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BREAST CANCER EPIDEMIOLOGY,CLASSIFICATION AND RISK FACTOR

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ABSTRACT- Breast cancer remains one of the leading causes of cancer-related morbidity and mortality worldwide. This journal explores the latest advancements in breast cancer research, covering key areas such as epidemiology, risk factors, early detection methods, molecular and genetic influences, novel treatment approaches, and patient care strategies. Emphasis is placed on innovative diagnostic tools, targeted therapies, and personalized medicine, which have significantly improved survival rates and treatment outcomes.

Keywords:
Breast Cancer, Oncology, Risk Factors, Early Detection, Diagnosis, Mammography, Genetic Mutations, BRCA1, BRCA2, Chemotherapy, Hormone therapy, Endocrine therapy, Targeted therapy Immunotherapy, Radiation therapy, Surgery (mastectomy, lumpectomy)PARP inhibitors, CDK4/6

1. INTRODUCTION

Breast cancer is one of the most prevalent and life-threatening malignancies affecting individuals worldwide, particularly women. It is a heterogeneous disease with various subtypes, risk factors, and treatment approaches. Despite significant advancements in early detection and therapy, breast cancer remains a major public health concern, contributing to high morbidity and mortality rates.

This journal aims to explore the latest research, clinical advancements, and emerging trends in breast cancer diagnosis, treatment, and prevention. By bringing together studies from various disciplines, including oncology, genetics, radiology, and patient care, we seek to enhance understanding and improve outcomes for patients. The articles featured will provide insights into innovative treatment modalities, biomarkers for early detection, and the impact of lifestyle and environmental factors on breast cancer development.

Breast cancer is the most frequently diagnosed malignancy in women worldwide, and around 70–

80% of patients with early-stage, non-metastatic disease can be cured. Advanced breast cancer with distant organ metastases is considered incurable with currently available therapies. On the molecular level, breast cancer is recognized as a heterogeneous disease, characterized by the activation of human epidermal growth factor receptor 2 (HER2, encoded by ERBB2), the activation of hormone receptors (oestrogen receptor and progesterone receptor), and/or the presence of BRCA mutations.

Treatment strategies are determined based on molecular subtype. A multidisciplinary approach is employed in the management of breast cancer, incorporating locoregional treatments (such as surgery and radiation therapy) and systemic therapies. Systemic therapies are utilized, including endocrine therapy for hormone receptor-positive disease, chemotherapy, anti-HER2 therapy for HER2-positive disease, bone-stabilizing agents, poly(ADP-ribose) polymerase inhibitors for BRCA mutation carriers, and, more recently, immunotherapy.

Future therapeutic concepts in breast cancer focus on the individualization of therapy, as well as on treatment de-escalation and escalation, based on tumor biology and early therapy response. In addition to further treatment innovations, ensuring equal worldwide access to therapeutic advances remains a major global challenge in breast cancer care.

The discovery of hormone receptor-positive breast cancer revolutionized treatment. In the 1970s, the introduction of tamoxifen, an anti-estrogen drug, marked the beginning of hormonal therapy, significantly benefiting patients with estrogen receptor (ER)-positive breast cancer. Later, aromatase inhibitors and ovarian suppression therapies further refined hormonal treatment.

The early 2000s witnessed major advancements in targeted therapy, particularly with the identification of HER2-positive breast cancer. The development of trastuzumab (Herceptin), a monoclonal antibody targeting HER2, drastically improved survival rates in HER2-positive patients. Since then, newer HER2targeted drugs such as pertuzumab and trastuzumabemtansine (T-DM1) have enhanced treatment efficacy.

Personalized Medicine and Immunotherapy (21st Century–Present) Recent years have seen a shift toward personalized and precision medicine in breast cancer treatment. Advances in genomic profiling and molecular diagnostics have enabled tailored therapies based on an individual's tumor biology. Tests like Oncotype DX and MammaPrint help assess recurrence risk and guide chemotherapy decisions, reducing unnecessary treatment exposure. Immunotherapy has emerged as a promising approach, particularly for triple-negative breast cancer (TNBC)

2. EPIDEMIOLOGY

Breast cancer is the most common malignant tumor in women in the world. Breast cancer patients account for as much as 36% of oncological patients. An estimated 2.089 million women were diagnosed with breast cancer in 2018 [1,2]. The incidence of this malignant tumor is increasing in all regions of the world, but the highest incidence occurs in industrialized countries. Almost half of

the cases on a global scale are in developed countries [2,3]. This trend is mainly due to the so-called Western lifestyle, associated with a poor diet, nicotinism, excessive stress and little physical activity [3]. In the case of breast cancer, mammography has become recognized as screening. The greatest value of mammography is observed in the group of women aged 50–69 years [1,3]. Classical mammography is characterized by 75–95% sensitivity and specificity at the level of 80–95% [4]. For women with suspected hereditary breast cancer, magnetic resonance mammography is used as a screening test. If a suspicious lesion is found in mammography, an ultrasound examination is performed and, if necessary, a thick needle biopsy along with a histopathological examination of the tumor.

