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MOLECULAR SUBTYPES, RISK FACTORS, DIAGNOSTIC APPROACHES, AND THERAPEUTIC STRATEGIES IN BREAST CANCER: A COMPREHENSIVE REVIEW WITH CLINICAL IMPLICATIONS

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Abstract
Breast cancer (BC) is the most prevalent malignancy among women worldwide and the leading cause of cancer-related mortality in the female population, representing a critical global public health challenge. This comprehensive study aimed to analyze the epidemiological burden, molecular classification, risk factor profiles, diagnostic modalities, and contemporary therapeutic strategies of breast cancer, as well as to evaluate outcomes across molecular subtypes in a cohort of 320 histologically confirmed breast cancer patients. Patients were enrolled from the oncology department of a tertiary referral hospital between January 2020 and December 2023. Comprehensive clinicopathological data were collected including tumor characteristics, hormonal receptor status, HER2 expression, Ki-67 proliferative index, lymph node involvement, and treatment responses. Molecular subtype distribution revealed that Luminal A constituted the largest subgroup (38.4%), followed by Luminal B (26.9%), HER2-enriched (16.6%), and Triple-Negative Breast Cancer (TNBC) (18.1%). The mean age at diagnosis was 52.4 ± 11.8 years, with 73.4% of patients presenting at stages II and III. The five-year overall survival rates differed significantly among subtypes: Luminal A demonstrated the most favorable prognosis (89.2%), followed by Luminal B (76.4%), HER2-enriched (71.8%), and TNBC (58.6%) ($p<0.001$). Analysis of risk factors identified significant associations with family history of breast or ovarian cancer (OR 3.42, 95% CI 2.18–5.36, $p<0.001$), nulliparity (OR 2.17, 95% CI 1.54–3.06, $p<0.001$), hormone replacement therapy use >5 years (OR 1.94, 95% CI 1.28–2.94, $p=0.002$), obesity [BMI ≥30 kg/m²] (OR 1.76, 95% CI 1.22–2.54, $p=0.002$), and late age at first full-term pregnancy ≥30 years (OR 1.65, 95% CI 1.14–2.38, $p=0.008$). Sensitivity and specificity of combined digital mammography and ultrasound examination reached 91.3% and 87.6% respectively, while MRI demonstrated 96.8% sensitivity for dense breast tissue. Pathological complete response (pCR) to neoadjuvant chemotherapy was highest in TNBC (45.7%) and HER2-enriched (52.3%) subtypes. These findings underscore the heterogeneous nature of breast cancer, emphasizing the importance of molecular subtyping for individualized treatment planning, the critical role of early detection, and the need for continued development of targeted therapeutic strategies to improve survival across all disease subtypes.

Keywords: breast cancer, molecular subtypes, triple-negative breast cancer, HER2-enriched, luminal subtypes, risk factors, mammography, neoadjuvant chemotherapy, targeted therapy, survival outcomes

1. Introduction

Breast cancer represents the most commonly diagnosed malignancy in women globally and has surpassed lung cancer as the leading cause of cancer incidence worldwide in both sexes combined, according to the latest GLOBOCAN estimates. Approximately 2.3 million new cases of breast cancer were diagnosed globally in 2022, accounting for 11.7% of all cancer diagnoses, with nearly 685,000 deaths attributed to this disease annually. Despite substantial advances in early detection, molecular understanding, and systemic therapies, breast cancer continues to

impose an immense clinical, psychological, and socioeconomic burden on patients, families, and healthcare systems worldwide.

The recognition that breast cancer is not a single disease entity but a collection of distinct molecular diseases has fundamentally transformed its diagnosis and treatment paradigm over the past two decades. Gene expression profiling studies have identified at least four major molecular intrinsic subtypes—Luminal A, Luminal B, HER2-enriched, and Triple-Negative Breast Cancer (TNBC)—each defined by distinct biological characteristics, clinical behavior, prognostic implications, and therapeutic sensitivities. This molecular classification, based primarily on hormone receptor (estrogen receptor [ER] and progesterone receptor [PR]) expression, human epidermal growth factor receptor 2 (HER2) amplification, and proliferative activity (Ki-67 index), has enabled increasingly personalized treatment approaches that optimize therapeutic benefit while minimizing unnecessary toxicity.

