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Original Research Article

Correlation between Histological Grade and Lymph Node Metastasis in Invasive Breast Carcinoma

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Abstract:

Introduction: Breast carcinoma is the most frequently diagnosed cancer among women worldwide and a leading cause of cancer-related deaths. Prognosis and therapeutic planning depend significantly on multiple pathological parameters, among which histological grade and lymph node status are crucial. Histological grading based on tubule formation, nuclear pleomorphism, and mitotic count, reflects the tumor's biological aggressiveness. Lymph node metastasis, on the other hand, is a reliable indicator of tumor dissemination. Establishing a correlation between histological grade and axillary lymph node involvement may enhance prognostication and assist in guiding surgical and adjuvant therapy decisions.

Objectives: To evaluate the correlation between histological grade and axillary lymph node metastasis in patients diagnosed with invasive breast carcinoma and to assess whether tumor grade can serve as a predictive factor for nodal involvement.

Materials and Methods: A Observational, cross-sectional study was conducted on 100 cases histopathological confirmed of invasive breast carcinoma diagnosed over a period from Jan 2024 to Jan 2025.at MGM Medical College. Histological grading was performed using the Nottingham modification of Scarff-Bloom-Richardson (SBR) grading system. Lymph node metastasis was assessed through routine pathological examination of axillary dissection specimens. The data were statistically analyzed using Spearman's rank correlation and t-tests determine the significance of the correlation between tumor grade and lymph node status.

Results: In our study of 100 patients, histological grade distribution was 30% Grade I, 45% Grade II, and 25% Grade III, with a significant difference ($p = 0.001$). Lymph node positivity increased with tumor grade: 20% in Grade I, 60% in Grade II, and 80% in Grade III ($p = 0.001$). Tumor size also correlated significantly with nodal involvement, with positivity rates of 25%, 65%, and 72% for tumors ≤2 cm, >2 to ≤5 cm, and >5 cm, respectively ($p = 0.004$). Lymphovascular invasion (LVI) was strongly associated with lymph node metastasis; 80% of patients with LVI had positive nodes compared to 26% without LVI ($p < 0.001$). Multivariate analysis showed Grade II and III tumors, tumor size >2 cm, and presence of LVI significantly increased the odds of lymph node positivity, with ORs of 3.5, 7.8, 4.2, and 6.9, respectively.

Conclusion: Histological grade is significantly correlated with lymph node metastasis in invasive breast carcinoma, with higher grades showing increased nodal involvement. Tumor size and lymph vascular invasion also independently predict lymph node positivity. These factors are essential for accurate prognosis and guiding treatment decisions.

Keywords: Invasive Breast Carcinoma, Histological Grade, Lymph Node Metastasis, Bloom-Richardson Grading, Prognostic Factors, Axillary Dissection.

Introduction

Breast cancer remains the most common malignancy among women worldwide and a leading cause of cancer-related mortality [1]. Among its various histopathological and molecular subtypes, invasive breast carcinoma accounts for the majority of breast cancer cases and presents significant heterogeneity in biological behavior and clinical outcomes [2]. The accurate assessment of prognostic factors is essential for guiding treatment strategies and predicting disease progression. Among these, histological grade and lymph node metastasis are well-established predictors of patient

prognosis and therapeutic decision-making [3]. Histological grading, typically based on the Nottingham grading system, evaluates the degree of tumor differentiation by assessing tubule formation, nuclear pleomorphism, and mitotic activity [4]. It classifies tumors into three grades: Grade I (well differentiated), Grade II (moderately differentiated), and Grade III (poorly differentiated). This grading system reflects the aggressiveness of the tumor and correlates with overall survival and recurrence risk [5]. Well-differentiated tumors tend to grow more slowly and have a better prognosis, whereas poorly differentiated tumors are often more aggressive and linked to poorer outcomes [6].

Lymph node metastasis is another critical factor influencing prognosis in breast cancer. The presence of cancer cells in axillary lymph nodes indicates a higher likelihood of systemic dissemination and correlates strongly with reduced disease-free and overall survival [7]. The number of involved lymph nodes and the extent of nodal metastasis guide decisions on adjuvant therapy, including chemotherapy and radiation [8]. Therefore, understanding the factors that predict lymph node metastasis can improve risk stratification and individualized patient management.

