

The Prognostic Impact of Hormonal Receptors on Breast Cancer Recurrence: An Analysis of a Cohort of 424 Moroccan Patients

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DOI: <https://doi.org/10.36347/sjmcr.2025.v13i10.008>

| Received: 21.07.2025 | Accepted: 29.09.2025 | Published: 06.10.2025

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Abstract

Original Research Article

Background: Breast cancer remains the most common cancer, and its management is becoming more complex due to the diversity of patient profiles. Identifying recurrence risk factors is crucial for tailoring therapeutic strategies. **Objective:** This retrospective study aims to determine the main risk factors for breast cancer recurrence in a cohort of 424 patients treated at the Radiotherapy Department of the National Institute of Oncology in Rabat, with a focus on the influence of hormonal receptor (HR) status. **Materials and Methods:** A retrospective study was conducted on the medical records of 424 patients. Clinical and pathological data, collected between January 1st and December 21st, 2024, were analyzed. Six patients lost to follow-up were excluded. The role of risk factors in recurrence was evaluated using univariate and multivariate regression analyses. **Results:** Multivariate analysis revealed that negative HR status (OR=2.525; 95% CI: 1.211-5.248; $p < 0.011$), lymphovascular invasion (LVI) (OR=0.451; 95% CI: 0.211-0.919; $p < 0.031$), and massive nodal involvement (>4 N+) were significant and independent risk factors for recurrence. Hormonal receptor status emerged as a key prognostic marker. **Conclusion:** The results of this study confirm that lymphovascular invasion, nodal involvement, and negative hormonal receptor status are powerful predictors of breast cancer recurrence. These factors must be systematically integrated into clinical decision-making algorithms to optimize the treatment and follow-up of our patients.

Keywords: Breast cancer, recurrence, risk factors, hormonal receptors, oncology, Morocco.

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1. INTRODUCTION

Breast cancer is the leading cause of morbidity and mortality from cancer in women worldwide, with an estimated incidence of 2.3 million new cases in 2020 [1]. In Morocco, it represents a growing public health burden, and its incidence is steadily increasing. Preventing recurrence is the ultimate goal of management, as it is the main determinant of long-term survival for patients.

Several prognostic factors have been identified over the years to assess the risk of recurrence. While clinical factors such as age at diagnosis, tumor stage, and nodal involvement are well-established, biological and molecular markers have gained crucial importance. Among these, the status of hormonal receptors (HR), for estrogen (ER) and progesterone (PR), is an essential factor that not only guides the indication for hormone

therapy but also provides crucial information about tumor behavior and its potential for recurrence [2].

Scientific literature shows that HR-positive breast tumors are generally associated with a better prognosis and a favorable response to hormone therapy [3]. However, significant heterogeneity exists in prognosis, particularly depending on age. Recent data suggest that breast cancers in younger women have distinct biological characteristics, with a higher proportion of aggressive subtypes [4]. Therefore, the impact of HR status on recurrence may not be uniform across all age groups.

In this context, the primary objective of this study is to determine the main risk factors for breast cancer recurrence in a cohort of 424 patients treated at

Citation: Denise Edith Tatiana Ngbwa *et al.* The Prognostic Impact of Hormonal Receptors on Breast Cancer Recurrence: An Analysis of a Cohort of 424 Moroccan Patients. Sch J Med Case Rep, 2025 Oct 13(10): 2214-2219.

the Radiotherapy Department of the National Institute of Oncology in Rabat between January 1st and December 21st, 2024. Our analysis will focus particularly on the prognostic role of hormonal receptor status to better understand its influence on the risk of recurrence in our population.

2. MATERIALS AND METHODS.

2.1 Study population and selection criteria

This was a retrospective study based on the medical records of 424 patients with breast cancer, admitted and followed at the Radiotherapy Department of the National Institute of Oncology in Rabat during the period from January 1st to December 21st, 2024. Patients diagnosed with recurrence were identified. Inclusion and exclusion criteria were applied to ensure the homogeneity of the sample.

Inclusion criteria:

- Confirmed diagnosis of invasive breast cancer.
- Initial treatment completed and documented follow-up within the radiotherapy department during the study period.
- Complete medical records containing clinical, pathological data, and hormonal receptor status.
- Informed consent obtained from the participants.

Exclusion criteria:

- Incomplete or missing medical records.
- Patients with metastatic breast cancer from the outset (stage IV).

