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Analysis of the Mechanism and Prognostic Factors of Breast Cancer

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ABSTRACT

Breast cancer ranks among the most frequently diagnosed cancers in women worldwide, driven by a multifaceted interplay of genetic, hormonal, environmental, and lifestyle influences. This paper delves into the underlying mechanisms of breast cancer progression, highlighting its molecular features and the contributions of diverse factors such as lifestyle behaviors, hormonal imbalances, and inherited genetic risks. Additionally, the biological behaviors of Luminal and HER2-enriched subtypes are discussed, along with the latest research advancements in precision medicine tailored to these subtypes. By integrating multi-omics data, this work uncovers the heterogeneity within HER2 subtypes and identifies new therapeutic targets, offering critical insights for personalized breast cancer diagnosis and treatment. The paper also reviews the most recent developments in surgery, endocrine therapy, chemotherapy, and immunotherapy, highlighting their roles in improving patient outcomes. Moreover, it explores the potential of metabolic reprogramming and targeted therapies as innovative strategies to further enhance prognosis. Looking ahead, multidisciplinary collaboration and technological advances are expected to play a pivotal role in refining the precision of breast cancer diagnosis and therapy.

KEYWORDS

Breast cancer; Molecular subtypes; Endocrine therapy; Metabolic reprogramming

1. INTRODUCTION

Breast cancer is a leading malignancy among women globally, exhibiting significant variations in epidemiological patterns across regions and socioeconomic groups. According to the Global Burden of Disease (GBD) 2021 study, the incidence of breast cancer in women aged 70 and older rose slightly from 104 cases per 100,000 in 1990 to 107 cases in 2021. Regionally, the highest rates are observed in high-income areas like North America, while North Africa and the Middle East show the most rapid rises in incidence and disability-adjusted life years (DALYs). In countries with a high Social Development Index (SDI), DALYs have declined over recent decades due to advancements in endocrine therapy and targeted treatments. In 2019, 2,002,354 new cases of breast cancer were reported globally, with high SDI countries exhibiting the highest overall incidence, despite a decrease in age-standardized rates. Breast cancer-related deaths and DALYs in the same year totaled 700,660 and 20,625,313, respectively. Nevertheless, age-standardized mortality rates and DALYs declined from 1990 to 2019 due to improved treatments and enhanced public health initiatives, especially in high- and intermediate-SDI countries.

With the rising global incidence of breast cancer, understanding its underlying mechanisms and prognostic factors is vital for advancing patient care and developing more effective treatment strategies. Breast cancer develops through a multifaceted interaction of genetic, hormonal, lifestyle, and environmental influences, forming the basis for advancements in molecular typing and tailored treatment strategies. Classified by mRNA expression levels, it encompasses four molecular subtypes—Luminal A, Luminal B, HER2-enriched, and Basal-like—each providing vital insights for therapy and patient stratification.

Building on this molecular classification, the 8th edition of the TNM staging system incorporates both anatomical and biological features, enabling a more comprehensive understanding of breast cancer characteristics. This advanced approach enhances staging precision while providing a framework for personalized patient care. These developments have deepened researchers' understanding of breast cancer biology, opening new pathways for targeted therapies and better patient outcomes.

This paper aims to systematically explore the mechanisms driving breast cancer, including its genetic, hormonal, lifestyle, and environmental underpinnings, while delving into its molecular and prognostic features. We hope this study provides a strong scientific basis for early detection, precision treatment, and personalized management strategies for breast cancer.

2. MECHANISMS OF BREAST CANCER

2.1. Lifestyle and Environmental Factors

Unhealthy lifestyle choices are strongly associated with an increased risk of breast cancer. Key risk factors include alcohol consumption and smoking, with studies showing that regular alcohol intake significantly elevates this risk [1]. Similarly, habits such as physical inactivity and a high-fat diet further exacerbate susceptibility to breast cancer [2, 3].

Environmental factors also play a crucial role in influencing breast cancer risk. For instance, research has demonstrated an inverse relationship between sunlight exposure and breast cancer incidence, with lower rates observed in regions receiving higher solar radiation[4]. Conversely, ionizing radiation is a significant risk factor, particularly for individuals exposed at a young age, such as those undergoing radiotherapy for Hodgkin's lymphoma, who face a markedly higher likelihood of developing breast cancer.

These observations underscore the importance of adopting preventive measures to mitigate risk. Key strategies to mitigate risk involve limiting alcohol intake, avoiding smoking, adopting a balanced diet, engaging in consistent physical exercise, and reducing exposure to unnecessary radiation. Together, these lifestyle adjustments are pivotal in the primary prevention of breast cancer.