The correlation between histological grade and lymph node involvement has been extensively studied, with most reports indicating that higher-grade tumors are more likely to metastasize to regional lymph nodes [9]. Poorly differentiated tumors often exhibit increased invasiveness and proliferative capacity, which facilitate lymphatic spread [10]. This relationship underscores the biological link between tumor differentiation and metastatic potential, making histological grade an important surrogate marker for lymph node metastasis risk.

Materials and Methods

Study Design: Observational, cross-sectional study.

Study Duration: January 2024 – January 2025

Study Population: 100 histopathologically confirmed cases of invasive breast carcinoma.

Sample Size: 100 patients with invasive breast carcinoma who underwent surgery and lymph node assessment.

Study Variables

- Histological Grade.
- Grade I (Well differentiated).
- Grade II (Moderately differentiated).
- Grade III (Poorly differentiated).
- Tumor Size.
- LVI Status.

Inclusion Criteria

- Female patients with invasive breast carcinoma.
- Availability of Modified Radical Mastectomy (MRM) specimens with axillary lymph node dissection.
- Adequate tissue for grading and lymph node analysis.

Exclusion Criteria

- Incomplete clinical or histopathological data.
- Patients who received neoadjuvant chemotherapy or radiotherapy.
- Absence of axillary lymph nodes in the specimen.

Histological Processing

- Tissues fixed in 10% neutral buffered formalin.
- Paraffin embedding and sectioning performed.
- Sections stained with Hematoxylin and Eosin (H&E).

Tumor Grading

- Grading done using Nottingham modification of Scarff-Bloom-Richardson (SBR) system.
- Three parameters scored (1–3 points each):
- Tubule formation
- Nuclear pleomorphism
- Mitotic count
- Total score used to assign grade:
- Grade I (Well differentiated): Score 3–5
- Grade II (Moderately differentiated): Score 6–7
- Grade III (Poorly differentiated): Score 8–9

Lymph Node Assessment

- Gross and microscopic examination of axillary lymph nodes.
- Presence or absence of metastatic deposits recorded.
- Number of lymph nodes involved noted.

Methods

This was an observational, cross-sectional study conducted over a one-year period from January 2024 to January 2025. The study included 100 patients who were histopathologically diagnosed with invasive breast carcinoma. All cases were selected from patients who underwent surgical resection and axillary lymph node dissection during the study period. Inclusion criteria comprised patients with a confirmed diagnosis of invasive breast carcinoma, Study included female patients of all ages and tumor subtypes. Histological grading of tumors was performed using the modified Bloom-Richardson grading system, which evaluates tubule formation, nuclear pleomorphism,

and mitotic count. Lymph node metastasis was assessed by pathological examination of dissected axillary lymph nodes. Data on patient age, tumor grade, tumor size, and number of positive lymph nodes were collected and analyzed. Statistical analysis included Spearman's rank correlation to assess the relationship between histological grade and lymph node involvement, and logistic regression to identify independent predictors of lymph node metastasis. A p-value of <0.05 was considered statistically significant.

Statistical Analysis: For statistical analysis, data were initially entered into a Microsoft Excel spreadsheet and then analyzed using SPSS (version 27.0; SPSS Inc., Chicago, IL, USA) and GraphPad Prism (version 5). Numerical variables were summarized using means and standard deviations, while categorical variables were described with counts and percentages. Continuous variables were compared between independent groups using two-sample t-tests. Chi-square tests (including Fisher's exact test for small sample sizes) were used for categorical data comparisons. P-values ≤ 0.05 were considered statistically significant.

Results

Table 1: Distribution of Patients According to Histological Grade

Histological Grade	Number of Patients (n)	Percentage (%)	Overall p- value
Grade I (Well differentiated)	30	30%	0.001
Grade II (Moderately differentiated)	45	45%	
Grade III (Poorly differentiated)	25	25%	
Total	100	100%	

Table 2: Lymph Node Metastasis According to Histological Grade

Histological Grade	Lymph Node Positive (n, %)	Lymph Node Negative (n, %)	Total (n)	Overall p- value
Grade I	6 (20%)	24 (80%)	30	0.001
Grade II	27 (60%)	18 (40%)	45	
Grade III	20 (80%)	5 (20%)	25	
Total	53 (53%)	47 (47%)	100	