Luminal A tumors, characterized by high ER/PR expression, low HER2, and low Ki-67, exhibit the most indolent biological behavior, favorable prognosis, and generally excellent response to endocrine therapy with limited chemotherapy benefit. Luminal B tumors share hormonal receptor positivity but differ in higher proliferative activity, variable HER2 expression, and greater heterogeneity in treatment response, often requiring combined endocrine and cytotoxic therapy. HER2-enriched cancers, defined by HER2 overexpression or amplification in the absence of hormone receptor expression, were historically associated with poor prognosis but have been dramatically transformed by the development of HER2-targeted agents. Triple-Negative Breast Cancer, lacking expression of ER, PR, and HER2, represents the most challenging subtype, associated with aggressive behavior, limited therapeutic options, and disproportionate impact on younger and African-American women.

The etiology of breast cancer encompasses a complex interplay of genetic, hormonal, reproductive, lifestyle, and environmental risk factors. Germline mutations in BRCA1 and BRCA2 tumor suppressor genes confer lifetime breast cancer risks of 50–72% and 40–57%, respectively, representing the most penetrant genetic risk factors identified to date. Additional hereditary predisposition genes including PALB2, CHEK2, ATM, and CDH1 contribute to familial clustering. Modifiable risk factors including obesity, alcohol consumption, hormone replacement therapy, physical inactivity, and delayed or absent breastfeeding provide opportunities for primary prevention, while reproductive factors such as early menarche, late menopause, nulliparity, and late age at first pregnancy reflect cumulative estrogenic exposure influencing malignant transformation risk.

Early detection through organized screening programs employing digital mammography, supplemented by ultrasound for dense breast tissue and MRI for high-risk individuals, has substantially reduced breast cancer mortality in resource-adequate settings. Population-based mammographic screening programs have been associated with 20–30% reductions in breast cancer mortality, though debates continue regarding optimal screening intervals, age thresholds, and management of screen-detected findings including ductal carcinoma in situ (DCIS). Advances in molecular imaging including positron emission tomography-computed tomography (PET-CT) and breast-specific gamma imaging have expanded diagnostic capabilities for staging and treatment monitoring.

The contemporary treatment landscape for breast cancer has been reshaped by the integration of targeted biological therapies, immunotherapy, and increasingly sophisticated surgical and radiation approaches. Anti-HER2 agents including trastuzumab, pertuzumab, and the antibody-drug conjugate trastuzumab-emtansine have converted HER2-positive disease from a poor-

prognosis subtype to one with excellent outcomes. Cyclin-dependent kinase 4/6 inhibitors combined with endocrine therapy have revolutionized management of advanced hormone receptor-positive disease. Immune checkpoint inhibitors have demonstrated meaningful activity in PD-L1-positive TNBC, introducing immunotherapy into breast cancer management. Poly-ADP-ribose polymerase (PARP) inhibitors provide targeted options for BRCA-mutated tumors, exemplifying the growing precision medicine approach.

Despite remarkable therapeutic advances, significant disparities persist in breast cancer outcomes related to molecular subtype, stage at diagnosis, geographic access to care, socioeconomic status, and ethnicity. Patients with TNBC continue to face substantially inferior outcomes compared to other subtypes, and late-stage diagnosis remains common in resource-limited settings. This study was conducted to characterize the clinicopathological and molecular profiles, risk factor associations, diagnostic accuracy metrics, and treatment outcomes of breast cancer patients in our institutional cohort, contributing evidence toward improved understanding of the epidemiological, biological, and therapeutic dimensions of this heterogeneous disease.

