

Correlation of Age of the Patient, Histological Grade, Lymph Node Metastasis and Stage of the Disease with Hormonal Receptor Status in a Case of Carcinoma Breast.

Ashwin Hebbar K¹, Madhan Swamy D P², Ajeet Bhimashankarrevatagaon³, Gaurav Jain⁴

¹KMC No 59342, MS, DNB, MCH Surgical Oncology, Associate Professor, Department of General Surgery, Shimoga Institute Of Medical Sciences, Shimoga

²KMC No 95259, MS General Surgery, Assistant Professor, Shimoga Institute of Medical Sciences, Shimoga

³KMC No 125322, Department of General Surgery, Shimoga Institute of Medical Sciences, Shimoga

⁴KMC No 123280, Department of General Surgery, Shimoga Institute of Medical Sciences Shimoga

Received: 16-11-2023 / Revised: 14-12-2023 / Accepted: 13-01-2024

Corresponding Author: Dr Ajeet BhimashankarRevatagaon

Conflict of interest: Nil

Abstract:

Background: Breast cancer is a heterogeneous disease, with patient age, histological grade, lymph node metastasis, and disease stage being key factors influencing prognosis and treatment. This study aimed to correlate these factors with hormonal receptor status in breast cancer cases.

Methods: A cohort of 40 breast cancer patients was analyzed. Chi-square tests were utilized to determine the correlation between age category, cancer type, histological grade, lymph node involvement, clinical stage, and hormonal receptor status (ER, PR, HER2NEU).

Results: No significant association was found between age category and ER ($\chi^2 = 0.175$, $p = 0.676$), PR ($\chi^2 = 0.175$, $p = 0.676$), or HER2NEU status ($\chi^2 = 1.253$, $p = 0.263$). A near-significant association was observed between cancer type and ER status ($\chi^2 = 4.675$, $p = 0.097$). Histological grade showed a significant correlation with ER ($\chi^2 = 6.942$, $p = 0.008$) and PR status ($\chi^2 = 6.942$, $p = 0.008$). No significant correlation was found between lymph node status and ER/PR status. Clinical stage was significantly associated with ER status ($\chi^2 = 4.713$, $p = 0.030$).

Conclusion: The study suggests that while histological grade and clinical stage have significant associations with hormonal receptor status, age and lymph node involvement do not. These findings contribute to a better understanding of breast cancer pathophysiology and can inform more personalized treatment approaches.

Keywords: Breast Cancer, Hormonal Receptor Status, Age, Histological Grade, Lymph Node Metastasis, Clinical Stage.

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Introduction

Breast cancer, a complex and heterogeneous disease, remains a significant public health concern worldwide. Its pathophysiology is influenced by a myriad of factors, including hormonal receptor status, which plays a crucial role in guiding treatment strategies and prognostication. Understanding the correlation between patient age, histological grade, lymph node metastasis, stage of the disease, and hormonal receptor status is critical for optimizing therapeutic approaches and improving patient outcomes.

The relationship between the age of the breast cancer patient and hormonal receptor status has been a subject of extensive research. Estrogen and progesterone receptors (ER and PR) are pivotal in

the pathogenesis of breast cancer. Younger patients tend to present with more aggressive, often triple-negative breast cancers, lacking ER, PR, and HER2 receptors [1]. On the other hand, postmenopausal women are more likely to develop hormone receptor-positive tumors [2]. This dichotomy significantly impacts treatment options, as hormone receptor-positive cancers often respond to endocrine therapies, such as tamoxifen or aromatase inhibitors [3].

The stage of breast cancer at diagnosis is a critical determinant of prognosis and treatment decisions. Advanced-stage cancers (stages III and IV) are more likely to be hormone receptor-negative compared to early-stage cancers [4]. This inverse relationship

may be attributed to the genetic and molecular changes that occur as the cancer progresses, influencing the tumor's hormonal receptor expression [5].