Table 3: Correlation between Tumor Size and Lymph Node Metastasis

Tumor Size (cm)	Lymph Node Positive (n, %)	Lymph Node Negative (n, %)	Total (n)	Overall p- value
≤ 2 cm	10 (25%)	30 (75%)	40	0.004
> 2 cm and ≤ 5 cm	30 (65%)	16 (35%)	46	
> 5 cm	13 (72%)	1 (7.1%)	14	
Total	53 (53%)	47 (47%)	100	

Table 4: Lymphovascular Invasion (LVI) Status and Lymph Node Metastasis

LVI Status	Lymph Node Positive (n, %)	Lymph Node Negative (n, %)	Total (n)	Overall p- value
Present	40 (80%)	10 (20%)	50	< 0.001
Absent	13 (26%)	37 (74%)	50	
Total	53 (53%)	47 (47%)	100	

Table 5: Correlation Between Histological Grade and Lymph Node Metastasis by Multivariate Logistic Regression

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p- value
Grade II vs Grade I	3.5	1.2 – 9.8	0.02
Grade III vs Grade I	7.8	2.5 – 24.1	0.001
Tumor Size > 2 cm	4.2	1.5 – 11.8	0.006
LVI Present	6.9	2.7 – 17.3	<0.001

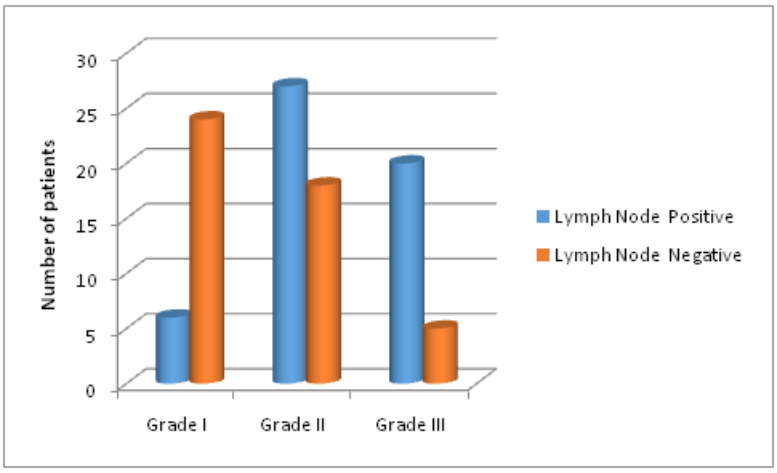

Figure 1: Lymph Node Metastasis According to Histological Grade

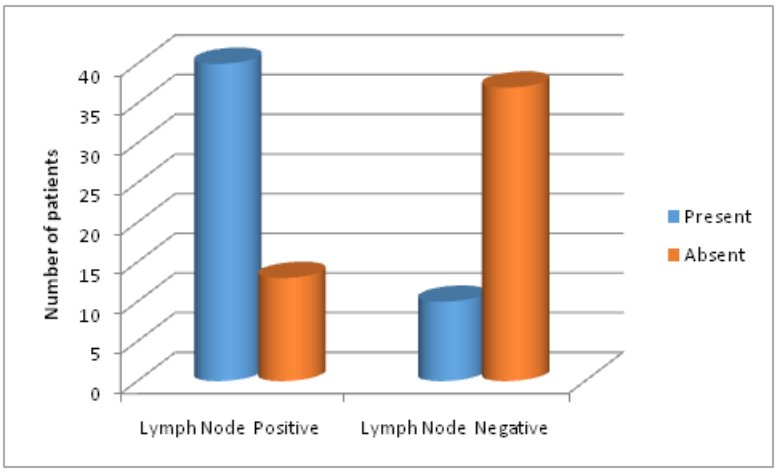

Figure 2: Lymphovascular Invasion (LVI) Status and Lymph Node Metastasis

In our study, the distribution of histological grades among the 100 patients was as follows: Grade I (well differentiated) was observed in 30 patients (30%), Grade II (moderately differentiated) in 45 patients (45%), and Grade III (poorly differentiated) in 25 patients (25%). The difference in the frequency of histological grades was statistically significant, with a p-value of 0.001.