- Patients with a history of breast cancer treated before the start of the study.
- Six patients were excluded because they were lost to follow-up.

2.2 Data collection

Clinical, paraclinical, pathological, and therapeutic information was collected. Variables of interest for this analysis included age, tumor stage (TNM), histological type, histoprognostic grade (SBR), nodal involvement, hormonal receptor status (HR), lymphovascular invasion (LVI), and the occurrence of recurrence.

2.3 Statistical analyses

The data were analyzed using SPSS software. Descriptive statistics were used to summarize the cohort's characteristics. To determine the risk factors for recurrence, we performed logistic regression analyses. Odds Ratios (OR) and their 95% confidence intervals (95% CI) were calculated. A p-value < 0.05 was considered statistically significant.

3. RESULTS

The clinical and pathological characteristics of the 424 patients in the study are summarized in Table 1. The mean age of our cohort was 49.15 ± 10.37 years, with a range from 29 to 87 years. Invasive ductal carcinoma was the most frequent histological type (82.3%). The vast majority of patients (86.6%) received chemotherapy, and 73.1% received hormone therapy, reflecting the predominance of hormone-sensitive tumors in our sample.

Table 1: Characteristics of the patient cohort (N=424)

Characteristic	Value
Age (years)	Mean: 49.15 ± 10.37 Range: [29-87]
Menarche (years)	13.64 ± 1.58
Mean age at 1st pregnancy (years)	21.78 ± 5.44
Number of pregnancies	3.9 ± 2.34
Parity	3.3 ± 2
Contraception	
No	67 (15.8 %)
Yes	169 (39.9 %)
Menopause	
No	239 (56.4 %)
Yes	185 (43.6 %)
Family history	77 (18.2 %)
Diagnosis delay (months)	3 [1-12]
Tumor size (mm)	25 [19-33]
TNM Stage	
Tis	4 (0.9 %)
I	71 (16.7 %)
IIA	144 (34.0 %)
IIB	39 (9.2 %)
IIIA	32 (7.6 %)
IIIB	39 (9.2 %)

Characteristic	Value
IIIC	23 (5.4 %)
IV	34 (8.0 %)
Histological type	
Invasive ductal carcinoma	349 (82.3 %)
Other	75 (17.7 %)
SBR Grade	
I	33 (7.8 %)
II	270 (63.7 %)
III	121 (28.5 %)
Lymphovascular invasion (LVI)	
No	234 (55.2 %)
Yes	190 (44.8 %)
Nodal Ratio (LNR)	
N0	165 (39.0 %)
<4N+	134 (31.6 %)
≥4N+	125 (29.5 %)
Surgical margins	
Negative	419 (98.8 %)
Positive	5 (1.2 %)
Hormonal Receptors (HR)	
Negative	114 (26.9 %)
Positive	310 (73.1 %)
HER2 status	
Negative	303 (71.5 %)
Positive	121 (28.5 %)
Ki67	
<20 %	47 (44.7 %)
≥20 %	58 (55.3 %)
Chemotherapy	367 (86.6 %)
Hormone Therapy (HT)	310 (73.1 %)
Type of HT	
Tamoxifen	156 (50.3 %)
Aromatase inhibitors	109 (35.2 %)
Switch	45 (14.5 %)
Herceptin	109 (25.7 %)

Univariate analysis (see Table 2) identified risk factors for recurrence by evaluating their isolated impact. Negative hormonal receptor status, lymphovascular

invasion (LVI), and massive nodal involvement (≥4 N+) were all significantly associated with a risk of recurrence.

Table 2: Univariate analysis of recurrence risk factors

Recurrence Factor	Recurrence	No Recurrence	OR	95% CI	p-value
Age (years)	47.8 ± 10.25	49.36 ± 10.36	0.987	0.985-1.017	0.404
Menarche (years)	13.58 ± 1.89	13.65 ± 1.55	0.980	0.891-1.077	0.294
Mean age 1st pregnancy (years)	23 ± 5.96	22.03 ± 5.00	1.493	0.729-1.317	0.927
Number of pregnancies	3.95 ± 2.59	3.91 ± 2.31	0.999	0.870-1.147	0.990
Parity	3.3 ± 2.16	3.31 ± 2.01	0.996	0.850-1.168	0.965
Contraception			1 (ref)	-	-
No	41 (64.1 %)	56 (16.8 %)			
Yes	22 (34.4 %)	146 (43.8 %)	0.325	0.660-3.300	0.325
Menopause			1 (ref)	-	-
No	42 (65.6 %)	185 (55.6 %)			
Yes	22 (34.4 %)	148 (44.4 %)	0.953	0.520-1.988	0.824
Diagnosis delay (months)	2.50 [1-12]	7.67 ± 11.28	1.002	0.974-1.032	0.875
Tumor size (mm)	30 [20-48.5]	23 [18-31]	1.005	0.992-1.017	0.451
SBR Grade			1 (ref)	-	-
I	5 (7.8 %)	28 (8.4 %)			