In 2018, there were 234,087 cases of breast cancer in the United States (crude rate: 85/105), 55,439 in the United Kingdom (crude rate: 94/105), 56,162 in France (crude rate: 99/105), 71,888 in Germany (crude rate: 85.4/105) and 66,101 in Japan (crude rate: 58/105) [2]. The highest incidence rate in the world is found in Belgium (crude rate: 113/105), and among the continents—in Australia (crude rate: 94/105) [2]. In Poland, breast cancer is also the most-commonly diagnosed malignant tumor in women. There is a steady increase in cases (1990, 8000 new cases; 2018, 20,203 new cases) [2]. The average incidence rate in Europe is 84/105 [2]. The lowest incidence occurs in the countries of Southeast Asia and Africa, where the standardized incidence rate does not exceed 25/105 [2]. The lowest incidence rates in 2018 were recorded in Bhutan (crude rate: 5/105) and the Republic of The Gambia (crude rate: 6.5/105) [2]. Despite the greater effectiveness of initial diagnostics or the rapid development of pharmacotherapy in recent years, breast cancer is the first cause of death from malignant tumors in women in the world. In 2018, 626,679 people died from breast cancer. Unlike morbidity, the highest mortality from this malignant tumor is recorded in developing countries [2] (Fiji, crude rate 36/105, highest rate; Somalia, crude rate 29/105; Ethiopia, crude rate 23/105; Egypt, crude rate 21/105; Indonesia, crude rate 17/105; Papua New Guinea, crude rate 25/105) [2], in which as much as 60% of all deaths from breast cancer occur. This trend is mainly related to the lack of screening, which is less than in developed countries, the availability of diagnostics and modern methods of treatment [5]. In contrast, the standardized death crude rate in Belgium 16.3/105, in the United States 13/105, and in Japan 9.3/105 [2]. The number of breast cancer cases in Poland is much lower than in EU countries (in 2013, the standardized incidence rate for Polish— 51.8, for the EU 106.6) [6]. The incidence of adult premenopausal women (20–49 years) has almost doubled over the past 30 years. Unfortunately, Polish women are still not very sensitive to prevention. They neglect their breasts and underestimate the importance of regular check-ups. Compared to other European countries, Polish women have a low incidence of preventative care—in the Netherlands, 80% of women report free mammogram prevention programs, in England 71%, and in Poland only 44% [6]. The percentage of 5-year survival due to breast cancer in Poland is 78.5%, differing significantly from, for example, the result of 90% achieved in the United States [7].

A. Early Understanding and Surgical Approaches (19th–Mid-20th Century)

Historically, surgeons treated breast cancer primarily with radical mastectomies, a concept William Halsted introduced in the late 19th century. At the time, doctors believed the disease was localized, leading them to adopt aggressive surgery as the standard approach. However, the severe psychological and physical consequences of radical mastectomies prompted the search for less invasive alternatives.

Emergence of Radiation and Chemotherapy (Mid- 20th Century)

In the mid-20th century, researchers revolutionized breast cancer treatment by integrating radiotherapy and chemotherapy. Studies confirmed that applying radiation therapy after surgery effectively reduced recurrence rates. The introduction of systemic chemotherapy, using agents like cyclophosphamide, methotrexate, and fluorouracil (CMF regimen), expanded treatment options and significantly improved survival rates.

B. Modern Paradigms in Breast Cancer Research and Treatment

Breast cancer research has undergone a paradigm shift in recent years, driven by advancements in genomics, precision medicine, and innovative therapeutic strategies. Modern approaches emphasize personalized treatment, minimally invasive diagnostics, and a deeper understanding of the tumor microenvironment.

3. Key Technological Advancements in Breast Cancer Research and Treatment

The landscape of breast cancer research and treatment has evolved significantly due to technological innovations. These advancements have improved early detection, treatment precision, and patient outcomes. The following are some of the key technologies and breakthroughs shaping modern breast cancer management

A. Genomic and Molecular Profiling

Next-Generation Sequencing (NGS): Enables detailed tumor genetic analysis, identifying mutations in genes like BRCA1, BRCA2, PIK3CA, TP53, and others to guide targeted therapy.