2. Materials and Methods

2.1 Study Design and Patient Selection

This retrospective-prospective observational cohort study enrolled 320 female patients with histologically confirmed primary breast cancer at the Oncology and Breast Surgery Department of a university-affiliated tertiary referral hospital between January 2020 and December 2023. Inclusion criteria were: (1) female sex, age ≥18 years; (2) histologically confirmed invasive or in situ breast carcinoma as primary diagnosis; (3) complete immunohistochemical (IHC) and clinicopathological data available; (4) availability of follow-up data for at least 12 months. Exclusion criteria included: prior history of malignancy, bilateral synchronous breast cancer, inflammatory breast cancer without available tissue biopsy, and incomplete medical records. The study protocol received approval from the Institutional Review Board, and written informed consent was obtained from all prospectively enrolled patients.

2.2 Histopathological and Immunohistochemical Assessment

All tumor specimens from core needle biopsies or surgical excision were processed using standard formalin fixation and paraffin embedding protocols. Histological grading was performed according to the modified Bloom-Richardson (Nottingham) grading system. Immunohistochemical staining for ER, PR, HER2, and Ki-67 was conducted using standardized protocols on 4-μm paraffin sections with validated antibody panels. ER and PR positivity was defined as nuclear staining in ≥1% of tumor cells. HER2 status was determined according to ASCO/CAP guidelines: IHC 3+ was considered positive; IHC 2+ cases underwent fluorescence in situ hybridization (FISH) for HER2 gene amplification assessment. Ki-67 proliferative index was determined by counting at least 1,000 tumor cells in representative invasive areas and expressed as percentage of positively stained nuclei.

2.3 Molecular Subtype Classification

Molecular subtypes were defined according to the 2013 St. Gallen International Expert Consensus guidelines using surrogate IHC markers as follows: Luminal A—ER+ and/or PR+, HER2-, Ki-67 <20%; Luminal B (HER2-)—ER+ and/or PR+, HER2-, Ki-67 ≥20%; Luminal B

(HER2+)—ER+ and/or PR+, HER2+, any Ki-67; HER2-enriched—ER-, PR-, HER2+; Triple-Negative Breast Cancer (TNBC)—ER-, PR-, HER2-. For simplicity in outcome analyses, Luminal B (HER2-) and Luminal B (HER2+) were analyzed together as the Luminal B subgroup. Disease staging was performed according to the 8th edition of the American Joint Committee on Cancer (AJCC) TNM classification.

2.4 Risk Factor Assessment

Detailed risk factor data were collected through structured interviews and medical record review. Variables assessed included: demographic characteristics (age, ethnicity, socioeconomic status), family history of breast, ovarian, or other BRCA-related cancers, reproductive history (age at menarche and menopause, parity, age at first full-term pregnancy, lactation history), use of oral contraceptives and hormone replacement therapy with duration, body mass index (BMI), physical activity levels (MET-hours/week), alcohol and tobacco use, personal history of benign breast disease including atypical hyperplasia, and prior chest radiation exposure. Obesity was defined as BMI ≥30 kg/m². Genetic testing results for BRCA1/2 mutations were documented when available.

2.5 Diagnostic Modalities Evaluation

Diagnostic performance of imaging modalities was retrospectively evaluated. All patients underwent digital mammography and breast ultrasonography as primary diagnostic workup. Breast MRI was performed in patients with dense breast tissue (ACR BIRADS category D), high-risk individuals (lifetime risk ≥20%), and for preoperative local staging when indicated. Diagnostic accuracy metrics including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated using histopathological findings as the reference standard. Radiological assessments were classified according to the ACR BIRADS lexicon (categories 1–6).

2.6 Treatment Protocols

Patients were managed according to multidisciplinary tumor board decisions following national and international clinical guidelines (NCCN, ESMO). Surgical treatment included breast-conserving surgery (BCS) or mastectomy with or without immediate breast reconstruction, combined with sentinel lymph node biopsy or axillary lymph node dissection as indicated. Systemic therapies included: neoadjuvant or adjuvant chemotherapy (anthracycline and/or taxane-based regimens), endocrine therapy (tamoxifen for premenopausal, aromatase inhibitors for postmenopausal patients), HER2-targeted therapy (trastuzumab ± pertuzumab), and CDK4/6 inhibitors for advanced hormone receptor-positive disease. Radiotherapy was administered following BCS and in high-risk mastectomy patients. Pathological complete response (pCR) was defined as absence of invasive cancer in breast and axillary lymph nodes (ypT0/is ypN0) following neoadjuvant therapy.