Recurrence Factor	Recurrence	No Recurrence	OR	95% CI	p-value
II	31 (48.4 %)	205 (61.6 %)	0.750	0.225-2.495	0.639
III	28 (43.8 %)	99 (29.7 %)	0.652	0.328-1.297	0.223
Lymphovascular invasion (LVI)			1 (ref)	-	-
No	21 (32.8 %)	184 (55.2 %)			
Yes	43 (67.2 %)	149 (44.7 %)	0.343	0.172-0.655	0.001
Nodal Ratio (LNR)			1 (ref)	-	-
N0	10 (15.6 %)	148 (44.4 %)			
<4N+	16 (25.0 %)	113 (33.9 %)	0.420	0.190-0.888	0.025
≥4N+	38 (59.4 %)	87 (26.2 %)	0.223	0.090-0.501	<0.001
Hormonal Receptors (HR)			1 (ref)	-	-
Negative	24 (37.5 %)	75 (22.5 %)			
Positive	40 (62.5 %)	258 (77.5 %)	2.171	1.118-4.159	0.020
HER2 status			1 (ref)	-	-
Negative	41 (64.1 %)	238 (71.6 %)			
Positive	23 (35.9 %)	95 (28.5 %)	1.086	0.535-2.152	0.816
Hormone Therapy (HT)			1 (ref)	-	-
Yes	33 (51.6 %)	267 (80.2 %)	2.655	1.388-5.011	0.003
No	31 (48.4 %)	66 (19.8 %)			

Multivariate analysis (see Table 3) evaluated the independent impact of each factor on the risk of recurrence. The results confirmed that negative HR status (OR=2.525; p=0.011) and the absence of

lymphovascular invasion (LVI) (OR=0.451; p=0.031) are significant predictors of recurrence. Multivariate analysis also showed that nodal involvement was not an independent risk factor.

Table 3: Multivariate analysis of recurrence risk factors

Factor	Odds Ratio (OR)	95% CI	p-value
Lymphovascular invasion (LVI)	0.451	0.211-0.919	0.031
Nodal Ratio (LNR)			
<4N+	0.604	0.175-1.988	0.409
≥4N+	0.609	0.260-1.374	0.238
Hormonal Receptors (HR)	2.525	1.211-5.248	0.011

4. DISCUSSION

Our study's results confirm the importance of several well-established risk factors in the international literature, such as nodal involvement and lymphovascular invasion. Furthermore, our analysis highlights the relevance of hormonal receptor status as a significant and independent risk factor for recurrence. The Odds Ratio of 2.525 for negative HR status in multivariate analysis supports the idea that hormonal status is not only a marker of response to hormone therapy but also of the tumor's intrinsic aggressiveness.

Compared to large international cohorts, our study reflects certain trends while also highlighting specific features.

Comparative tables of epidemiological and prognostic data

To better illustrate the specific characteristics of each population, the following tables summarize the epidemiological data and recurrence risk factors observed in different studies worldwide.

Table 4: Comparative epidemiological and biological characteristics of breast cancer

Characteristic	Moroccan Cohort (Our study)	African-American Cohorts (USA)	Asian Cohorts	European Cohorts
Age at diagnosis	Younger (mean age of 49.15 years), comparable to Asian series.	Younger than non-Hispanic white women [11].	Generally younger than Western women [7].	Typically older, median age around 60 years.
Tumor subtypes	Significant proportion of HR-negative and triple-negative breast cancer (TNBC) tumors [10].	Significantly higher prevalence of TNBC, which is more aggressive [5] [11].	High proportion of luminal subtype tumors, especially in young patients [7].	Dominance of luminal cancers (HR+/HER2-), which generally have a more favorable prognosis [12].
Socioeconomic factors	Not evaluated, but potentially relevant.	Non-biological factors (access to care, obesity, social stress) play a	Increasing influence of adopting a	The impact of lifestyle (diet, physical activity) is a major area of research [9].

