clear surgical margins, or contraindications to radiotherapy.

Management of the axillary lymph nodes depends on clinical stage, tumor characteristics, and whether neoadjuvant systemic therapy has been given. In clinically node-negative disease, sentinel lymph node biopsy is commonly used for axillary staging, while axillary lymph node dissection is reserved for selected patients.[4]

Chemotherapy

Chemotherapy may be administered as neoadjuvant, adjuvant, or treatment for recurrent or metastatic disease. Neoadjuvant chemotherapy can reduce tumor size, increase the possibility of breast-conserving surgery, and treat micrometastatic disease at an early stage. It also provides an opportunity to assess treatment response, particularly in aggressive breast cancer subtypes such as triple-negative and HER2-positive disease.

The use of molecular subtyping and multigene assays can further help identify patients who are more likely to benefit from chemotherapy and avoid unnecessary treatment in selected patients.[4]

Triple-Negative Breast Cancer

Triple-negative breast cancer (TNBC) is an aggressive subtype characterized by the absence of estrogen receptor, progesterone receptor, and HER2 expression. It is associated with a higher risk of early recurrence and limited treatment options compared with hormone receptor-positive breast cancer.

Chemotherapy remains an important component of TNBC treatment, particularly in the neoadjuvant setting. Pathological complete response following neoadjuvant therapy can provide important prognostic information. For patients with *BRCA1/2* mutations, PARP inhibitors may provide therapeutic benefit, while antibody-drug conjugates such as sacituzumab govitecan offer options for selected advanced or treatment-resistant cases. Immune checkpoint inhibitors targeting the PD-1/PD-L1 pathway, when combined with chemotherapy, have also improved outcomes in selected patients.[5]

Future research should focus on personalized treatment strategies, combination therapies, and approaches to overcome tumor heterogeneity and treatment resistance.

Conclusions and Perspectives

Breast cancer remains a major global health challenge because of its complex biology, diverse clinical subtypes, and potential for recurrence and metastasis. Advances in imaging, molecular diagnostics, and genetic testing have improved early detection and helped guide individualized treatment.

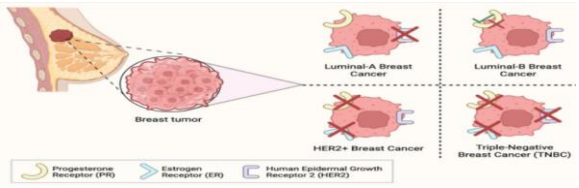


Figure 1: *GPER-mediated signaling pathways involved in triple-negative breast cancer progression, including angiogenesis, epithelial–mesenchymal transition, invasion, migration, and metastasis. Reproduced from Zhang et al.*[6]

Current management increasingly combines surgery, systemic therapy, targeted therapy, immunotherapy, and molecularly guided approaches according to tumor subtype and patient characteristics. Continued research is essential to improve diagnostic accuracy, overcome treatment resistance, and develop more effective personalized therapies.[6]

Increasing public awareness, improving access to appropriate screening and diagnostic services, and strengthening collaboration among healthcare professionals and researchers are also essential for reducing the global burden of breast cancer. A comprehensive approach integrating prevention, early detection, accurate diagnosis, effective treatment, and patient education can contribute substantially to improving outcomes and reducing breast cancer-related mortality.[7]

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