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PREDICTORS OF PATHOLOGICAL COMPLETE RESPONSE FOLLOWING NEOADJUVANT CHEMOTHERAPY IN BREAST CANCER: A SINGLE-CENTER STUDY FROM THE ROYAL MEDICAL SERVICES, JORDAN

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ABSTRACT

Background: Achieving pathological complete response (pCR) after neoadjuvant chemotherapy (NAC) is one of the most well-established surrogate markers for improved prognosis in breast cancer. Predictive factor identification for pCR is important especially in optimizing treatment approaches in adjuvant settings. **Objectives:** To identify clinicopathological factors with pCR among breast cancer patients treated with NAC at the Royal Medical Services in Jordan. **Methods:** This retrospective study was comprised of 262 patients with invasive breast cancer who underwent NAC from (January 2022) to (December 2023) followed by surgical intervention. HR (hormone receptor) status, HER-2 expression, lymph node involvement, tumor grade, and age were assessed. Predictors of pCR were determined using logistic regression analysis. **Results:** Among them, twenty-one percent of patients achieved pCR. On a multivariate analysis, the presence of HR (hormone receptor) negative tumors (OR=2.708, p=0.005), positive HER-2 tumors (OR=2.271, p=0.012), and no lymph node metastasis (OR=2.607, p=0.015) greatly increased the chances of pCR. The predictors remained non-significant for pCR. **Conclusion:** Negative HR, positive HER-2, and no nodal involvement were independent predictors of pCR in this cohort of Jordanians. Those results warrant changes to clinical practice for molecular subtype evaluation prior to NAC.

KEYWORDS: Cancer of the breast, pathological complete response, chemotherapy, neoadjuvant therapy, predictors, hormonal receptors, HER2, Hashemite kingdom of Jordan.

INTRODUCTION

Chemotherapy is an integral aspect of care for patients with locally advanced and/or high-risk breast cancer, mostly in the neoadjuvant setting. It serves to downsize the tumor, allow for breast-conserving surgery, and evaluate the in vivo systemic therapy efficacy along with effect on adjuvant treatment. Achieving a pathological complete response (pCR) or absence of invasive cancer in the breast and axillary lymph nodes is associated with better recurrence-free and overall survival, especially amongst aggressive subtypes.

Despite the importance of pCR, not all patients universally reach this treatment milestone. A range of predictive factors has been studied extensively in patients in Western countries, including hormone receptor (HR) status, HER-2 overexpression, nodal involvement, and tumor grade. Data from the Middle East, and particularly Jordan, remain limited.

Defining the clinical and pathological predictors of pCR in breast cancer patients treated with NAC at the Royal Medical Services, a primary referral hospital in Jordan, is the objective of this research. Comprehending these factors from our population may help in tailoring treatment approaches to improve oncological results.

Methods

Study Design and Setting

This study was conducted at the Royal Medical Services (RMS), a tertiary healthcare institution in Jordan. It was a retrospective cohort study which included patients treated in [insert years, e.g., 2022–2023] with histologically confirmed breast cancer who received neoadjuvant chemotherapy followed by surgery.

Inclusion criteria

Female patientzs with invasive breast carcinoma.
Received a complete course of NAC.
Underwent definitive surgical procedure accompanied by a final histopathological examination.

Available comprehensive clinical and pathological data.

Exclusion criteria
Metastatic disease at diagnosis.
Did not complete the prescribed chemotherapy.
Missing or incomplete records.
Data Collection

Patient records were screened to extract relevant Demographic and Clinical information such as
Age at diagnosis. Hormone receptor status (ER/PR). HER-2 receptor status. Tumor's histologic grade. Status of the axillary lymph nodes. Presence of lymphovascular invasion (LVI). Toward the end of the study period, the participants will have undergone the study evaluations.
A pCR was defined as no evidence of invasive cancer in the breast and axillary lymph nodes (ypT0/is ypN0) after the final histopathological examination.

Statistical analysis
The data summary was done with descriptive statistics. Bivariate analyses were conducted using chi-square tests and independent t-tests. The independent predictors of pCR were determined using multivariate binary logistic regression analysis, and results were presented as odds ratios (OR) with 95% confidence intervals (CI). All variables with p-value less than 0.05 in univariate analysis were included in the regression model. LVI was removed from the model because of quasi-complete separation. Statistical significance was considered to be p-value less than 0.05.