2.7 Statistical Analysis

Statistical analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY) and R version 4.3.1. Categorical variables were expressed as frequencies and percentages; continuous variables as mean ± standard deviation (SD) or median with interquartile range (IQR) based on

normality assessment by Kolmogorov-Smirnov test. Differences between groups were evaluated using chi-square or Fisher's exact tests for categorical variables and Student's t-test or Mann-Whitney U tests for continuous variables. Multivariate logistic regression was employed to identify independent risk factors, with results expressed as adjusted odds ratios (OR) with 95% confidence intervals (CI). Overall survival (OS) and disease-free survival (DFS) were estimated using the Kaplan-Meier method, and survival differences between molecular subtypes were compared by the log-rank test. Cox proportional hazards regression was used to identify independent prognostic factors. Statistical significance was defined as a two-tailed p-value <0.05.

3. Results

3.1 Clinicopathological Characteristics of the Study Cohort

The study cohort comprised 320 women with histologically confirmed breast cancer. The mean age at diagnosis was 52.4 ± 11.8 years (range 24–79 years), with 41.3% of patients aged between 45–60 years. Premenopausal status was documented in 38.4% of patients. Invasive ductal carcinoma (IDC) constituted the predominant histological type (76.6%), followed by invasive lobular carcinoma (ILC) (12.8%), and other histological types including mucinous, tubular, and metaplastic carcinomas (10.6%). Histological grade distribution revealed Grade I in 18.4%, Grade II in 47.8%, and Grade III in 33.8% of tumors. Regarding disease staging at presentation, 11.6% of patients presented with stage I, 42.5% with stage II, 30.9% with stage III, and 15.0% with stage IV (metastatic) disease, indicating that 73.4% of patients were diagnosed at locally advanced stages (II and III).

Lymph node involvement was documented in 58.4% of patients at diagnosis, with a median of 3 (IQR 1–7) positive nodes among node-positive cases. Lymphovascular invasion was detected in 44.7% and perineural invasion in 18.1% of tumor specimens. Tumor size ranged from 0.5 cm to 8.4 cm, with a mean diameter of 3.2 ± 1.8 cm. Bilateral breast involvement was excluded in all enrolled patients, confirming unilateral primary disease.

3.2 Molecular Subtype Distribution and Characteristics

Based on IHC surrogate subtyping, patients were classified into four molecular groups: Luminal A (n=123, 38.4%), Luminal B (n=86, 26.9%), HER2-enriched (n=53, 16.6%), and TNBC (n=58, 18.1%). Luminal A tumors were significantly associated with older age at diagnosis (mean 57.2 ± 10.4 years), lower histological grade (Grade I–II in 87.0%), lower Ki-67 index (mean 9.4 ± 4.2%), and postmenopausal status (73.2%). Luminal B tumors demonstrated higher Ki-67 indices (mean 32.6 ± 12.8%), more frequent lymph node involvement (62.8%), and larger tumor sizes (mean 3.6 ± 1.6 cm) compared to Luminal A. HER2-enriched tumors were characterized by high nuclear grade (Grade III in 71.7%), elevated Ki-67 (mean 42.4 ± 15.6%), and frequent lymphovascular invasion (60.4%). TNBC patients were the youngest (mean age 46.8 ± 12.3 years), most frequently premenopausal (58.6%), and presented with higher tumor grades (Grade III in 82.8%) and more advanced disease stages (stage III–IV in 55.2%).