Gene Expression Assays: Tools like Oncotype DX, MammaPrint, and Prosigna (PAM50) help predict recurrence risk and personalize treatment plans.

B. Targeted and Immunotherapy Innovations

CDK4/6 Inhibitors: Drugs like palbociclib, ribociclib, and abemaciclib improve outcomes for hormone receptor-positive breast cancer.

HER2-Targeted Therapies: New-generation drugs such as trastuzumab deruxtecan (T-DXd), neratinib, and tucatinib offer enhanced efficacy. Checkpoint Inhibitors: Immunotherapy agents like pembrolizumab (Keytruda) improve survival in triple-negative breast cancer (TNBC).

C. Liquid Biopsy and Non-Invasive Diagnostics

Circulating Tumor DNA (ctDNA): Detects residual disease, recurrence, and therapy resistance through a simple blood test..

D. AI and Machine Learning in Breast Cancer Management

AI in Imaging: Machine learning algorithms improve mammogram, MRI, and ultrasound accuracy, reducing false positives. Mammography and Advanced Imaging AI in Drug Discovery: Accelerates the identification of new breast cancer drugs and treatment pathways. Digital Breast Tomosynthesis (DBT): Provides 3D breast imaging, improving early cancer detection and reducing recall rates.

4. Risk Factors in Breast Cancer

The precise cause of carcinogenesis has not yet been determined, but several risk factors associated with the development of breast cancer have been identified. Among the most significant, as indicated by epidemiological data, are gender, age, and the economic status of a given country. Hormonal factors, particularly those related to the duration of estrogen exposure, as well as reproductive factors such as the number of children born, the age at first childbirth, and breastfeeding, are also considered influential.

Great importance is attributed to genetic predisposition, the use of hormone replacement therapy, an unhealthy diet, and obesity in the development of breast cancer. Additionally, hormonal contraception, alcohol consumption, and early-life exposure to ionizing radiation are recognized as significant risk factors.

A. Liquid Biopsies

Non-Invasive Monitoring: Liquid biopsies detect circulating tumor DNA in the blood, allowing for real-time monitoring of tumor progression and response to treatment without invasive procedures. Circulating Tumor Cells (CTCs) – Cancer cells that have detached from the primary tumor and entered the bloodstream.

Circulating Tumor DNA (ctDNA) – Fragments of DNA shed by tumor cells, useful for detecting mutations and monitoring treatment response.

Extracellular Vesicles (EVs) – Small vesicles containing tumor-derived genetic material and proteins, offering insights into cancer progression. MicroRNAs (miRNAs) – Small RNA molecules involved in gene regulation, acting as potential biomarkers for breast cancer detection.

Clinical Applications:

Early Detection & Screening – Identifies cancerrelated mutations before symptoms appear. Treatment Monitoring – Tracks tumor evolution and response to therapy in real time.

Minimal Residual Disease (MRD) Detection – Detects lingering cancer cells post-treatment to predict recurrence.

Drug Resistance Identification – Helps in adjusting treatment strategies based on emerging resistance mechanisms.

B. Radionomics

Advanced Imaging Analysis: Radiomics involves extracting large amounts of features from radiographic medical images using datacharacterization algorithms, aiding in the prediction of disease prognosis and treatment response.

C. Cryaoblation

Minimally Invasive Treatment: Cryoablation is being studied as a potential alternative to lumpectomy for small breast cancers, offering a less invasive option with promising preliminary results**.** These developments represent a shift towards more precise, personalized, and less invasive strategies in breast cancer care, aiming to improve patient outcomes and quality of life.

D. Mild Breast Changes

An increased risk of developing breast cancer is associated with the presence of benign changes in the mammary glands. Some benign lesions, including benign neoplasms such as atypical ductal hyperplasia (ADH) or atypical lobular hyperplasia (ALH), have been found to increase the risk by four to five times. Proliferative lesions without atypia, such as a stellate scar or fibrotic adenoma, have been shown to elevate the risk up to two times.

In a cohort study conducted by Hartmann et al., the risk of breast cancer in patients with various types of benign lesions was assessed. The relative risk of developing breast cancer for the entire study cohort was determined to be 1.56 (95% CI, 1.45–1.68). This risk remained elevated for 25 years following biopsy. Among women with benign lesions without proliferation, the relative risk of developing breast cancer was calculated at 1.27 (95% CI, 1.15–1.41). In cases where mild proliferative lesions were present but without atypia, the relative risk was measured at 1.88 (95% CI, 1.66–2.12). The highest relative risk was observed in women with benign proliferative lesions with atypia (such as atypical ductal hyperplasia, atypical lobular hyperplasia, or both), reaching as high as 4.24 (95% CI, 3.26–5.41). It was also found that the earlier benign changes were diagnosed (before the age of 55), the greater the risk of developing the malignant tumor in question.