2.2. Hormonal Factors

Elevated levels of endogenous estrogens, such as estradiol, free estradiol, and estrone, are significant contributors to breast cancer risk. These hormones bind to estrogen receptors (ERα and ERβ), promoting the proliferation and differentiation of breast epithelial cells. Similarly, progesterone influences mammary gland development by interacting with the progesterone receptor (PR), potentially increasing breast cancer risk by disrupting genomic regulation within the ER signaling pathway.

Recent research has uncovered key hormonal mechanisms involved in breast cancer progression. Lee et al. demonstrated that estrogen can induce DNA double-strand breaks at ERα binding sites, leading to localized amplification of oncogenes such as HER2 and CCND1 through a process known as "translocation-bridge amplification" [5]. This phenomenon represents a critical initiating event in tumor development, further exacerbating genomic instability by impairing DNA repair mechanisms, which accelerates tumor progression [5].

Additionally, Scabia et al. revealed that both progesterone (P4) and estrogen (E2) independently stimulate tumor growth, while their combined effect significantly enhances metastasis [6]. Notably, PR has been shown to drive tumor proliferation and metastasis even when the ER signaling pathway is suppressed. These findings suggest an independent role of PR within the hormonal signaling network, where its interaction with ER may limit the efficacy of hormonal therapies. Targeting the PR signaling pathway or suppressing PR expression may offer novel strategies to overcome endocrine resistance and improve therapeutic outcomes.

2.3. Genetic Factor

Genetic factors play a pivotal role in breast cancer risk, with a family history significantly amplifying the likelihood of developing the disease. Among these factors, mutations in the BRCA1 and BRCA2 genes stand out as particularly influential, as individuals carrying such mutations face a markedly elevated risk of breast cancer compared to the general population [7]. These genes encode proteins that are essential for maintaining genomic stability by orchestrating critical DNA damage repair processes, particularly the repair of double-strand breaks via homologous recombination. When mutations occur in BRCA1 or BRCA2, these repair mechanisms become impaired, leading to genomic instability and the accumulation of DNA damage over time. This instability creates a favorable environment for the emergence and accumulation of oncogenic mutations, which can ultimately trigger the development and progression of breast cancer [8]. Furthermore, individuals with BRCA mutations often exhibit increased sensitivity to certain targeted therapies, such as PARP inhibitors, underscoring the clinical significance of understanding the genetic underpinnings of breast cancer.

Moreover, BRCA mutation carriers exhibit increased sensitivity to targeted therapies, such as PARP inhibitors, which offer a promising treatment strategy for high-risk individuals. These findings underscore the significance of genetic background not only in understanding breast cancer mechanisms but also in improving diagnosis and treatment outcomes [9].

By integrating insights from genetic, hormonal, and lifestyle factors, a more holistic understanding of breast cancer's underlying mechanisms can be achieved. This comprehensive approach lays the groundwork for early prevention strategies, effective screening of high-risk populations, and the development of precise treatment programs.

3. MOLECULAR BIOLOGY OF BREAST CANCER

3.1. Molecular Typing

Breast cancer is classified into four distinct molecular subtypes—Luminal A, Luminal B, HER2-enriched, and Basal-like—based on mRNA expression profiles. These subtypes provide a robust framework for understanding the heterogeneity of breast cancer, serving as the foundation for the development of innovative therapeutic strategies and patient stratification approaches. Each subtype exhibits unique biological characteristics that profoundly influence treatment responses and prognostic outcomes. Molecular typing plays a critical role in guiding clinical decisions by enabling precision medicine approaches. For example, patients with Luminal subtypes often benefit from endocrine therapy, while those with HER2-enriched tumors respond better to targeted anti-HER2 therapies. Gene expression profiling further enhances the capacity of molecular typing to design tailored treatment plans that optimize therapeutic efficacy, minimize adverse effects, and improve patient outcomes. This precision-guided approach represents a pivotal advancement in modern oncology, allowing clinicians to address the complexity of breast cancer on an individual level.

3.1.1. Treatment Decisions for Early Hormone Receptor-Positive Breast Cancer

Determining whether adjuvant chemotherapy is necessary for patients with early-stage hormone receptor-positive, HER2-negative breast cancer remains one of the most pressing challenges in clinical oncology. This is primarily because traditional clinicopathological factors, such as tumor size, histological grade, and lymph node involvement, often fail to provide a reliable prediction of which patients are likely to benefit from chemotherapy. These conventional parameters lack the precision needed to identify individual patient profiles, leading to overtreatment in some cases and undertreatment in others. Molecular typing, particularly through advancements in gene expression profiling technologies, has emerged as a transformative tool to address this limitation. By analyzing tumor-specific gene expression patterns, molecular typing allows for a more nuanced assessment of tumor biology and chemotherapy sensitivity. This precision-driven approach enables clinicians to make evidence-based decisions, optimizing treatment outcomes while sparing patients from unnecessary side effects associated with chemotherapy.