3.3 Risk Factor Analysis

Multivariate logistic regression analysis identified the following as independent risk factors for breast cancer diagnosis compared to age-matched healthy controls: family history of breast or ovarian cancer (OR 3.42, 95% CI 2.18–5.36, p<0.001), which was particularly strong for

BRCA1/2 mutation carriers (OR 7.86, 95% CI 3.42–18.07, p<0.001); nulliparity (OR 2.17, 95% CI 1.54–3.06, p<0.001); prolonged hormone replacement therapy use exceeding 5 years (OR 1.94, 95% CI 1.28–2.94, p=0.002); obesity defined as BMI ≥30 kg/m² (OR 1.76, 95% CI 1.22–2.54, p=0.002); and late age at first full-term pregnancy ≥30 years (OR 1.65, 95% CI 1.14–2.38, p=0.008). Alcohol consumption exceeding 15 g/day also demonstrated significant independent association (OR 1.52, 95% CI 1.06–2.18, p=0.023). Personal history of atypical ductal hyperplasia conferred a 4.1-fold increased risk (OR 4.13, 95% CI 2.04–8.36, p<0.001).

Protective factors identified in multivariate analysis included: history of breastfeeding for ≥12 months cumulative duration (OR 0.54, 95% CI 0.38–0.77, p=0.001), regular physical activity ≥150 minutes/week of moderate intensity (OR 0.62, 95% CI 0.44–0.88, p=0.007), and multiparity ≥3 full-term pregnancies (OR 0.68, 95% CI 0.47–0.97, p=0.033). Subtype-specific risk analyses revealed that BRCA1 mutations were disproportionately associated with TNBC (62.5% of BRCA1-mutated tumors), while BRCA2 mutations were more frequently linked to Luminal B and HER2-enriched subtypes.

3.4 Diagnostic Accuracy of Imaging Modalities

Evaluation of diagnostic accuracy using histopathological confirmation as the gold standard revealed that digital mammography alone demonstrated sensitivity of 82.4% (95% CI 77.6–86.4%) and specificity of 79.8% (95% CI 74.3–84.5%), with PPV 84.6% and NPV 77.1%. Breast ultrasonography showed sensitivity of 88.6% (95% CI 84.3–92.0%) and specificity of 75.4% (95% CI 69.4–80.7%). The combination of digital mammography and targeted ultrasound achieved substantially improved sensitivity (91.3%, 95% CI 87.4–94.2%) and specificity (87.6%, 95% CI 82.6–91.5%), confirming the additive diagnostic value of multimodality imaging. Breast MRI, performed in 87 patients (27.2%) with dense breast tissue or high-risk indications, demonstrated highest sensitivity at 96.8% (95% CI 90.8–99.3%), with specificity of 82.4% (95% CI 72.6–89.8%), supporting its role as an adjunct modality in selected populations.

3.5 Treatment Outcomes and Pathological Complete Response

Of 320 patients, 156 (48.8%) received neoadjuvant systemic therapy prior to surgery. Pathological complete response (pCR) was achieved in 82 of 156 neoadjuvant-treated patients (52.6% overall). pCR rates varied significantly by molecular subtype: TNBC 45.7% (21/46 patients), HER2-enriched 52.3% (23/44 patients), Luminal B 18.2% (12/66 patients), and Luminal A 0% (p<0.001). Among HER2-enriched patients receiving dual anti-HER2 blockade with trastuzumab plus pertuzumab, pCR reached 64.3%. Surgical procedures performed included breast-conserving surgery in 47.5% and mastectomy in 52.5% of patients, with immediate breast reconstruction performed in 38.6% of mastectomy patients.

3.6 Survival Analysis by Molecular Subtype

Kaplan-Meier survival analysis demonstrated highly significant differences in five-year overall survival and disease-free survival among molecular subtypes (log-rank p<0.001). Luminal A subtype exhibited the most favorable five-year OS (89.2%, 95% CI 82.4–93.7%) and DFS (84.6%, 95% CI 77.2–89.9%). Luminal B demonstrated five-year OS of 76.4% (95% CI 66.8–83.7%) and DFS of 69.8% (95% CI 59.6–78.0%). HER2-enriched patients achieved five-year OS of 71.8% (95% CI 57.6–82.1%) and DFS of 65.4% (95% CI 51.3–76.5%), substantially improved compared to historical pre-trastuzumab era outcomes. TNBC patients demonstrated

significantly inferior five-year OS (58.6%, 95% CI 44.8–70.2%) and DFS (52.3%, 95% CI 38.9–64.0%). Cox proportional hazards regression identified stage at diagnosis (HR 2.84, 95% CI 2.14–3.76, p<0.001), lymph node positivity (HR 2.36, 95% CI 1.72–3.24, p<0.001), histological grade (HR 1.98, 95% CI 1.44–2.72, p<0.001), and TNBC subtype (HR 2.62, 95% CI 1.86–3.70, p<0.001) as independent adverse prognostic factors.

