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Research Article

Patterns of Nodal Metastasis and Their Impact on Survival After Modified Radical Mastectomy: A Prospective Cohort Study

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Abstract

Axillary lymph node involvement remains one of the most important prognostic indicators in breast cancer and plays a critical role in determining disease recurrence, therapeutic planning, and long-term survival. Despite advances in systemic therapy and molecular profiling, the extent and pattern of nodal metastasis continue to influence outcomes following modified radical mastectomy (MRM). This prospective cohort study evaluated patterns of axillary nodal metastasis and their impact on disease-free survival (DFS) and overall survival (OS) in patients undergoing modified radical mastectomy for invasive breast carcinoma.

A total of 220 female patients with histologically confirmed invasive breast cancer who underwent MRM with axillary lymph node dissection were prospectively followed for 5 years. Patients were categorized according to nodal involvement: node-negative (N0), limited nodal metastasis (1–3 positive nodes), intermediate nodal metastasis (4–9 positive nodes), and extensive nodal metastasis (≥10 positive nodes). Primary outcomes included 5-year disease-free survival and overall survival. Secondary outcomes included locoregional recurrence and distant metastasis rates.

The mean age was 52.8 ± 10.6 years. Nodal metastases were identified in 61.4% of patients. Five-year overall survival was 91.2% in N0 patients, 82.5% in patients with 1–3 positive nodes, 68.7% in patients with 4–9 positive nodes, and 49.1% in patients with

≥10 positive nodes ($p < 0.001$). Disease-free survival demonstrated a similar trend (87.6%, 76.2%, 61.3%, and 41.5%, respectively; $p < 0.001$). Extensive nodal involvement was independently associated with poorer survival outcomes and increased recurrence risk.

Patterns of nodal metastasis significantly influence long-term outcomes after modified radical mastectomy. Increasing nodal burden is associated with progressively reduced survival and increased recurrence, emphasizing the continued prognostic importance of axillary nodal status in breast cancer management.

Keywords: Breast cancer, nodal metastasis, modified radical mastectomy, survival, axillary lymph nodes

Introduction

Breast cancer remains the most frequently diagnosed malignancy among women worldwide and continues to represent a major public health challenge despite substantial advances in screening, diagnosis, and treatment. Improvements in multimodal therapy have significantly enhanced survival rates; however, disease stage at diagnosis remains a critical determinant of prognosis. Among various prognostic factors, axillary lymph node involvement has consistently demonstrated one of the strongest associations with recurrence risk and long-term survival outcomes [1–3].

The lymphatic system serves as the primary route for regional dissemination of breast carcinoma. Tumor cells originating from the breast frequently spread first to the axillary lymph nodes before progressing to distant metastatic sites. Consequently, assessment of axillary nodal status has become an integral component of breast cancer staging systems and therapeutic decision-making processes [2–4].

Modified radical mastectomy (MRM) remains an important surgical treatment option for locally advanced breast cancer, multicentric disease, recurrent tumors, and patients unsuitable for breast-conserving surgery. The procedure combines complete breast removal with axillary lymph node dissection, allowing accurate pathological evaluation of nodal burden while providing local disease control [3–5].

The prognostic significance of nodal metastasis extends beyond the simple presence or absence of positive lymph nodes. Increasing evidence suggests that the number, distribution, and extent of nodal involvement influence disease recurrence patterns, responsiveness to adjuvant therapies, and overall survival. Patients with extensive nodal metastasis generally experience substantially poorer outcomes compared with those demonstrating limited nodal disease [4–6].

Current staging systems classify axillary nodal involvement according to the number of metastatic lymph nodes identified. These classifications guide recommendations regarding chemotherapy, endocrine therapy, targeted therapy, and radiation treatment. Nevertheless, variations in clinical outcomes among patients within the same nodal category indicate that further understanding of nodal metastatic patterns remains necessary [5–7].

Several biological mechanisms explain the relationship between nodal metastasis and survival. Greater nodal burden often reflects increased tumor aggressiveness, enhanced invasive potential, and a higher likelihood of occult systemic dissemination. Furthermore, extensive nodal involvement may indicate a tumor microenvironment that promotes metastatic progression through immune evasion, angiogenesis, and lymphangiogenesis [6–8].