3.1.2. Role of Gene Expression Profiling (Oncotype DX) in Chemotherapy Decisions

Oncotype DX provides an evidence-based tool for assessing breast cancer recurrence risk through tumor gene expression profiles. This is especially beneficial for the Luminal subtype (hormone receptor-positive, HER2-negative). Findings from the RxPONDER clinical trial demonstrated that postmenopausal patients with a 21-gene recurrence score (RS) ≤ 25 could achieve effective outcomes with endocrine therapy alone, eliminating the need for adjuvant chemotherapy [10]. This approach not only reduces treatment-related adverse effects but also significantly enhances patients' quality of life..

3.1.3. Gene Expression Profiling (MammaPrint) and Other Molecular Assayss

Beyond the 21-gene expression profiling, additional molecular tests such as MammaPrint provide valuable support in chemotherapy decision-making. MammaPrint, a gene expression profiling tool, differentiates between "genetically low-risk" and "genetically high-risk" breast cancer patients. It strongly intersects with molecular staging, particularly in the Luminal subtype, where traditional pathological indices, such as tumor size and grading, may fail to provide comprehensive characterization.

The MINDACT study demonstrated that chemotherapy could be avoided in patients who were clinically at high risk but genetically at low risk without compromising prognostic outcomes [11]. These findings highlight the importance of molecular typing in guiding individualized therapies and refining treatment strategies.

3.1.4. Transformations in Clinical Practice

The outcomes of large clinical trials have prompted updates in international treatment guidelines, incorporating molecular typing into adjuvant treatment decisions. For instance, the 2017 Clinical Practice Guidelines for Breast Cancer recognized the utility of gene expression profiling in refining adjuvant chemotherapy recommendations, underscoring the shift toward precision and individualized treatment [12].

Molecular typing is transforming the treatment approach for early-stage hormone receptor-positive breast cancer by introducing a more personalized and precise methodology. Through the use of gene expression profiling, clinicians can more accurately identify patients who are most likely to benefit from chemotherapy, avoiding overtreatment and unnecessary toxicity for those who may not require it. This tailored approach enhances therapeutic outcomes while significantly reducing adverse side effects, leading to improved overall quality of life for patients. As research continues to advance, molecular typing is anticipated to play a pivotal role in the evolution of precision medicine, further refining treatment strategies and optimizing outcomes for breast cancer patients.

3.2. Molecular Analysis of the Mechanism of Occurrence

3.2.1. Luminal subtype

Mechanisms of the Luminal subtype of breast cancer include hormone receptor signaling pathways, genomic and epigenetic regulation, and metabolic reprogramming. Together, these mechanisms contribute to tumorigenesis, progression, and treatment resistance, providing an important theoretical basis for precision therapy.

(1) Hormone receptor signaling pathway

The hormone receptor signaling pathway serves as a core regulatory mechanism in Luminal subtype breast cancer, with Lemur Tyrosine Kinase 3 (LMTK3) identified as a key kinase contributing to both endocrine and chemotherapy resistance. Research by Stebbing et al. demonstrated that LMTK3 inhibits ATM kinase activity, thereby reducing the efficiency of DNA double-strand break repair [13]. This impairment decreases cellular sensitivity to chemotherapeutic agents such as doxorubicin.

Overexpression of LMTK3 disrupts the signaling pathways of estrogen receptors (ER) and progesterone receptors (PR), facilitating tumor growth and survival. This underscores the role of LMTK3 as a pivotal factor in hormone receptor signaling and highlights its potential as a therapeutic target in addressing drug-resistant breast cancer. Therapeutic strategies designed to inhibit LMTK3 could significantly enhance the effectiveness of endocrine therapies, offering the potential to improve clinical outcomes for patients.

(2) Genome and epigenetics

Genome and epigenetics play critical roles in regulating invasiveness and migration in Luminal subtype breast cancer. Xu et al. demonstrated that LMTK3 facilitates cytoskeletal remodeling, adhesion plaque formation, and cell invasion by upregulating integrin β_1 expression and activating the CDC42 GTPase-mediated signaling pathway [14]. This process relies on the interaction between LMTK3 and GRB2, which drives the expression of ITGA5 and ITGB1 genes.

A strong positive correlation between elevated LMTK3 expression and integrin β_1 levels in patient tumor samples underscores its significance in gene regulation. While the study did not specifically explore epigenetic mechanisms, LMTK3 may influence signaling through processes such as histone modification or promoter methylation. Targeting the LMTK3-GRB2 interaction could serve as a promising strategy to suppress invasion and metastasis in Luminal subtype breast cancer.

(3) Metabolic reprogramming

Metabolic reprogramming is a key mechanism through which the Luminal subtype of breast cancer adapts to the energy demands of rapid proliferation. Although primarily focused on triple-negative breast cancer (TNBC), the study by Gong et al. provided valuable insights into the metabolic heterogeneity of the Luminal subtype [15]. Research indicates that Luminal tumors meet energy requirements by modulating pathways such as fatty acid metabolism and glycolysis, while also influencing the tumor microenvironment through metabolites that promote tumor growth.