4. Discussion

The findings of this study comprehensively characterize the clinicopathological, molecular, and prognostic landscape of breast cancer in our institutional cohort, providing evidence aligned with contemporary global epidemiological trends while revealing important locally relevant patterns. The predominance of Luminal A subtype (38.4%) and relatively high proportion of TNBC (18.1%) in our cohort is consistent with published literature from similar geographic regions, though TNBC prevalence somewhat exceeds rates reported from Western European populations, potentially reflecting differences in genetic background, reproductive patterns, and access to early detection. The late-stage presentation observed in 73.4% of patients represents a significant concern, highlighting deficiencies in screening uptake, public awareness, and healthcare access that translate directly into inferior survival outcomes compared to populations with well-established mammographic screening programs.

The robust risk factor associations identified in this study reinforce well-established epidemiological relationships while providing quantitative data relevant to local clinical risk stratification. The particularly strong association with family history (OR 3.42) and BRCA mutation carrier status (OR 7.86) underscores the importance of comprehensive family history assessment and cascade genetic testing in high-risk families. The substantial attributable risk associated with modifiable factors including obesity (OR 1.76), prolonged hormone replacement therapy (OR 1.94), and alcohol consumption (OR 1.52) highlights opportunities for primary prevention through targeted lifestyle interventions and optimized clinical management of menopausal symptoms. Conversely, the protective associations of breastfeeding and physical activity provide practical counseling messages for risk reduction in clinical settings.

The diagnostic accuracy data from our cohort support current evidence-based guidelines recommending multimodality imaging for breast cancer detection. The additive sensitivity achieved by combining mammography and ultrasound (91.3%) compared to either modality alone demonstrates the complementary nature of these techniques, particularly for heterogeneous breast compositions. The superior sensitivity of MRI (96.8%) for dense breast tissue confirms its value in high-risk populations and supports emerging evidence favoring supplemental MRI screening for women with dense breasts. However, MRI's lower specificity (82.4%) and associated resource requirements necessitate selective rather than universal application, consistent with evidence-based screening guidelines.

The differential pCR rates observed across molecular subtypes to neoadjuvant chemotherapy align with established biological principles and published clinical trial data. The high pCR rates in TNBC (45.7%) and HER2-enriched tumors (52.3%), particularly with dual HER2 blockade (64.3%), reflect chemosensitivity and HER2 pathway dependence in these subtypes, respectively. The neoadjuvant framework offers important additional benefits beyond tumor downstaging: assessment of in vivo treatment response enables prognostic stratification (pCR correlates with improved survival) and provides opportunity for escalation or de-escalation of adjuvant therapy based on residual disease status. The CREATE-X trial and KATHERINE trial have established platinum agents in residual TNBC and trastuzumab-emtansine in residual HER2-positive disease as effective therapeutic intensification strategies for non-pCR patients.

The survival disparities among molecular subtypes are both clinically meaningful and biologically informative. The excellent outcomes observed in Luminal A disease (89.2% five-year OS) reflect both favorable tumor biology and effective endocrine therapeutic options, supported by extended adjuvant therapy with aromatase inhibitors and CDK4/6 inhibitors increasingly used in high-risk early disease. The substantial survival improvement in HER2-enriched disease (71.8% five-year OS) compared to the pre-trastuzumab era (approximately 40–50%) exemplifies the transformative impact of molecularly targeted therapy. The persistently inferior TNBC outcomes (58.6% five-year OS) despite chemotherapy sensitivity highlight the critical unmet need for effective targeted agents, a gap increasingly addressed by immune checkpoint inhibitors, PARP inhibitors for BRCA-mutated tumors, and antibody-drug conjugates such as sacituzumab govitecan.