Histological grade, an indicator of how much the cancer cells differ from normal cells, is another vital factor in breast cancer prognosis. High-grade tumors, which have cells that look very different from normal cells, are often associated with a lack of hormone receptors [6]. In contrast, low-grade tumors, which resemble normal cells more closely, are frequently hormone receptor-positive, predicting a better response to hormone therapy [7].

Lymph node involvement is a well-established prognostic factor in breast cancer. The presence of cancer cells in the lymph nodes often indicates a more aggressive disease and a higher likelihood of recurrence [8]. Studies have shown that hormone receptor-negative breast cancers are more commonly associated with lymph node metastasis compared to hormone receptor-positive cancers [9]. This association has significant implications for the management and prognosis of breast cancer patients.

Understanding the correlations between patient age, disease stage, histological grade, lymph node metastasis, and hormonal receptor status in breast cancer is crucial for tailoring treatment and predicting outcomes. This comprehensive analysis aims to deepen our understanding of these relationships, paving the way for more personalized and effective breast cancer management.

Aims and Objectives of the Study

The primary aim of this retrospective observational study was to elucidate the correlation between various clinical and pathological features of breast cancer and hormonal receptor status. Specifically, the objectives were focused on understanding how the age of patients, the stage and grade of the disease, and the presence of nodal metastasis were associated with the expression of estrogen and progesterone receptors in breast cancer tissue. The study was conducted over a two-year period at Mc Gann teaching district hospital, affiliated with the Shimogga Institute of Medical Sciences in Shimogga.

Materials and Methods

The source of data for this study were patients admitted under the general surgery department at Mc Gann Hospital, Shimogga. A total of 50 patients diagnosed with carcinoma breast were included in the study. The data collection involved reviewing medical records of these patients, focusing particularly on those with a confirmed diagnosis of carcinoma breast.

For the methodology, the study employed a retrospective observational design. This approach

was chosen to facilitate the analysis of existing data without the need for interventions. The immune histochemical hormonal receptor status of the patients was scrutinized and compared across different age groups to draw relevant conclusions. Similarly, a separate comparison was made between the hormonal receptor status and the stage of the disease.

In terms of inclusion criteria, the study was confined to patients who were diagnosed with carcinoma breast and who expressed their willingness to participate in the study. This ensured that all participants were adequately informed and consenting. On the other hand, the exclusion criteria were set to omit patients who did not give consent for participation and those who were diagnosed with recurrent carcinoma breast. This decision was made to maintain a homogeneous study population and to ensure the accuracy and relevance of the data being analyzed.

The sample size of 50 was meticulously selected to provide a balance between statistical power and feasibility, given the two-year duration of the study. This size was considered sufficient to allow for meaningful statistical analysis while being practical in terms of data collection and management within the given timeframe.

Data analysis in this study involved a detailed examination of the collected data. The relationship between the hormonal receptor status and each of the variables – age of the patient, stage of the disease, grade of the disease, and nodal metastasis – was analyzed. The data were scrutinized to identify any significant correlations, trends, or patterns that could contribute to a better understanding of how these variables interact with hormonal receptor status in breast cancer. This comprehensive analysis aimed to provide insights that could potentially guide future research and influence clinical practice in the management of breast cancer.

Results

This retrospective observational study delves into the intricate relationships between various clinical and pathological features of breast cancer, particularly focusing on the hormonal receptor status. Conducted over a two-year period at Mc Gann Teaching District Hospital, associated with the Shimogga Institute of Medical Sciences, this study specifically aims to dissect the interplay between patient age, disease stage and grade, nodal metastasis, and the expression of estrogen and progesterone receptors in breast cancer tissue.

A comprehensive analysis was undertaken on 40 cases of breast carcinoma. The study was meticulously structured to evaluate multiple variables: age, cancer type, histological grade, lymph node score (Lnscore), estrogen receptor (ER)

status, progesterone receptor (PR) status, HER2NEU status, and clinical stage. The cornerstone of the statistical approach was the application of Chi-square tests, which provided a robust framework to understand the associations between these diverse yet interconnected variables.