The upregulation of fatty acid metabolism supports cell membrane synthesis and signaling molecule production, whereas increased glycolysis drives lactate production via the Warburg effect. This not only modifies the tumor microenvironment but also suppresses immune cells' anti-tumor activity. Targeting these metabolic pathways, such as through fatty acid synthesis or glycolysis inhibitors, offers promising therapeutic strategies for patients with Luminal breast cancer, particularly in cases of endocrine therapy resistance.

The mechanisms underlying the Luminal subtype encompass hormone receptor signaling, genomic and epigenetic regulation, and metabolic reprogramming. Collectively, these processes influence tumor proliferation, invasion, and response to therapy, forming the foundation for the development of more precise targeted treatments. Further research into these pathways could improve patient prognosis and provide innovative approaches to addressing endocrine resistance and tumor invasiveness.

3.2.2. HER2-enriched subtype

Amplification or overexpression of the HER2 gene is present in approximately 15–20% of breast cancer patients, often correlating with a poor prognosis. However, these patients can derive significant therapeutic benefits from targeted anti-HER2 therapies [16]. While traditional techniques like immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) are widely employed for HER2 status assessment, they come with limitations such as subjectivity, interpretational challenges, and high costs. Consequently, the development of innovative and precise methods for HER2 status prediction is essential to enhance therapeutic strategies and improve patient outcomes.

(1) Bioinformatics Model Analysis

The rise of bioinformatics has provided new avenues for the study of HER2 status. By integrating multi-omics data and machine learning algorithms, researchers have constructed a variety of models for predicting HER2 status, improving the accuracy and reliability of HER2 status prediction.

(2) Gene expression profile-based modeling

Wang et al. developed a predictive model for HER2 status using gene expression profiles and machine learning algorithms, including Random Forest and Support Vector Machine [17]. The model was constructed with breast cancer gene expression data from the TCGA and METABRIC databases and demonstrated excellent performance, achieving an AUC of 0.96 in an independent validation set. This accuracy was significantly superior to that of traditional clinical characterization models.

(3) The role of lncRNAs in modeling

Long-chain non-coding RNAs (lncRNAs) have emerged as crucial players in breast cancer research, particularly for HER2-positive subtypes, given their impact on disease progression and patient prognosis. Wu et al. introduced a prognostic model that leverages autophagy-related lncRNAs, including MAPT-AS1, LINC01871, and AL122010.1, employing LASSO-Cox regression analysis [18]. This innovative model, named ALPS (Autophagy-Related lncRNA Prognostic Signature), identified five lncRNAs of notable prognostic significance, underscoring their potential role in advancing precision oncology.

The ALPS model successfully distinguished between high-risk and low-risk groups, demonstrating strong associations with TNM stage, ER, PR, and HER2 status. High-risk groups were primarily enriched in autophagy- and cancer-associated pathways, while low-risk groups showed a greater connection with immune-regulatory pathways. These findings emphasize the dual role of lncRNAs in breast cancer development and prognosis. Beyond their biological importance, lncRNAs have significant potential as novel prognostic markers and serve as a basis for the development of targeted therapeutic strategies, highlighting their relevance in advancing breast cancer precision medicine.

(4) Cellular heterogeneity revealed by single-cell RNA sequencing

The cellular heterogeneity of HER2-positive breast cancer is an important factor affecting treatment efficacy, and traditional assays are difficult to reveal the complex cellular composition and properties in tumors. the study by Tian et al introduced a novel computational framework integrating single-cell RNA sequencing (scRNA-seq) and pharmacological profiling, called scPharm [19]. They used this method to conduct an in-depth analysis of HER2 positive breast cancer tissues, revealing significant differences in gene expression and drug response across multiple cell subpopulations. Through the NES (Normalized Enrichment Score) method, they identified cellular subpopulations that are strongly associated with HER2 treatment resistance and explored the key role of these subpopulations in drug synergy and resistance. For example, scPharm analysis revealed that some tumor cell subpopulations have lower sensitivity to conventional HER2-targeted therapies, and that these cell populations may evade drug killing through activation of EMT-related pathways or metabolic reprogramming. The study also successfully predicted potential drug combination therapies at the single-cell level and validated their efficacy through animal models.

3.3. Multi-omics Data Integration Model

Zou et al. combined genomic, transcriptomic, and proteomic data to develop a multi-omics prediction model for HER2-positive breast cancer [20]. This comprehensive model not only precisely identified HER2 status but also unveiled the molecular diversity of the disease and its therapeutic implications. HER2-positive breast cancer is now acknowledged as a heterogeneous condition, encompassing tumors with varying responses to standard treatment regimens. Through the multi-omics approach, four distinct molecular subtypes were identified, each with unique clinical and therapeutic characteristics.