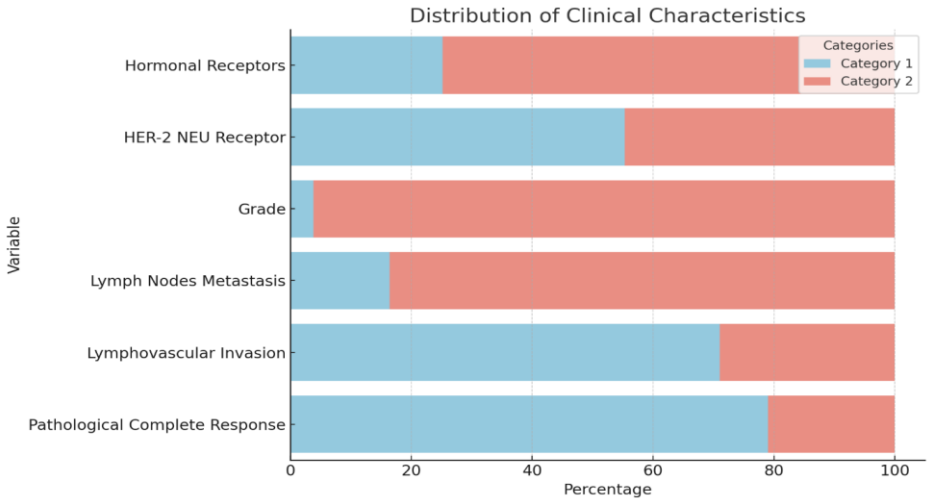
Ethical approval
The Jordanian Royal Medical Services' Institutional Review Board (IRB) in Amman, Jordan approved this study.

RESULTS

Patient characteristics
A total of 262 patients with invasive breast cancer who received neoadjuvant chemotherapy were included. The mean age was 50.6 years (SD = 10.9), with a range of 25 to 78 years.

The majority of patients were hormone receptor (HR) positive (74.8%), and 44.7% were HER-2 NEU positive. Lymph node metastasis was found in 83.6%, and lymphovascular invasion (LVI) was present in 29%. Overall, pathological complete response (pCR) was achieved in 55 patients (21%).

Table 1: Summary of clinical characteristics.



Bivariate analysis
Several clinicopathological variables were significantly associated with pCR on univariate analysis:
Table 2: Bivariate Analysis of pCR Predictors.

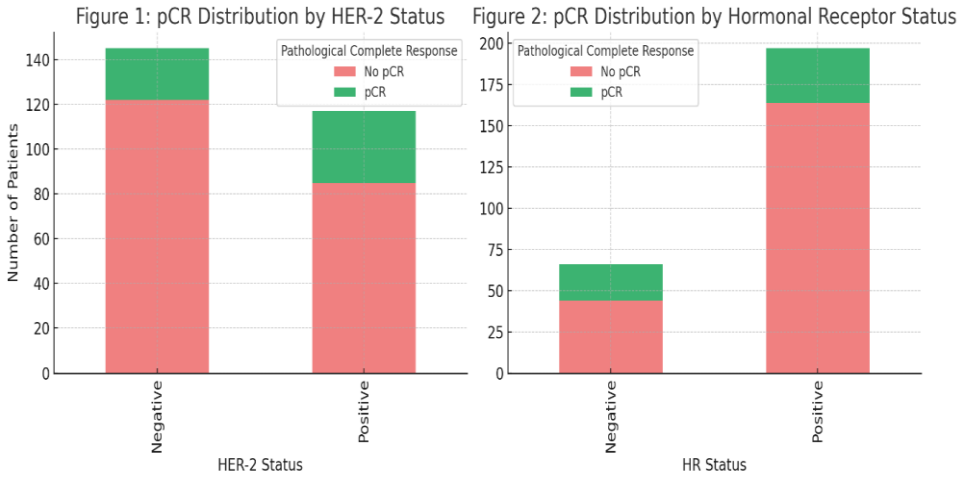
- HR-negative status was associated with a higher rate of pCR (33.3% vs. 16.8%, p = 0.004).
- HER-2 positivity was significantly associated with pCR (27.4% vs. 15.9%, p = 0.023).
- Lymphovascular invasion was absent in all patients who achieved pCR (100% of LVI-positive patients had no pCR, p < 0.001).
- Neither tumor grade nor age was significantly associated with pCR.

Figure 1: pCR Distribution by HER-2 Status
Figure 2: pCR Distribution by Hormonal Receptor Status
These figures illustrate the higher likelihood of achieving pCR among HER-2 positive and HR-negative subgroups.

Table 2: Bivariate Analysis of pCR Predictors.

Variable	pCR - No (n, %)	pCR - Yes (n, %)	p-value
Hormonal Receptors	44 (66.7%)	22 (33.3%)	0.004
HER-2 NEU Receptor	122 (84.1%)	23 (15.9%)	0.023
Tumor Grade	98 (77.2%)	29 (22.8%)	0.588

Lymphovascular Invasion	76 (100%)	0 (0%)	<0.001
Age (Mean ± SD)	51.05 ± 11.23	49.02 ± 9.81	0.223



Multivariate logistic regression analysis

A binary logistic regression model was used to assess independent predictors of pCR, excluding LVI due to quasi-complete separation.

Table 3: Multivariate logistic regression results.

- HR-negative status: OR = 2.708, 95% CI = 1.360–5.392, p = 0.005
- HER-2 positive status: OR = 2.271, 95% CI = 1.196–4.313, p = 0.012
- Absence of lymph node metastasis: OR = 2.607, 95% CI = 1.207–5.629, p = 0.015
- Age and tumor grade were not statistically significant in the multivariate model.