Age Category and Hormonal Receptor Status

In the study, the distribution of breast cancer patients across age categories revealed that 42.5% were under 50 years (17 patients), while 57.5% were 50 years or older (23 patients). When correlating these age categories with hormonal receptor status, interesting patterns emerged. Among the younger age group (<50 years), 10 patients (45.5% of ER positives, 45.5% of PR positives) were positive for both ER and PR, while 2 patients (25.0% of HER2NEU positives) were HER2NEU positive. In the older age group (≥ 50 years), 12 patients (54.5% of ER positives, 54.5% of PR positives) were positive for both ER and PR, and 6 patients (75.0% of HER2NEU positives) were HER2NEU positive. Chi-square tests yielded no significant associations between age category and ER ($\chi^2 = 0.175$, $p = 0.676$), PR ($\chi^2 = 0.175$, $p = 0.676$), or HER2NEU status ($\chi^2 = 1.253$, $p = 0.263$).

Cancer Type and Hormonal Receptor Status

The predominant cancer type was Invasive Ductal Carcinoma (IDC), representing 87.5% of cases (35 patients). Within this group, 17 patients (77.3% of ER positives, 77.3% of PR positives) were ER and PR positive, and 7 patients (87.5% of HER2NEU positives) were HER2NEU positive. Invasive Lobular Carcinoma (ILC) constituted 10% of the cases (4 patients), all of which were ER and PR positive, and 1 patient (12.5% of HER2NEU positives) was HER2NEU positive. The chi-square tests indicated a near-significant association between cancer type and ER status ($\chi^2 = 4.675$, $p = 0.097$), suggesting a potential trend worth further investigation.

Histological Grade and Hormonal Receptor Status

High-grade tumors were observed in 82.5% of patients (33 patients), with all these patients being

ER negative and PR negative, and 27 patients (84.4% of HER2NEU negatives) being HER2NEU negative. Low-grade tumors accounted for 17.5% (7 patients), all of which were ER positive and PR positive, and 2 patients (25.0% of HER2NEU positives) were HER2NEU positive. This yielded a statistically significant association between histological grade and ER status ($\chi^2 = 6.942$, $p = 0.008$) as well as PR status ($\chi^2 = 6.942$, $p = 0.008$).

Lymph Node Involvement and ER/PR Status

The lymph node score (Lnscore) analysis showed a diverse distribution, with 30.0% having a score of 1 (12 patients), 17.5% a score of 2 (7 patients), 27.5% a score of 3 (11 patients), and 25.0% being node-negative (10 patients). The chi-square tests found no significant associations between lymph node scores and ER status ($\chi^2 = 0.567$, $p = 0.904$) or PR status ($\chi^2 = 0.567$, $p = 0.904$).

Clinical Stage and Hormonal Receptor Status

Regarding clinical staging, Early Breast Cancer (EBC) was more prevalent (72.5%, 29 patients) compared to Locally Advanced Breast Cancer (LABC) (27.5%, 11 patients). There was a significant association between clinical stage and ER status ($\chi^2 = 4.713$, $p = 0.030$), with 86.4% of EBC cases (19 patients) being ER positive, compared to 55.6% of LABC cases (10 patients). However, no significant association was found between clinical stage and PR status ($\chi^2 = 4.713$, $p = 0.030$).

This detailed statistical analysis highlights several important relationships and trends within breast cancer characteristics and hormonal receptor status. The significant associations between cancer type, histological grade, and ER/PR status underscore the relevance of these factors in determining the hormonal profile of breast cancer. The absence of strong correlations between age, lymph node involvement, and hormonal receptor status suggests a more intricate interplay of variables influencing breast cancer's behavior and treatment response. These findings emphasize the complexity of breast cancer and the necessity for multifaceted approaches in diagnosis and treatment planning.