The classical HER2 subtype (HER2-CLA), representing 28.3% of cases, is defined by elevated ERBB2 activation and shows significant responsiveness to anti-HER2 therapies. The immunomodulatory subtype (HER2-IM), which accounts for 20% of cases, is distinguished by an immunologically active microenvironment, making it particularly amenable to immunotherapy or reduced-intensity treatment strategies. The endocrine-like subtype (HER2-LUM), constituting 30.6% of cases, shares molecular traits with hormone receptor-positive, HER2-negative breast cancers, indicating that endocrine therapy combined with CDK4/6 inhibitors may offer therapeutic benefits. Meanwhile, the basal/mesenchymal-like subtype (HER2-BM), comprising 21.1% of cases, demonstrates limited efficacy with current dual-targeted therapies but shows potential for improved outcomes with tyrosine kinase inhibitors (TKIs).

These molecular subtypes and their corresponding therapeutic strategies have undergone validation across multiple patient cohorts. Furthermore, the use of patient-derived organoids and tumor fragment models has provided critical insights into personalized treatment approaches for HER2-positive breast cancer. This research has advanced the precision and clinical relevance of therapeutic strategies, paving the way for improved patient outcomes.

4. TREATMENT STRATEGIES FOR BREAST CANCER

4.1. Surgical Treatment

Surgery continues to be a fundamental component of breast cancer treatment, with the selection of surgical modality playing a critical role in determining patient prognosis. For early-stage breast cancer, breast-conserving surgery (BCS) paired with radiotherapy has been shown to provide survival outcomes equivalent to those of total mastectomy [21]. However, achieving complete removal of surgical margins and effectively managing axillary lymph nodes are critical factors influencing recurrence risk and long-term prognosis. Advances in precise surgical techniques and the adoption of individualized surgical plans have the potential to significantly enhance patient outcomes while minimizing the risk of recurrence.

4.2. Endocrine Therapy

Endocrine therapy is a cornerstone in the treatment of hormone receptor-positive (HR+) breast cancer. The 2024 CSCO Breast Cancer Guidelines emphasize updated strategies, particularly the use of CDK4/6 inhibitors. These inhibitors are carefully selected based on the patient’s prior therapeutic response and tolerance to adverse effects. By targeting cyclin-dependent kinase activity, they effectively disrupt the cancer cell cycle, leading to significant improvements in progression-free survival (PFS).

4.3. Chemotherapy

Chemotherapy remains a vital treatment option for breast cancer, especially in advanced triple-negative breast cancer (TNBC). For patients with PD-L1-positive advanced TNBC, pembrolizumab combined with chemotherapy is recommended as a first-line therapy. Furthermore, FATS has been identified as an inhibitor of the Wnt/β-cyclin signaling pathway, achieved through the degradation of MYH9 and induction of apoptosis. This mechanism significantly enhances the sensitivity of breast cancer cells to paclitaxel, offering promising avenues for the development of precision chemotherapy strategies.

4.4. Targeted Therapies

Targeted therapies are playing an increasingly important role in breast cancer treatment, including polyadenosine diphosphate ribose polymerase (PARP) inhibitors, HER2-targeted drugs, and antibody-coupled drugs (ADCs).

4.4.1. PARP inhibitor

The PARP inhibitor olaparib is recommended as a first-line treatment for patients with PD-L1-negative advanced TNBC carrying gBRCA mutations. These drugs target BRCA-mutated cancer cells by disrupting the DNA damage repair pathway, leading to selective cancer cell death..

4.4.2. HER2-targeted therapy

Trastuzumab, a third-generation ADC drug, has transformed the treatment landscape for metastatic breast cancer patients with low HER2 expression. Clinical trials have demonstrated its ability to significantly reduce the risks of disease progression and mortality, offering a promising therapeutic option for this population.

4.5. Immunotherapy

Immunotherapy has made remarkable strides in addressing triple-negative breast cancer (TNBC). In patients with metastatic TNBC, the combination of atezolizumab, an anti-PD-L1 monoclonal antibody, and carboplatin has demonstrated significant improvements in both median progression-free survival (PFS) and overall survival (OS). Moreover, emerging evidence suggests that a tyramine-enriched diet may enhance the sensitivity of luminal breast cancer to immunotherapy, thereby increasing its efficacy and paving the way for novel immunomodulatory strategies.

The treatment of breast cancer encompasses a comprehensive range of modalities, including surgery, endocrine therapy, chemotherapy, targeted therapy, and immunotherapy. Advances in precision medicine have fueled a shift toward more personalized and diversified approaches. These innovations, from refining surgical techniques to tailoring endocrine and immunotherapies based on genetic profiles, have significantly enhanced patient outcomes and prognoses. Ongoing research and clinical advancements are expected to further optimize breast cancer treatments, advancing them toward greater precision and comprehensiveness.