Additionally, it has been suggested that in women with atypical hyperplasia whose first-degree relatives have been treated for breast cancer, the risk of developing this malignant tumor is increased by as much as nine times.

E. Immunotherapy Advancements

Checkpoint inhibitors (e.g., pembrolizumab) for triple-negative breast cancer.Personalized cancer vaccines under development to boost immune response.

Personalized cancer vaccines under development to boost immune response.

F. Organoids & 3D Cell Culture Models

Patient-derived tumor organoids (PDTOs) allow for personalized drug testing.

3D cultures mimic tumor environments for better research outcomes.

Microbiome Research & Breast Cancer

Studies exploring gut and breast tissue microbiota's role in cancer progression.

Potential for probiotic-based interventions in breast cancer prevention.

Theranostics (Therapy + Diagnostics)

Dual-purpose agents enabling simultaneous imaging and targeted therapy.

Example: Radiopharmaceuticals detecting and treating metastases in one step.

Breast cancer research is a dynamic field, with numerous journals dedicated to advancing our understanding of the disease. Here are some prominent journals that publish significant findings in breast cancer research

Breast Cancer Research and Treatment

This journal focuses on the treatment and investigation of breast cancer, targeting a wide audience including clinical researchers, epidemiologists, immunologists, and cell biologists. It publishes original research, reviews, and discussions on controversial issues. According to the Journal Citation Reports, the journal has a 2020 impact factor of 4.872.

npj Breast Cancer

An open-access journal published by Nature, npj Breast Cancer covers a broad spectrum of breast cancer research, including molecular biology, genetics, and clinical studies. It aims to facilitate the rapid dissemination of high-quality research findings to the global community.

5. Challenges and Future Prospects

Breast cancer research and treatment face numerous challenges across different aspects of the disease.

Here are some of the key challenges: Early Detection & Diagnosis

Limitations in Screening: Mammograms may not detect tumors in dense breast tissue. False Positives & Negatives: Misdiagnosis can lead to unnecessary treatments or delayed care.

Lack of Universal Biomarkers: No single test can reliably detect all breast cancer subtypes early.

A. Challenges

1. Heterogeneity of the Disease

Breast cancer consists of multiple subtypes (e.g., HER2+, triple-negative, luminal A/B), each requiring different treatment approaches. Personalized therapies are difficult to standardize across diverse patient populations.

.2.Resistance to Therapy

Many patients develop resistance to chemotherapy, targeted therapy, or hormone therapy.Mechanisms of drug resistance remain poorly understood in some cases.

3. Limited Early Detection in Some Cases

Dense breast tissue can mask tumors in mammography. Current screening methods may miss aggressive or fast-growing tumors.

4. Access to Advanced Treatments

High costs of targeted therapies and immunotherapy limit accessibility. Disparities exist in treatment availability across different regions and socioeconomic groups**.**

5. Tumor Microenvironment Complexity

The role of the immune system, stromal cells, and extracellular matrix in tumor progression is still being explored.Immunotherapy is effective in some subtypes but not universally applicable.

6. Recurrence and Metastasis

Predicting and preventing metastatic progression remains a major challenge.Dormant cancer cells can evade treatment and reactivate years later.

B. Future Prospects

1. Advancements in Early Detection AI-driven imaging and molecular biomarkers for better early diagnosis.Blood-based screening methods, including advanced liquid biopsies.

2. Precision Medicine & Genomics

Genomic sequencing to tailor treatments based on tumor mutations.CRISPR and gene-editing technologies for targeted therapies.

3. New Therapeutic Approaches

Next-generation immunotherapies, including cancer vaccines and adoptive cell therapies. Development of new antibody-drug conjugates (ADCs) for specific subtypes.

4. Combination Therapies

Combining immunotherapy with chemotherapy or radiation for enhanced effectiveness.

