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Molecular Profile of Breast Cancer in Young Women Under 40 Years: Experience from the Oncology-Radiotherapy Department of Mohammed VI University HospitaL Marrakech, Morocco

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Abstract **Original Research Article**

Breast cancer in young women is relatively uncommon but often exhibits aggressive biological and clinical characteristics. The molecular landscape of these tumors remains poorly described in North African populations. This study aimed to characterize the molecular profile of breast cancer in young women in the Marrakech region of Morocco and to evaluate its correlation with clinicopathological features and prognostic implications. We conducted a retrospective analysis of breast cancer cases diagnosed and treated at the Oncology-Radiotherapy Department, Mohammed VI University Hospital Center of Marrakech. Data were extracted from institutional records January 2018 and December 2024, with a specific subgroup of women younger than 40 years. Clinical, pathological, therapeutic, and immunohistochemical data (ER, PR, HER2, Ki-67) were analyzed, and molecular subtypes were classified according to St. Gallen 2015 guidelines. Associations between molecular subtypes, treatment modalities, recurrence, metastasis, and survival were assessed. Young women accounted for 10.7% of breast cancer cases (mean age 34 years). Molecular classification showed a predominance of Luminal B (42.1%), followed by Luminal A (23%), HER2-enriched (20%), and Triple-negative (14.5%). Aggressive subtypes (HER2-enriched and triple-negative) were associated with high grade (SBR III, 64%-68%), larger tumor size (T2–T3, 70-72%), lymph node invasion (65%), vascular emboli (26-28%), and higher rates of distant metastasis at diagnosis (HER2-enriched 18%, Triple-negative 20%). Recurrence was highest in TNCB (48%) and HER2-enriched (42%) tumors. Mortality was highest in HER2-enriched (45%) and Triple-negative (40%). The 5-year disease-free survival was highest in Luminal A (72%), intermediate in Luminal B (56%), and lowest in HER2-enriched (41%) and Triple-negative (36%). Breast cancer in Moroccan women under 40 years is characterized by a high prevalence of aggressive molecular subtypes, which correlates with adverse clinicopathological features, high recurrence rates, and poor survival outcomes. These findings underscore the critical need for early detection programs and improved access to targeted therapies for young breast cancer patients in this region.

Keywords: Breast Cancer, Young Women, Molecular Subtypes, Morocco, Prognosis, Targeted Therapy.

INTRODUCTION

Breast cancer is the leading cause of cancer-related death in women worldwide [1]. While the majority of cases are diagnosed after the age of 50, approximately 7–12% occur in women under 40 years [2]. Breast cancer in young women is consistently associated with a more advanced stage at diagnosis, higher histological grade, and a higher prevalence of aggressive molecular phenotypes [3]. These patients often face unique clinical challenges due to fertility concerns, significant psychosocial impact, and limited access to targeted therapies in low- and middle-income countries [4].

In Morocco, breast cancer represents the most frequently diagnosed malignancy in women, with a concerning rise in incidence among younger populations [5]. Despite the clinical significance of early-onset disease, data on its molecular characteristics in North African women remain scarce. A detailed understanding of these tumor profiles is crucial for refining diagnostic strategies, improving prognostication, and guiding personalized treatment decisions.

This study therefore aims to characterize the molecular profile of breast cancer in women younger than 40 years treated at the Oncology-Radiotherapy Department, Mohammed VI University Hospital Center of Marrakech, Morocco and to investigate its correlation with clinicopathological features, treatment patterns, and survival outcomes.

MATERIALS AND METHODS

Study design and setting:

A retrospective descriptive and analytical study was conducted in the Oncology-Radiotherapy Department, Mohammed VI University Hospital Center of Marrakech, Morocco. Data were retrospectively collected from medical and pathological records between January 2018 and December 2024.

Study Population :

The study included all female patients under the age of 40 years diagnosed with primary invasive breast carcinoma. Patients with incomplete immunohistochemistry (IHC) or treatment data were excluded from the analysis.