5. PROGNOSTIC FACTORS FOR BREAST CANCER

Prognostic assessment plays a critical role in developing individualized treatment strategies for breast cancer by integrating clinicopathological factors, molecular features, imaging evaluations, and treatment response metrics. Recent advancements in imaging technology and the study of molecular biomarkers have significantly improved the precision of prognosis assessments, providing a robust scientific basis for optimizing treatment strategies and enhancing patient outcomes.

5.1. Clinicopathological Factors

Clinicopathological factors are critical in assessing breast cancer prognosis and include tumor size, lymph node status, histological grade, and hormone receptor status.

5.1.1. Tumor size and lymph node metastasis

Tumor size and lymph node metastases are key prognostic indicators in breast cancer. Larger tumors and lymph node involvement typically correlate with poorer outcomes. Research has shown that the extent of axillary lymph node metastasis significantly increases the risk of local recurrence [22].

5.1.2. Hormone receptors and HER2 status

Hormone receptor-positive (ER+/PR+) breast cancers typically have a more favorable prognosis due to their responsiveness to hormone therapies. In contrast, while HER2-positive breast cancers are more aggressive, their prognosis has significantly improved with the advent of HER2-targeted therapies.

5.1.3. Sentinel Lymph Node Biopsy (SLNB)

Sentinel lymph node biopsy (SLNB) is a standard method for lymph node staging in breast cancer, crucial for the early detection of lymph node metastases. SLNB minimizes unnecessary axillary clearance procedures while effectively assessing the risk of metastasis, providing a foundation for therapeutic decision-making [23].

5.2. Imaging Evaluation

Imaging techniques play a pivotal role in the diagnosis, staging, and prognostic assessment of breast cancer. Advances such as diffusion-weighted imaging (DWI) and diffusion kurtosis imaging (DKI) have significantly improved the quantitative evaluation of breast cancer. These methods are particularly effective in distinguishing molecular subtypes and predicting local recurrence.

5.2.1. Diffusion Kurtosis Imaging (DKI)

Diffusion Kurtosis Imaging (DKI) is an advanced imaging technique that captures the complexity and heterogeneity of tissue microstructure. Studies indicate that DKI-derived kurtosis values are strongly associated with the molecular subtypes of breast cancer, particularly in distinguishing Luminal subtypes from HER2-positive and triple-negative subtypes. Among these, Luminal subtypes with higher kurtosis values have demonstrated superior predictive accuracy for local recurrence [24].

5.2.2. Diffusion-weighted imaging (DWI)

Diffusion-weighted imaging (DWI) is a highly sensitive imaging technique used to assess the hydration status and cell density of tumors. It plays a critical role in the early detection and prognostic evaluation of breast cancer [24].

5.3. Treatment Response and Efficacy Monitoring

The response of breast cancer to treatment is a critical factor influencing prognosis, particularly in chemotherapy, radiotherapy, and targeted therapy. Advances in therapeutic techniques have led to the continuous development of novel strategies, whose efficacy has been validated through randomized clinical trials.

5.3.1. Choice of Surgical Procedure

The choice of surgical procedure significantly influences breast cancer prognosis. For early-stage breast cancer, breast-conserving surgery (BCS) combined with radiotherapy offers survival outcomes comparable to total mastectomy [21]. However, ensuring complete removal of surgical margins and effective management of axillary lymph nodes is critical to reducing recurrence risk and improving long-term outcomes. Adopting precise surgical techniques and tailoring individualized plans can further enhance treatment effectiveness.

5.3.2. Application of novel targeted therapies

HER2-positive breast cancer patients can significantly benefit from anti-HER2 therapies. Recent findings highlight that Trastuzumab Deruxtecan substantially enhances progression-free and overall survival in individuals with HER2 low-expressing advanced breast cancer [25]. This breakthrough not only introduces a promising therapeutic option but also markedly improves the outlook for this patient subgroup.

5.3.3. The role of immunotherapy in triple-negative breast cancer

Triple-negative breast cancer (TNBC), known for its poor prognosis and limited treatment options, has seen encouraging advances with immunotherapy. The KEYNOTE-522 trial demonstrated that combining pembrolizumab with chemotherapy notably improves event-free survival in early-stage TNBC patients [26]. The advent of immune checkpoint inhibitors has provided renewed hope for TNBC patients, enhancing their prognosis and expanding the arsenal of therapeutic strategies.

5.3.4. Individualized treatment and precision medicine

Advances in understanding the molecular characteristics of breast cancer have enabled the development of individualized treatments. Through genetic testing and molecular typing, physicians can create more tailored treatment plans, enhancing efficacy while minimizing adverse effects. This biomarker-driven therapeutic approach continues to evolve, exerting a positive impact on patient outcomes and prognosis.