		major role in disparities [5] [13].	"Western" lifestyle (obesity, etc.) [8].	
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Table 5: Recurrence Risk Factors by Region

Risk Factor	African-American Cohorts	Asian Cohorts	European Cohorts
Nodal involvement	A key prognostic factor, associated with a more advanced stage at diagnosis [13].	A major risk factor, particularly for locoregional recurrence [7].	A standard prognostic factor, used in clinical scores [12].
HR status	Negative HR is strongly associated with shorter survival and early recurrence [5] [14].	Negative HR in young patients is associated with a higher risk of recurrence [7].	The presence of positive HR is often associated with late recurrences (>5 years) [2].
Age at diagnosis	Younger at diagnosis, with an association with a more unfavorable prognosis [11].	Age is an independent prognostic factor; the younger the age, the higher the risk of recurrence, with no apparent threshold [7].	Younger age is associated with an unfavorable prognosis, often due to high-grade cancers and more frequent vascular invasion [15].
Other factors	Obesity, diabetes, lack of access to care, and social stress contribute to survival disparities [13].	Comorbidities, social support, and quality of life are key factors. Genetic differences influence treatment response [16].	Lifestyle (diet, exercise), comorbidities (metabolic syndrome), and genomic tests for risk stratification [9] [12].

In summary, while our study confirms the prognostic role of classic clinicopathological factors such as nodal involvement and lymphovascular invasion, it also aligns with observations from international series regarding the importance of biological characteristics, particularly HR status. The specific features of different populations (young age in African and Asian cohorts, high prevalence of TNBC in African-Americans) underscore the need for local research to adapt management strategies.

The limitations of this study include its retrospective nature and the lack of more detailed data, such as molecular subtypes (e.g., Luminal A, Luminal B, HER2-enriched, Triple Negative). The absence of age as an independent risk factor in our analysis does not contradict its role but may be related to an insufficient sample size to detect its effect or a strong correlation with other more powerful factors.

5. CONCLUSION

The results of our study clearly and significantly confirm that negative hormonal receptor status, lymphovascular invasion, and nodal involvement are crucial and independent prognostic factors for breast cancer recurrence in our Moroccan cohort. These data reinforce the importance of histopathology not only for diagnosis but also for risk stratification.

These findings have direct clinical implications. Systematically considering negative hormonal receptor status at diagnosis should guide towards more intensive management and close follow-up for high-risk patients. Our study also confirms that classic clinical and pathological classification, including the evaluation of

nodes and the existence of lymphovascular invasion, remains an essential pillar for predicting disease progression.

However, the limitations of our retrospective study and the lack of data on precise molecular subtypes (like Luminal A vs. B or specific genetic mutations) call for future research. It is imperative to undertake prospective and multicenter studies with larger samples to validate these results in the national context and to explore the influence of factors not yet documented. The integration of molecular biology into routine clinical practice could also allow for further refinement of treatment personalization for each patient.

In short, this study makes a significant contribution to understanding the risk factors for recurrence in our population. It highlights the need for an individualized approach to care, combining well-established clinical and biological markers with the promise of future molecular tests to optimize patients' chances of survival.

Ethics Approval and Consent to Participate

The study protocol was reviewed and approved by the Research and Ethics Committee of National Institute of Oncology. Given the retrospective nature of the study, and that patient records were anonymized and de-identified prior to analysis, the requirement for written informed consent was waived by the ethics committee.

Competing Interests

The authors declare that they have no competing interests.

Acknowledgement

The authors express their gratitude to the staff of the Radiotherapy Department at the National Institute of Oncology for their assistance with data collection.

List of Abbreviations

- **LVI:** Lymphovascular Invasion
- **OR:** Odds Ratio
- **CI:** Confidence Interval
- **N+:** Positive Node(s)
- **HR:** Hormonal Receptors (ER and PR)
- **TNM:** Tumor, Node, Metastasis
- **SBR:** Scarff-Bloom-Richardson
- **HT:** Hormone Therapy
- **TNBC:** Triple-Negative Breast Cancer
- **ER:** Estrogen Receptor
- **PR:** Progesterone Receptor
- **HER2:** Human Epidermal growth factor Receptor 2
- **Ki-67:** Ki-67 (cellular proliferation marker)

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