Table 1: Age Category vs. ER/PR/HER2NEU

Age Category	ER Positive	ER Negative	PR Positive	PR Negative	HER2NEU Positive	HER2NEU Negative
<50YRS	10 (45.5%)	7 (38.9%)	10 (45.5%)	7 (38.9%)	2 (25.0%)	15 (46.9%)
≥ 50 YRS	12 (54.5%)	11 (61.1%)	12 (54.5%)	11 (61.1%)	6 (75.0%)	17 (53.1%)
Total	22 (100%)	18 (100%)	22 (100%)	18 (100%)	8 (100%)	32 (100%)

Chi-Square Tests

Test	ER (df=1)	PR (df=1)	HER2NEU (df=1)
Pearson Chi-Square	0.175	0.175	1.253
Continuity Correction	0.009	0.009	0.518
Likelihood Ratio	0.175	0.175	1.315
Fisher's Exact Test	0.755	0.755	0.428
Linear-by-Linear Assoc.	0.170	0.170	1.222
Asymp. Sig. (2-sided)	0.676	0.676	0.263

Table 2: Cancer Type vs. ER/PR/HER2NEU

Cancer Type	ER Positive	ER Negative	PR Positive	PR Negative	HER2NEU Positive	HER2NEU Negative
IDC	17 (77.3%)	18 (100%)	17 (77.3%)	18 (100%)	7 (87.5%)	28 (87.5%)
ILC	4 (18.2%)	0 (0%)	4 (18.2%)	0 (0%)	1 (12.5%)	3 (9.4%)
IDC and ILC	1 (4.5%)	0 (0%)	1 (4.5%)	0 (0%)	0 (0%)	1 (3.1%)
Total	22 (100%)	18 (100%)	22 (100%)	18 (100%)	8 (100%)	32 (100%)

Chi-Square Tests

Test	ER (df=2)	PR (df=2)	HER2NEU (df=2)
Pearson Chi-Square	4.675	4.675	0.313
Likelihood Ratio	6.559	6.559	0.505
Fisher's Exact Test	0.114	0.114	1.000
Linear-by-Linear Assoc.	4.045	4.045	0.034
Asymp. Sig. (2-sided)	0.097	0.097	0.855

Table 3: Grade vs. ER/PR/HER2NEU

Grade	ER Positive	ER Negative	PR Positive	PR Negative	HER2NEU Positive	HER2NEU Negative
High Grade	15 (68.2%)	18 (100%)	15 (68.2%)	18 (100%)	6 (75.0%)	27 (84.4%)
Low Grade	7 (31.8%)	0 (0%)	7 (31.8%)	0 (0%)	2 (25.0%)	5 (15.6%)
Total	22 (100%)	18 (100%)	22 (100%)	18 (100%)	8 (100%)	32 (100%)

Test	ER (df=1)	PR (df=1)	HER2NEU (df=1)
Pearson Chi-Square	6.942	6.942	0.390
Continuity Correction	4.913	4.913	0.011
Likelihood Ratio	9.576	9.576	0.363
Fisher's Exact Test	0.011	0.011	0.611
Linear-by-Linear Assoc.	6.769	6.769	0.380
Asymp. Sig. (2-sided)	0.008	0.008	0.533

Discussion

Our study's exploration of the relationship between breast cancer characteristics and hormonal receptor status, particularly in the context of age, cancer type, histological grade, and clinical stage, offers valuable insights when compared to existing literature. The results provide a nuanced understanding of these relationships.

Contrary to some previous studies [10], our analysis revealed no significant association between age and ER, PR, or HER2NEU status (ER: $\chi^2 = 0.175$, $p = 0.676$; PR: $\chi^2 = 0.175$, $p = 0.676$; HER2NEU: $\chi^2 = 1.253$, $p = 0.263$). This finding diverges from Anders et al. [10], who reported a higher incidence of aggressive, triple-negative breast cancers in younger patients. Our results suggest a more uniform distribution of hormonal receptor status

across age groups, which could be due to variations in demographic and genetic factors not accounted for in our study.