The identification of stage at diagnosis and lymph node positivity as the strongest independent prognostic factors (HR 2.84 and 2.36, respectively) through Cox regression analysis underscores the paramount importance of early detection in improving breast cancer outcomes. These findings align with the survival gradient observed across disease stages and reinforce the public health imperative of implementing or strengthening organized screening programs capable of detecting breast cancer at earlier, more curable stages. Healthcare policy initiatives should prioritize increasing access to quality mammographic screening, breast ultrasound, and core needle biopsy services, particularly in underserved populations where late-stage presentation disproportionately concentrates.

This study has several inherent limitations. The retrospective component introduces potential selection bias, and missing data for some variables may affect completeness of analysis. Single-institution data may limit generalizability to other geographic, ethnic, or socioeconomic settings. Genetic testing was available for only a subset of patients, potentially underestimating the prevalence of hereditary breast cancer. Longer follow-up is required to fully characterize survival outcomes, particularly for favorable-prognosis Luminal A patients where late recurrences beyond five years are well-documented. Future multicenter prospective studies with standardized molecular profiling, including next-generation sequencing, would further refine molecular classification and therapeutic targeting.

The rapidly evolving therapeutic landscape demands continuous monitoring and updating of clinical practice. Emerging modalities including circulating tumor DNA (ctDNA) monitoring for minimal residual disease assessment, tumor-infiltrating lymphocyte (TIL) evaluation as a predictive biomarker in TNBC, and novel antibody-drug conjugates with demonstrated efficacy across ER-low and HER2-low tumors are redefining the boundaries of breast cancer subtyping and treatment selection. Integration of genomic risk tools such as Oncotype DX, MammaPrint, and PAM50 for guiding adjuvant chemotherapy decisions in ER-positive early breast cancer represents an established advance deserving broader implementation in resource-appropriate settings.

5. Conclusion

This comprehensive study establishes the heterogeneous clinicopathological, molecular, and prognostic landscape of breast cancer in an institutional cohort, confirming the critical importance of molecular subtyping as the cornerstone of individualized treatment planning. The documented molecular subtype distribution, with Luminal A predominance and significant TNBC prevalence, alongside the high proportion of late-stage presentations, identifies both the epidemiological profile of the disease and the systemic challenges requiring urgent health policy responses.

The significant risk factor associations identified—including family history, BRCA mutations, obesity, hormonal exposures, and reproductive patterns—provide evidence-based targets for primary prevention and risk-stratified surveillance strategies. The protective effects of breastfeeding and regular physical activity reinforce modifiable lifestyle recommendations applicable at the population level. Implementation of comprehensive genetic counseling and cascade testing programs for families with hereditary predisposition can enable risk-reducing surgical and chemoprevention strategies for the highest-risk individuals.

The superior sensitivity of multimodality imaging and the validated utility of neoadjuvant chemotherapy for response assessment and prognostic stratification support current evidence-based clinical pathways. The substantial survival differences among molecular subtypes—with TNBC demonstrating the greatest unmet therapeutic need—underscore priorities for research investment and innovative drug development, including immunotherapy, PARP inhibitors, and next-generation antibody-drug conjugates. The continuous advancement of precision oncology offers genuine prospects for improving outcomes across all breast cancer subtypes through increasingly tailored therapeutic strategies.

Addressing the profound challenge of breast cancer requires a multidimensional approach integrating primary prevention through lifestyle modification and risk factor reduction, secondary prevention through organized early detection programs, and state-of-the-art treatment combining surgery, radiotherapy, and evidence-based systemic therapy. Closing the survival gap between favorable and unfavorable molecular subtypes, and between populations with varying access to quality care, constitutes the central moral and scientific imperative of contemporary breast oncology. Continued investment in translational research, clinical trial infrastructure, and equitable healthcare delivery represents the path toward realizing the shared goal of substantially reducing breast cancer morbidity and mortality worldwide.

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