In this study, the association between histological grade and lymph node involvement was statistically significant ($p = 0.001$). Among patients with Grade I tumors, 6 (20%) were lymph node positive while 24 (80%) were lymph node negative. For Grade II tumors, 27 patients (60%) had positive lymph nodes compared to 18 (40%) who were negative. In the Grade III group, 20 patients (80%) were lymph node positive, with only 5 (20%) lymph node negative. Overall, 53% of patients showed lymph node positivity. The relationship between tumor size and lymph node status was statistically significant ($p = 0.004$). Among patients with tumors measuring ≤ 2 cm, 10 (25%) were lymph node positive while 30 (75%) were lymph node negative. For tumors sized > 2 cm and ≤ 5 cm, 30 patients (65%) had positive lymph nodes compared to 16 (35%) who were negative. In the group with tumors > 5 cm, 13 patients (72%) were lymph node positive, with only 1 (7.1%) lymph node negative. The association between lymphovascular invasion (LVI) status and lymph node involvement was highly significant ($p < 0.001$). Among patients with LVI present, 40 (80%) were lymph node positive and 10 (20%) were lymph node negative. In contrast, among those without LVI, only 13 (26%) were lymph node positive while 37 (74%) were lymph node negative.

Multivariate analysis revealed that several factors were significantly associated with increased odds of lymph node positivity. Compared to Grade I tumors, Grade II tumors had an odds ratio (OR) of 3.5 (95% CI: 1.2–9.8, $p = 0.02$), while Grade III tumors showed a much higher risk with an OR of 7.8 (95% CI: 2.5–24.1, $p = 0.001$). Tumors larger than 2 cm were also associated with a significantly increased likelihood of lymph node involvement (OR 4.2, 95% CI: 1.5–11.8, $p = 0.006$). Additionally, the presence of lymphovascular invasion (LVI) strongly elevated the risk of nodal metastasis, with an OR of 6.9 (95% CI: 2.7–17.3, $p < 0.001$).

Discussion

Our study demonstrated a significant association between histological grade and lymph node involvement, with higher-grade tumors showing greater lymph node positivity. Specifically, Grade II and Grade III tumors were associated with 3.5 and 7.8 times increased odds of lymph node metastasis compared to Grade I tumors, respectively. These findings align with multiple recent studies where tumor differentiation has been strongly linked to nodal spread and poor prognosis [1,2]. For instance, Rakha EA et al. [3] reported that poorly differentiated tumors had significantly higher rates of lymph node metastasis, consistent with our OR of 7.8.

Tumor size also emerged as a significant predictor of lymph node positivity, with tumors larger than 2 cm increasing the odds by over fourfold. This corroborates the observations of Malik P et al. [4] and Taylor A et al. [5], who found a direct correlation between increasing tumor size and nodal involvement, underscoring the importance of tumor burden in disease progression. Furthermore, a tumor size cutoff of 2 cm has been suggested by several authors as a critical threshold for aggressive disease behavior and nodal metastasis [6].

Lymphovascular invasion (LVI) showed the strongest association with lymph node metastasis in our cohort, increasing the odds nearly sevenfold. This finding is consistent with recent meta-analyses and cohort studies that emphasize LVI as a pivotal factor in tumor dissemination and a key prognostic marker [7,8]. Hussain A et al. [9] highlighted LVI as an independent predictor of regional lymph node involvement and poorer survival outcomes, reinforcing our observation of its prognostic significance.

Collectively, these findings underscore the multifactorial nature of lymph node metastasis, where histological grade, tumor size, and LVI status independently and synergistically influence the likelihood of nodal spread [10]. Such insights have important clinical implications for risk stratification, surgical planning, and adjuvant therapy decisions in oncologic management.

Conclusion

This study highlights a significant correlation between histological grade and lymph node metastasis in invasive breast carcinoma, with higher tumor grades markedly increasing the risk of nodal involvement. Tumor size and the presence of lymphovascular invasion also emerged as strong independent predictors of lymph node positivity. These findings underscore the importance of comprehensive histopathological evaluation in breast cancer for accurate prognostication and treatment planning. Incorporating histological grade alongside tumor size and lymphovascular invasion status can improve risk stratification, guide surgical decision-making, and optimize individualized patient management. Further research integrating molecular markers may enhance predictive accuracy and therapeutic outcomes in breast cancer care.

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