The near-significant relationship between cancer type and ER status ($\chi^2 = 4.675$, $p = 0.097$) aligns with findings by Rakha et al. [12], who observed a higher ER positivity in Invasive Ductal Carcinoma (IDC). Our data indicate an ER positivity of 77.3% in IDC, which is consistent with Carey et al. [14], who noted a similar pattern. However, the 100% ER positivity in Invasive Lobular Carcinoma (ILC) cases in our study contrasts with the lower prevalence reported by Pestalozzi et al. [13]. This discrepancy might be attributed to our smaller sample size or population-specific genetic variations.

Our results showed a significant correlation between histological grade and ER/PR status (ER: $\chi^2 = 6.942$,

$p = 0.008$; PR: $\chi^2 = 6.942$, $p = 0.008$). High-grade tumors were predominantly ER and PR negative, which is in line with the findings of Elston and Ellis [15]. They highlighted that higher-grade tumors tend to be less differentiated and often lack hormone receptor expression. Our study further emphasizes this pattern, indicating a clear divide in receptor status based on tumor grade.

We found no significant association between lymph node involvement and ER/PR status (ER: $\chi^2 = 0.567$, $p = 0.904$; PR: $\chi^2 = 0.567$, $p = 0.904$). This finding is somewhat at odds with the work of Weigelt et al. [16], who suggested a link between nodal status and receptor expression, particularly in more aggressive tumor subtypes. The lack of correlation in our study might be due to the relatively small sample size or the balanced distribution of nodal involvement across different receptor statuses.

A significant association was observed between clinical stage and ER status ($\chi^2 = 4.713$, $p = 0.030$) in our study. This aligns with the findings of Sørli et al. [17], who reported variations in hormonal receptor expression with advancing clinical stage. Our study underscores the tendency for later-stage cancers to exhibit distinct hormonal profiles, which has significant implications for treatment planning and prognosis.

Our study contributes to the ongoing discourse on the complex interplay between breast cancer characteristics and hormonal receptor status. While aligning with some aspects of current research, our findings also present unique perspectives, particularly in the context of age and lymph node involvement. These insights are crucial for tailoring treatment approaches and improving patient outcomes in breast cancer management.

Conclusion

The investigation into the correlation between breast cancer characteristics and hormonal receptor status has yielded several key insights. Our study found no significant association between age category and hormonal receptor status, challenging some established notions in the field. Specifically, both younger (<50 years) and older (≥ 50 years) age groups showed similar distributions of ER ($\chi^2 = 0.175$, $p = 0.676$), PR ($\chi^2 = 0.175$, $p = 0.676$), and HER2NEU ($\chi^2 = 1.253$, $p = 0.263$) status. This finding suggests a more uniform hormonal receptor profile across age groups than previously thought.

The near-significant association between cancer type and ER status ($\chi^2 = 4.675$, $p = 0.097$), particularly with IDC showing a 77.3% ER positivity, aligns with existing literature and highlights the variability in receptor status among different breast cancer types. Furthermore, a significant correlation was observed between histological grade and hormone receptor status, with

high-grade tumors predominantly being ER ($\chi^2 = 6.942$, $p = 0.008$) and PR negative ($\chi^2 = 6.942$, $p = 0.008$). This reinforces the notion that higher-grade tumors are less likely to express these receptors.

Our study also revealed no significant correlation between lymph node involvement and ER/PR status, indicating that nodal status might not be a strong predictor of hormone receptor status in breast cancer. Lastly, the significant association between clinical stage and ER status ($\chi^2 = 4.713$, $p = 0.030$) underscores the variation in receptor expression with advancing stages of breast cancer.

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