Histopathological evaluation:

Tumor histology was classified according to the World Health Organization (WHO) 2019 classification of breast tumors. Histological grading was performed using the modified Scarff-Bloom-Richardson (SBR) system.

Immunohistochemistry and molecular subtyping:

IHC was performed for estrogen receptor (ER), progesterone receptor (PR), HER2, and Ki-67. Molecular subtypes were defined according to the St. Gallen 2015 consensus [6]:

- Luminal A: ER+ and/or PR+, HER2-, Ki-67 low (<14%)
- Luminal B (HER2-negative): ER+ and/or PR+, HER2-, Ki-67 high (≥14%)
- Luminal B (HER2-positive): ER+ and/or PR+, HER2+
- HER2-enriched: ER-, PR-, HER2+
- Triple-Negative Breast Cancer (TNBC): ER-, PR-, HER2-

Treatment and follow-up:

Treatment strategies were collected, including surgery, chemotherapy, radiotherapy, endocrine therapy, and targeted anti-HER2 therapy. Follow-up data were reviewed to assess recurrence, metastasis, and survival outcomes.

Statistical analysis:

Data were analyzed with SPSS v25. Correlations between molecular subtypes, treatment, recurrence, metastasis, and clinicopathological parameters were tested using chi-square test. Survival data were analyzed descriptively based on follow-up records.

RESULTS

Epidemiological features:

Out of 2040 breast cancer cases, 220 (10.7%) involved women <40 years. The mean age at diagnosis was 34 years (range 22–39). Age distribution analysis revealed that 18% of patients were aged 20–29, 64% were 30–35 years, and 18% were 36–39 years.

Histological characteristics:

The predominant histological type was invasive ductal carcinoma (87%), followed by lobular carcinoma (6%) and others (7%). High-grade tumors (SBR III) were frequent (64%).

Distribution of Molecular Subtypes:

The distribution of molecular subtypes in this cohort of young women is shown in Figure 1. Luminal B was the most frequent subtype (42.1%), followed by Luminal A (23.0%), HER2-enriched (20.4%), and Triple-negative (14.5%).

Correlation with clinicopathological features and metastasis:

As detailed in Table 1, aggressive subtypes (HER2-enriched and Triple-negative) showed strong correlations with adverse pathological features. High histological grade (SBR III) was observed in 64-68% of these tumors. Larger tumor size (T2-T3) was more frequent in the HER2-enriched (72%) and Triple-negative (70%) groups. Lymph node involvement and the presence of vascular emboli were also higher in these aggressive subtypes. Distant metastases at diagnosis were present in 18% of HER2-enriched and 20% of Triple-negative cases.

Treatment patterns and evolution:

Almost all patients underwent surgical intervention, with mastectomy being more common. Chemotherapy was administered to 85% of patients. Radiotherapy was delivered to 90% of patients, especially those with nodal involvement. Endocrine therapy was prescribed for all patients with Luminal subtypes. Targeted anti-HER2 therapy (trastuzumab) was administered to HER2+ patients when accessible.

Survival Outcomes:

During a median follow-up of 48 months, the overall recurrence rate was 32%. Recurrence was most common in Triple-negative (48%) and HER2-enriched (42%) tumors. The highest mortality rates were observed in the HER2-enriched (45%) and Triple-negative (40%) groups. The estimated 5-year disease-free survival (DFS) was highest for Luminal A tumors (72%), intermediate for Luminal B (56%), and lowest for HER2-enriched (41%) and Triple-negative (36%) subtypes (Figure 2).