The model had good calibration (Hosmer-Lemeshow p = 0.964) and an overall accuracy of 79.9%. The Nagelkerke R^2 was 11.8%, indicating a modest but meaningful predictive value.

Table 3: Multivariate logistic regression results.

Predictor	Odds Ratio (OR)	95% CI	p-value
Hormonal Receptor Negative	2.708	1.360–5.392	0.005
HER-2 NEU Positive	2.271	1.196–4.313	0.012
Lymph Node Negative	2.607	1.207–5.629	0.015
Age (continuous)	0.98	0.953–1.009	0.178
Grade (ref: G3)	NS	-	>0.05

DISCUSSION

Key clinicopathological factors linked to achieving pathological complete response (pCR) after neoadjuvant chemotherapy (NAC) in patients with breast cancer were identified in this single-center study carried out at the Royal Medical Services in Jordan. Our results show that the absence of lymph node involvement, HER-2 positivity, and hormone receptor (HR) negativity are all important independent predictors of pCR. These findings are in line with international research and provide insightful information for modifying treatment plans in comparable medical environments.

Status of Hormone Receptors and pCR

Compared to HR-positive tumors, our analysis showed that HR-negative tumors have a significantly higher chance of achieving pCR. This finding is in line with previous research showing that HR-negative breast cancers, especially triple-negative breast cancer (TNBC), have higher chemosensitivity and, as a result, higher pCR rates. For example, according to a study by Spring et al., the pCR rate for TNBC patients was roughly 34%, while that of HR-positive/HER2-negative patients were only 16%. Because HR-negative tumors don't rely on hormonal growth signals and have a higher proliferative index, they may be more sensitive to chemotherapy.

HER-2 Positivity and Treatment Response

Another important predictor of pCR in our cohort was HER-2 positive status. This result is consistent with research showing that increased response to NAC is linked to HER-2 overexpression, particularly when paired with HER-2 targeted treatments like pertuzumab and trastuzumab. HER-2 positivity was found to be significantly associated with higher pCR rates in a thorough meta-analysis that included 5,768 patients with HER-2 overexpressing breast cancer in the neoadjuvant setting. The effectiveness of HER-2 targeted treatments emphasizes how crucial a precise HER-2 assessment is in directing therapeutic choices.

Lymph Node Status and pCR

In our study, higher pCR rates were independently linked to the lack of lymph node metastases. This is consistent with other studies' findings that patients with node-negative disease have a higher chance of achieving pCR after NAC. For instance, stage, HER2 status, and lack of vascular invasion are linked to higher pCR in cases of locally advanced breast cancer undergoing neoadjuvant therapy, according to a study examining the factors influencing pCR. A more advanced stage of the disease and possible chemotherapy resistance may be indicated by the presence of lymph node metastases.

Tumor Grade and Age

Our analysis revealed no significant correlation between pCR and tumor grade or patient age, which is in contrast to some other studies. In some situations, higher tumor grade has been associated with higher pCR rates; however, not all studies have found this correlation. Similarly, age has not been a good indicator of pCR; some studies find no significant association between age and pCR, while others suggest that younger patients may have higher pCR rates. These differences show that more research is necessary to determine how these factors affect treatment response prediction.

Lymphovascular Invasion (LVI)

Since none of the patients with lymphovascular invasion (LVI) achieved pCR, LVI was not included in our multivariate analysis because of quasi-complete separation. This result implies that LVI may be linked to a decreased chance of obtaining pCR, possibly as a result of its function in promoting tumor growth and chemotherapy resistance. Our capacity to reach firm conclusions is, however, limited by the exclusion of LVI from the analysis, and more investigation is necessary to fully examine this relationship.

Clinical consequences

There are important clinical ramifications when HR negativity, HER-2 positivity, and lack of lymph node involvement are found to be predictors of pCR. By helping to stratify patients according to their chances of reaching pCR, these variables can help guide treatment planning and decision-making. In order to achieve pCR, which is linked to better long-term results, patients with HR-negative, HER-2 positive, and node-negative tumors, for example, may be evaluated for more aggressive NAC regimens.

Limitations

There are various restrictions on this study. Its single-center setting and retrospective design might restrict how broadly the results can be applied. Furthermore, our comprehension of LVI's influence on pCR is limited by its exclusion from the multivariate analysis because of data limitations. To confirm and build on these findings, prospective, multicenter studies with bigger sample sizes and thorough data collection are required in the future.

CONCLUSION

The absence of lymph node metastases, hormone receptor negativity, and HER-2 positivity were shown to be significant independent predictors of pathological complete response (pCR) after neoadjuvant chemotherapy in patients with breast cancer in this single-center retrospective study from the Royal Medical Services in Jordan. These results support the crucial role that molecular subtyping plays in forecasting treatment response and are in line with international literature.

Finding patients who are more likely to experience pCR can help with resource allocation, outcome optimization, and treatment strategy personalization—especially in healthcare systems with limited resources. To confirm these predictors and deepen our understanding of tumor biology in the Jordanian population, more prospective, multicenter studies in the area are necessary.

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