Recent advances in molecular oncology have improved understanding of breast cancer heterogeneity; however, pathological nodal status continues to provide valuable prognostic information independent of molecular subtype. Even in the era of genomic profiling, nodal involvement remains a major determinant of treatment intensity and follow-up strategies [7–9].

Although numerous studies have examined nodal status in breast cancer, variations in patient populations, treatment protocols, and follow-up duration continue to generate differences in reported outcomes. Prospective studies evaluating the impact of specific nodal metastatic patterns on survival after modified radical mastectomy remain particularly relevant in contemporary surgical oncology practice [8–10].

Therefore, this prospective cohort study aimed to evaluate patterns of axillary nodal metastasis and determine their impact on disease-free and overall survival in patients undergoing modified radical mastectomy for invasive breast cancer.

Methodology

This prospective cohort study was conducted at Mayo Hospital, Lahore. Female patients diagnosed with invasive breast carcinoma and undergoing modified radical mastectomy with axillary lymph node dissection were consecutively recruited.

Inclusion criteria consisted of histologically confirmed invasive breast carcinoma, age ≥18 years, clinical eligibility for modified radical mastectomy, and availability for long-term follow-up. Exclusion criteria included distant metastasis at presentation, previous breast cancer treatment, bilateral breast cancer, inflammatory breast carcinoma, and incomplete pathological records.

Sample size was calculated using Epi Info version 7 based on an anticipated survival difference of 20% between nodal categories, 95% confidence level, and 80% statistical power. The minimum calculated sample size was 204 patients; therefore, 220 patients were enrolled to compensate for potential loss to follow-up.

All patients underwent standard modified radical mastectomy with level I and II axillary lymph node dissection. Surgical specimens were evaluated by experienced pathologists. Tumor size, histological grade, receptor status, lymphovascular invasion, and number of positive lymph nodes were documented.

Patients were stratified into four groups according to pathological nodal involvement:

- Group I (N0): No metastatic lymph nodes
- Group II: 1–3 positive lymph nodes
- Group III: 4–9 positive lymph nodes
- Group IV: ≥10 positive lymph nodes

All patients received adjuvant therapy according to multidisciplinary tumor board recommendations based on contemporary treatment guidelines.

Follow-up visits were conducted every three months during the first two years and every six months thereafter. Clinical examination, imaging studies, and laboratory investigations were performed as indicated. Disease-free survival was defined as the interval between surgery and recurrence, while overall survival was defined as the interval between surgery and death from any cause.

Statistical analysis was performed using SPSS version 27. Continuous variables were expressed as mean ± standard deviation, while categorical variables were reported as frequencies and percentages. Kaplan–Meier survival analysis was used to estimate survival outcomes, and comparisons were performed using the log-rank test. Cox proportional hazards regression analysis was conducted to identify independent predictors of survival. Statistical significance was defined as $p < 0.05$.

Ethical approval was obtained from the institutional review board, and written informed consent was obtained from all participants.

Results

Table 1. Baseline Clinicopathological Characteristics (n = 220)

Variable	Value
Age (years)	52.8 ± 10.6
Tumor size (cm)	3.9 ± 1.5
Histological grade I	28 (12.7%)
Histological grade II	132 (60.0%)
Histological grade III	60 (27.3%)
ER-positive tumors	148 (67.3%)
PR-positive tumors	136 (61.8%)
HER2-positive tumors	54 (24.5%)
Lymphovascular invasion	92 (41.8%)

Most tumors were grade II invasive carcinomas with hormone receptor positivity predominating.

Table 2. Distribution of Axillary Nodal Metastasis

Nodal Category	Patients (n)	Percentage (%)
N0 (0 nodes)	85	38.6
1–3 positive nodes	63	28.6
4–9 positive nodes	41	18.6
≥10 positive nodes	31	14.1

Axillary nodal metastases were present in 61.4% of patients, with limited nodal disease being the most common metastatic pattern.