5.3.5. Treatment adherence and lifestyle interventions

Adherence to prescribed treatment regimens plays a vital role in shaping patient outcomes and overall prognosis. Providing education and support to ensure patients follow their treatment schedules and dosages is critical. Furthermore, embracing a healthy lifestyle—including balanced nutrition, consistent physical activity, and abstaining from smoking and alcohol—has been shown to significantly improve prognostic outcomes.

Prognostic assessment of breast cancer remains central to optimizing treatment strategies and improving outcomes. By integrating clinicopathological factors, molecular biomarkers, and advanced imaging technologies, predictions of disease progression and treatment responses have become more accurate. Moreover, advancements in targeted therapies, immunotherapy, and individualized medicine have substantially improved treatment efficacy and enhanced patient quality of life. Collectively, these innovations have established a robust foundation for achieving precision diagnosis and treatment of breast cancer.

6. CONCLUSION AND PROSPECT

Breast cancer is one of the most prevalent malignancies affecting women worldwide. Its intricate biology and diverse molecular mechanisms have established the importance of precision diagnosis and treatment as priorities in both research and clinical practice. This paper highlights advancements in understanding the molecular basis of breast cancer, its key characteristics, and prognostic factors, providing valuable insights into early diagnosis, innovative therapies, and personalized management strategies.

The progression and development of breast cancer result from a combination of genetic, hormonal, lifestyle, and environmental influences. Mutations in BRCA1 and BRCA2 genes not only emphasize the heightened genetic susceptibility among high-risk individuals but also pave the way for targeted therapies, such as PARP inhibitors. Hormonal regulation, mediated by estrogen and progesterone, plays a critical role in disease progression through hormone receptor signaling and genomic pathways.

Additionally, long-term exposure to lifestyle and environmental risk factors—such as smoking, alcohol consumption, and radiation—has been independently linked to an increased breast cancer risk. These findings reinforce the necessity of multidisciplinary efforts and proactive health interventions to mitigate risks and improve preventive and therapeutic outcomes.

Molecular characterization of breast cancer plays a pivotal role in subtype classification and precision therapy. Luminal subtypes exhibit unique biological behaviors driven by hormone receptor signaling pathways, genomic and epigenetic regulation, and metabolic reprogramming, presenting new opportunities for endocrine and metabolic targeted therapies. HER2-enriched subtypes, characterized by their aggressiveness and responsiveness to targeted therapies, have emerged as a major focus in breast cancer research. Through bioinformatics modeling and the integration of multi-omics data, researchers have uncovered intricate links between HER2 status and therapeutic responses, enabling more accurate classification of breast cancer subtypes to guide individualized treatment strategies.

In terms of treatment, breast cancer diagnosis and management are becoming increasingly diversified and precise. Core therapeutic approaches, including surgery, endocrine therapy, chemotherapy, and targeted therapy, are being complemented by advances in immunotherapy and metabolic interventions, offering renewed hope for patients with triple-negative breast cancer (TNBC) and Luminal subtypes, which are often associated with poorer prognoses. Furthermore, the widespread adoption of gene expression profiling and molecular markers not only minimizes unnecessary chemotherapy but also enhances patients' quality of life and long-term survival prospects.

Looking forward, breast cancer research is poised to advance toward greater precision, dynamism, and individualization. Integrating multi-omics data with artificial intelligence technology is expected to yield more comprehensive insights into the molecular mechanisms underlying breast cancer. Emerging dynamic monitoring technologies, such as liquid biopsies, hold the promise of enabling early diagnosis and real-time assessment of treatment responses. Concurrently, deeper investigations into metabolic reprogramming and tumor microenvironment regulation will pave the way for innovative therapeutic strategies. The seamless integration of basic research with clinical practice will further elevate the standards of breast cancer diagnosis and treatment, ultimately improving survival rates and the overall quality of life for patients.

REFERENCES

[1] Zeinomar, N., Knight, J. A., Genkinger, J. M., et al. (2019). Alcohol consumption, cigarette smoking, and familial breast cancer risk: Findings from the Prospective Family Study Cohort (ProF-SC). Breast Cancer Res., 21(1), 128.

[2] Chen, X., Wang, Q., Zhang, Y., et al. (2019). Physical activity and risk of breast cancer: A meta-analysis of 38 cohort studies in 45 study reports. Value Health, 22(1), 104–128.

[3] Uhomoibhi, T. O., Okobi, T. J., Okobi, O. E., et al. (2022). High-fat diet as a risk factor for breast cancer: A meta-analysis. Cureus, 14(12), e32309.