Dual-target inhibitors to overcome resistance mechanisms**.**

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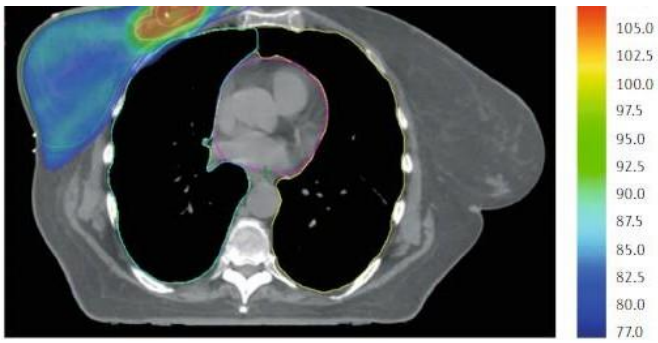
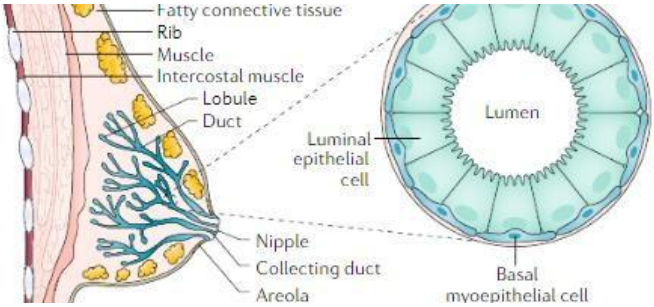
5. Patient-Centered Care & Survivorship Programs

Personalized rehabilitation and mental health support for long-term survivors.Integration of digital health tools (e.g., wearable devices) for monitoring patient outcomes.

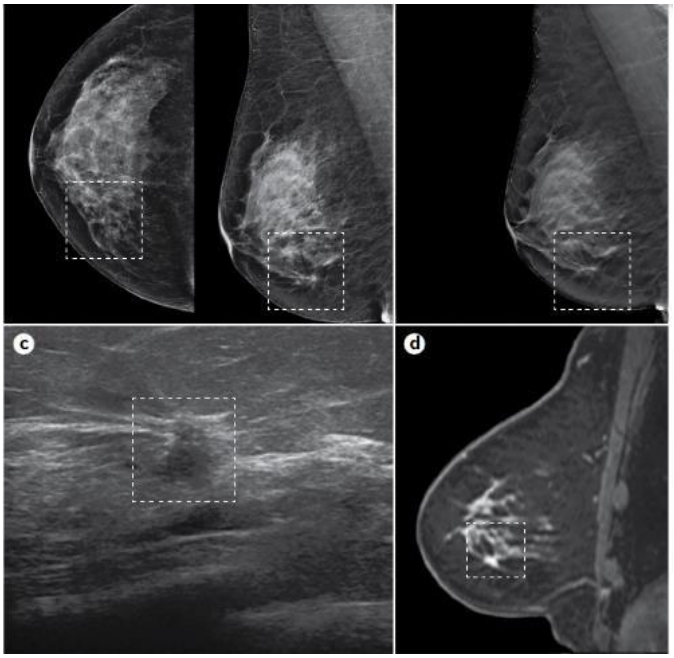
Radiation therapy for breast cancer



6. Advances in AI and Big Data AI algorithms to improve diagnosis, prognosis, and treatment selection.Machine learning models analyzing large patient datasets to identify new treatment patterns. Lifestyle and other environmental factors Breast cancer epidemiology pattern differences across countries are further compounded by cultural factors, lifestyle factors and national awareness campaigns increase in breast cancer incidence between 1980 and the late 1990s is likely due to changes in reproductive factors, with advanced maternal age for first pregnancy, and an increase in awareness and mammography screening.



Breast cancer imaging



Conclusion

Breast cancer remains a significant global health challenge, requiring continuous advancements in research, diagnosis, and treatment. Despite improvements in early detection, targeted therapies, and personalized medicine, challenges such as treatment resistance, tumor heterogeneity, and disparities in access to care persist. Emerging technologies, including AI-driven diagnostics, immunotherapy, and liquid biopsies, offer promising avenues for improving patient outcomes. Future research should focus on developing more effective and less toxic treatments, improving early detection methods, and addressing socioeconomic barriers to ensure equitable healthcare access. A multidisciplinary approach combining clinical research, patient-centered care, and innovative technology will be crucial in advancing breast cancer prevention, treatment, and survivorship.

Key Takeaways:

1.Advancements in Early Detection & Diagnosis

AI-powered imaging and molecular biomarkers improve early detection.Liquid biopsies offer noninvasive cancer monitoring.Personalized
screening strategies based on genetic risk factors.

.**2.Innovations in Treatment & Therapy** Targeted therapies (e.g., antibody-drug conjugates, PARP inhibitors) improve outcomes.

3.Challenges & Future Directions Drug resistance and major challenges.Disparities in access to advanced treatments persist globally.

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