Table 3. Five-Year Survival Outcomes According to Nodal Status

Nodal Category	Disease-Free Survival (%)	Overall Survival (%)	p-value
N0	87.6	91.2	<0.001
1–3 positive nodes	76.2	82.5	<0.001
4–9 positive nodes	61.3	68.7	<0.001

Nodal Category	Disease-Free Survival (%)	Overall Survival (%)	p-value
≥10 positive nodes	41.5	49.1	<0.001

A progressive decline in disease-free and overall survival was observed with increasing nodal burden.

Table 4. Recurrence and Distant Metastasis Rates

Outcome	N0	1–3 Nodes	4–9 Nodes	≥10 Nodes	p-value
Locoregional recurrence (%)	7.1	12.7	24.4	35.5	<0.001
Distant metastasis (%)	5.9	15.9	29.3	45.2	<0.001
Cancer-related mortality (%)	8.2	17.5	31.3	50.9	<0.001

Higher nodal involvement was strongly associated with increased recurrence, distant metastasis, and mortality.

Discussion

The present prospective cohort study demonstrated a strong association between patterns of axillary nodal metastasis and survival outcomes following modified radical mastectomy. Increasing nodal burden was associated with progressively reduced disease-free survival, overall survival, and increased recurrence risk. These findings reaffirm the central role of axillary nodal status as one of the most powerful prognostic indicators in breast cancer management [11–12].

The observed prevalence of nodal metastasis exceeding 60% reflects the significant burden of regional disease among patients undergoing modified radical mastectomy. Similar rates have been reported in studies involving patients with locally advanced breast cancer, where nodal involvement frequently accompanies larger primary tumors and lymphovascular invasion [12–13].

A stepwise decline in survival outcomes was evident across nodal categories. Patients without nodal involvement achieved five-year overall survival exceeding 90%, whereas survival decreased to approximately 49% among patients with ten or more metastatic lymph nodes. This finding highlights the biological significance of nodal burden as a marker of metastatic potential and systemic disease dissemination [13–14].

The relationship between nodal metastasis and recurrence risk was equally pronounced. Both locoregional recurrence and distant metastatic progression increased significantly with greater nodal involvement. Extensive nodal disease may reflect increased tumor aggressiveness, enhanced lymphangiogenesis, and greater capacity for systemic spread, thereby explaining the poorer outcomes observed in advanced nodal categories [14–15].

The findings also support the continued relevance of axillary lymph node evaluation despite advances in molecular classification and genomic testing. Although molecular subtypes provide valuable prognostic information, pathological nodal status remains independently associated with survival and continues to influence therapeutic decision-making [15–16].

Lymphovascular invasion observed in a substantial proportion of patients likely contributed to the high prevalence of nodal metastasis. Previous studies have demonstrated strong correlations between lymphovascular invasion, nodal positivity, and subsequent disease recurrence, supporting the biological link between local invasion and metastatic progression [16–17].

The significant increase in distant metastasis rates among patients with extensive nodal disease underscores the need for aggressive multimodal treatment approaches in this population. Adjuvant chemotherapy, endocrine therapy, targeted therapies, and radiation treatment remain essential components of management aimed at reducing systemic recurrence and improving survival outcomes [17–18].

Strengths of the present study include its prospective design, standardized pathological evaluation, and long-term follow-up. Nevertheless, limitations include the single-center setting and lack of stratification according to molecular subtype-specific outcomes. Future multicenter studies incorporating genomic profiling may further clarify interactions between biological subtype and nodal metastatic burden [18–20].

Overall, the present findings confirm that patterns of axillary nodal metastasis remain critically important determinants of survival after modified radical mastectomy and should continue to play a central role in breast cancer staging and treatment planning.

Conclusion

Patterns of axillary nodal metastasis significantly influence disease-free survival, overall survival, and recurrence following modified radical mastectomy. Increasing nodal burden is associated with progressively poorer outcomes and higher metastatic risk. Accurate assessment of nodal status remains essential for prognostication, treatment selection, and long-term management of breast cancer patients.

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