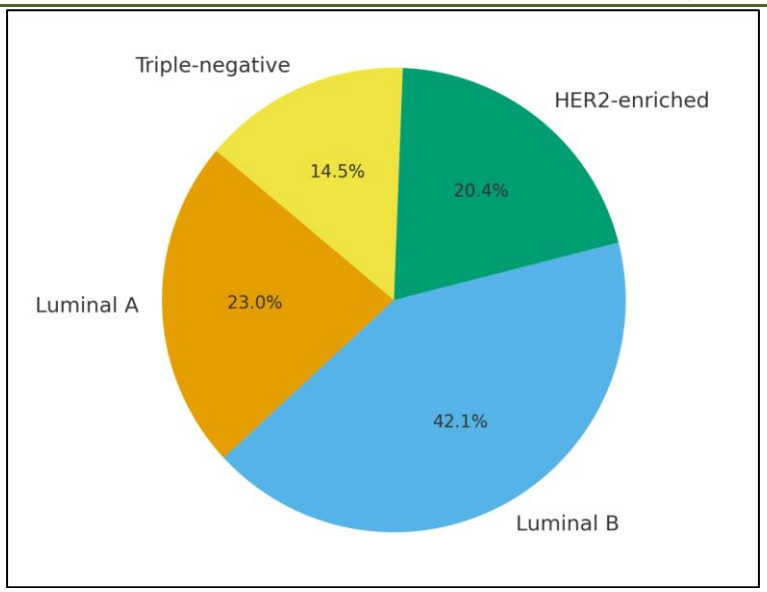

Figure 1. Distribution of molecular subtypes in young women

Table 1. Association between molecular subtypes, prognostic factors, and metastasis

Factor	Luminal A	Luminal B	HER2-enriched	Triple-negative
High SBR grade (III)	32%	44%	64%	68%
Tumor size (T2–T3)	41%	49%	72%	70%
Lymph node invasion	48%	55%	65%	65%
Vascular emboli	15%	20%	28%	26%
Metastasis at diagnosis	6%	9%	18%	20%

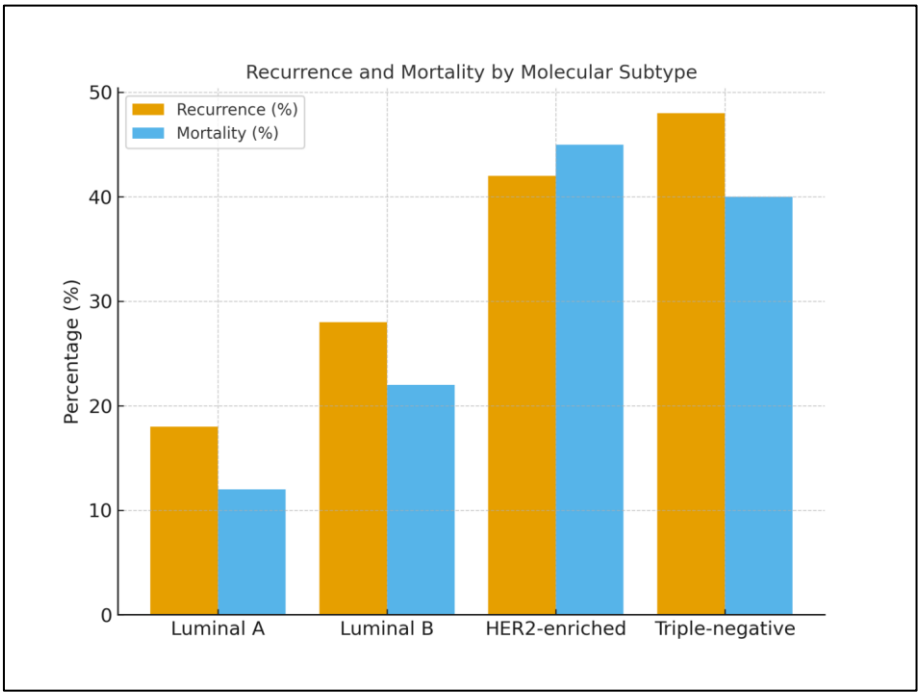

Figure 2. Reccurrence and mortality by Molecular Subtype

DISCUSSION

This study provides one of the first comprehensive analyses of breast cancer molecular profiles in young Moroccan women. We report that early-onset breast cancer constitutes 10.7 % of all breast cancer cases, consistent with global reports ranging between 7–12% [7].

Our findings highlight a pronounced predominance of aggressive molecular subtypes. This pattern aligns with international studies demonstrating

that breast cancer in young women is more likely to be associated with biologically aggressive phenotypes [8,9].