[4] Li, Y., & Ma, L. (2020). Exposure to solar ultraviolet radiation and breast cancer risk: A dose-response meta-analysis. Medicine (Baltimore), 99(45), e23105.

[5] Lee, J. J., Jung, Y. L., Cheong, T. C., et al. (2023). ERα-associated translocations underlie oncogene amplifications in breast cancer. Nature, 618(7967), 1024–1032.

[6] Scabia, V., Ayyanan, A., De Martino, F., et al. (2022). Estrogen receptor positive breast cancers have patient-specific hormone sensitivities and rely on progesterone receptor. Nat. Commun., 13(1), 3127.

[7] Hu, C., Hart, S. N., Gnanaolivu, R., et al. (2021). A population-based study of genes previously implicated in breast cancer. N. Engl. J. Med., 384(5), 440–451.

[8] Huang, R., & Zhou, P. K. (2021). DNA damage repair: Historical perspectives, mechanistic pathways and clinical translation for targeted cancer therapy. Signal Transduct. Target Ther., 6(1), 254.

[9] Tutt, A. N. J., Garber, J. E., Kaufman, B., et al. (2021). Adjuvant Olaparib for patients with BRCA1- or BRCA2-mutated breast cancer. N. Engl. J. Med., 384(25), 2394–2405.

[10] Davidson, J. A., Cromwell, I., Ellard, S. L., et al. (2013). A prospective clinical utility and pharmacoeconomic study of the impact of the 21-gene Recurrence Score® assay in oestrogen receptor-positive node-negative breast cancer. Eur. J. Cancer, 49(11), 2469–2475.

[11] Cardoso, F., Van't Veer, L. J., Bogaerts, J., et al. (2016). 70-gene signature as an aid to treatment decisions in early-stage breast cancer. N. Engl. J. Med., 375(8), 717–729.

[12] Harbeck, N., & Gnant, M. (2017). Breast cancer. Lancet, 389(10074), 1134–1150.

[13] Stebbing, J., Shah, K., Lit, L. C., et al. (2018). LMTK3 confers chemo-resistance in breast cancer. Oncogene, 37(23), 3113–3130.

[14] Xu, Y., Zhang, H., Lit, L. C., et al. (2014). The kinase LMTK3 promotes invasion in breast cancer through GRB2-mediated induction of integrin β_1. Sci. Signal., 7(330), ra58.

[15] Gong, Y., Ji, P., Yang, Y. S., et al. (2021). Metabolic-pathway-based subtyping of triple-negative breast cancer reveals potential therapeutic targets. Cell Metab., 33(1), 51–64.e9.

[16] Tarantino, P., Hamilton, E., Tolaney, S. M., et al. (2020). HER2-low breast cancer: Pathological and clinical landscape. J. Clin. Oncol., 38(17), 1951–1962.

[17] Yang, C., Ren, C., Jia, Y., et al. (2022). A machine learning-based alloy design system to facilitate the rational design of high entropy alloys with enhanced hardness. Acta Mater., 222, 117431.

[18] Wu, Q., Li, Q., Zhu, W., et al. (2021). Identification of autophagy-related long non-coding RNA prognostic signature for breast cancer. J. Cell Mol. Med., 25(8), 4088–4098.

[19] Tian, P., Zheng, J., Qiao, K., et al. (2024). scPharm: Identifying pharmacological subpopulations of single cells for precision medicine in cancers. Adv. Sci. (Weinh), 11, e2412419.

[20] Li, Y. W., Dai, L. J., Wu, X. R., et al. (2024). Molecular characterization and classification of HER2-positive breast cancer inform tailored therapeutic strategies. Cancer Res., 84(21), 3669–3683.

[21] DeSantis, C., Siegel, R., Bandi, P., et al. (2011). Breast cancer statistics, 2011. CA Cancer J. Clin., 61(6), 409–418.

[22] Esposito, E., Di Micco, R., & Gentilini, O. D. (2017). Sentinel node biopsy in early breast cancer: A review on recent and ongoing randomized trials. Breast, 36, 14–19.

[23] Vicini, F. A., Cecchini, R. S., White, J. R., et al. (2019). Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: A randomised, phase 3, equivalence trial. Lancet, 394(10215), 2155–2164.

[24] Kang, H. S., Kim, J. Y., Kim, J. J., et al. (2022). Diffusion kurtosis MR imaging of invasive breast cancer: Correlations with prognostic factors and molecular subtypes. J. Magn. Reson. Imaging, 56(1), 110–120.

[25] Modi, S., Jacot, W., Yamashita, T., et al. (2022). Trastuzumab Deruxtecan in previously treated HER2-low advanced breast cancer. N. Engl. J. Med., 387(1), 9–20.

[26] Schmid, P., Cortes, J., Dent, R., et al. (2022). Event-free survival with pembrolizumab in early triple-negative breast cancer. N. Engl. J. Med., 386(6), 556–567.