The correlation between molecular profiles and adverse clinicopathological features is striking. HER2-enriched and triple-negative tumors were more frequently associated with higher grade, larger tumor size, nodal metastasis, vascular emboli, and distant metastases. These associations have also been documented in international cohorts, where young women often present with systemic spread at diagnosis and poorer prognostic indicators [10,11]. The biological aggressiveness of these subtypes likely contributes to the elevated recurrence and mortality observed in our population.

Treatment patterns followed international standards but revealed significant disparities in access to targeted therapy. The limited use of trastuzumab, often due to cost, likely contributed to the poor outcomes observed in the HER2-enriched subgroup [12].

Survival analysis in our cohort further confirmed the unfavorable prognosis of aggressive subtypes. Luminal A patients had the best outcomes, while HER2-enriched and Triple-negative had the lowest disease-free survival, in line with previous reports [13,14].

Strengths and limitations:

The main strength of this study is its focus on a specific, understudied population. The limitations are inherent to its retrospective design, including potential selection bias and incomplete long-term follow-up. Future prospective studies incorporating genetic sequencing are warranted.

CONCLUSION

Breast cancer in Moroccan women under 40 years is characterized by a high prevalence of aggressive molecular subtypes.These molecular profiles correlate with adverse clinicopathological features, advanced stage at diagnosis, higher recurrence rates, and poor survival outcomes. Our findings highlight a pressing need for enhanced early detection programs and for health policy initiatives that ensure equitable access to essential targeted therapies to improve the prognosis for young breast cancer patients in Morocco.

REFERENCES

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin. 2021;71(3):209-249.
2. Fredholm H, Eaker S, Frisell J, Holmberg L, Fredriksson I, Lindman H. Breast cancer in young women: poor survival despite intensive treatment. PLoS One. 2009;4(11):e7695.
3. Anders CK, Johnson R, Litton J, Phillips M, Bleyer A. Breast cancer before age 40 years. Semin Oncol. 2009;36(3):237-249.
4. Howard-Anderson J, Ganz PA, Bower JE, Stanton AL. Quality of life, fertility concerns, and behavioral health outcomes in younger breast cancer survivors: a systematic review. J Natl Cancer Inst. 2012;104(5):386-405.
5. El Fakir S, Najdi A, Khazraji YC, et al. Trends in breast cancer incidence and mortality in Morocco, 2005-2015. Lancet Glob Health. 2018;6:S30.
6. Coates AS, Winer EP, Goldhirsch A, et al. Tailoring therapies—improving the management of early breast cancer: St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2015. Ann Oncol. 2015;26(8):1533-1546.
7. Johnson RH, Chien FL, Bleyer A. Incidence of breast cancer with distant involvement among women in the United States, 1976 to 2009. JAMA. 2013;309(8):800-805.
8. Azim HA Jr, Partridge AH. Biology of breast cancer in young women. Breast Cancer Res. 2014;16(4):427.
9. Cancello G, Maisonneuve P, Rotmensz N, et al. Prognostic and predictive value of centrally reviewed expression of estrogen and progesterone receptors in a randomized trial comparing letrozole and tamoxifen adjuvant therapy for postmenopausal early breast cancer: BIG 1-98. J Clin Oncol. 2007;25(25):3846-3852.
10. Carey LA, Perou CM, Livasy CA, et al. Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. JAMA. 2006;295(21):2492-2502.
11. Keegan TH, DeRouen MC, Press DJ, Kurian AW, Clarke CA. Occurrence of breast cancer subtypes in adolescent and young adult women. Breast Cancer Res. 2012;14(2):R55.
12. Ginsburg O, Bray F, Coleman MP, et al. The global burden of women's cancers: a grand challenge in global health. Lancet. 2017;389(10071):847-860. Abubakar M, et al. Prognostic value of Ki-67 in young women with breast cancer. *Breast Cancer Res Treat*. 2016.
13. Loibl S, et al. Survival of young patients with triple-negative breast cancer. *Breast Care*. 2014.
14. Loibl S, et al. Survival of young patients with triple-negative breast cancer. Breast Care. 2014.a