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Original Research Article

PROGNOSTIC IMPACT OF MARGINAL ADIPOSE TISSUE INVASION IN BREAST CARCINOMA: A CLINICOPATHOLOGICAL STUDY OF 150 CASES

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ABSTRACT

Background: Marginal adipose tissue invasion (ATI) has been proposed as a potential indicator of tumour aggressiveness in invasive ductal carcinoma of the breast, yet its prognostic significance remains insufficiently explored. **Materials and Methods:** A total of 150 mastectomy specimens were evaluated for ATI, lymphovascular invasion (LVI), lymph node metastasis, tumour grade, hormone receptor status, St. Gallen risk stratification, and predicted 10-year survival. Clinicopathological correlations were analyzed using chi-square and ANOVA tests. **Result:** ATI was present in 61.3% of cases and showed a significant association with lymph node metastasis (p=0.0001) and estrogen receptor positivity (p=0.025). No significant differences were observed in tumour grade, tumour size, progesterone receptor status, or LVI. ATI-positive cases demonstrated slightly lower predicted 10-year survival, though this difference was not statistically significant. **Conclusion:** Marginal adipose tissue invasion correlates strongly with nodal metastasis and may serve as an additional marker of tumour aggressiveness in breast carcinoma. Its prognostic value appears enhanced when considered alongside LVI, supporting its potential role in risk assessment, particularly when lymph node sampling is limited.

INTRODUCTION

Breast carcinoma represents a clinically and pathologically heterogeneous group of malignancies. Among these, infiltrating ductal carcinoma—also termed infiltrating carcinoma NOS—constitutes the most common subtype, characterized by the absence of distinguishing special features and accounting for the majority of invasive mammary carcinomas.[1,2] Numerous clinical and pathological parameters have been explored in an effort to better predict prognosis in breast cancer patients. Traditional prognostic indicators include tumour size, histologic grade, vascular invasion, presence of an in situ component, lymphatic tumour emboli, and overall stromal characteristics. At the same time, molecular markers consist of hormone receptor status, p53 expression, and HER2/neuamplification.[3]

Lymphatic dissemination is recognized as a key pathway in breast cancer metastasis, with functional lymphatics at the tumour periphery facilitating nodal spread. Tumour cell morphology and proliferative capacity also influence metastatic potential. Emerging evidence suggests that tumour cells' ability to invade surrounding tissues is an equally significant prognostic factor. Despite this, the prognostic role of marginal adipose tissue invasion and the extent of invasive spread into adipose tissue has not been thoroughly evaluated.[4,5] The present study aims to assess marginal adipose tissue invasion at the tumour margin and determine its prognostic significance in invasive ductal carcinoma of the breast.

MATERIALS AND METHODS

This study was conducted in the Department of Pathology among 150 patients diagnosed with invasive ductal carcinoma of the breast who underwent mastectomy with axillary lymph node dissection at the Government Medical College, Thrissur, from 2011 to 2012. All mastectomy specimens processed during this period that met the inclusion criteria were evaluated. All histologically confirmed invasive ductal carcinoma cases were included. Exclusion criteria comprised special histologic subtypes such as mucinous, lobular, medullary, or squamous cell carcinoma, bilateral breast cancer, distant metastasis, malignancies at other sites, and patients who had received neoadjuvant chemotherapy.

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Breast and axillary lymph node tissues were fixed in 10% formalin and processed according to standard histopathology protocols. Gross examination included measuring the tumour's maximum dimension. Tissues were serially sectioned, embedded in paraffin, and stained with hematoxylinand eosin. Lymph nodes were dissected in their entirety, processed, and screened microscopically for metastasis. Both micrometastasis (≤2 mm) and macrometastasis were recorded, while reactive changes without malignant infiltration were excluded from metastasis reporting.

Adipose tissue and marginal adipose tissue invasion (ATI) were defined using strict morphological criteria. Pure adipose tissue was identified as clusters of more than 20 adipocytes without intervening fibrous tissue. Marginal ATI was diagnosed when more than 20 malignant cells were found in direct contact with or within adipose tissue. Cases with unequivocal invasion were categorized as ATI-positive, while those with doubtful features were classified as ATI-negative. Lymphovascular invasion (LVI) was defined as the presence of tumour emboli within endothelial-lined lymphatic or vascular spaces; cases showing clear tumour emboli were labelled LVI-positive, and equivocal cases were recorded as LVI-negative.

Histologic grading of tumours was performed using the Nottingham modification of the Bloom–Richardson system, which evaluates three components: tubule formation, nuclear pleomorphism, and mitotic count. Each parameter was scored 1-3, and the total score was used to assign tumour grade I (3–5), II (6–7), or III (8–9). This standardized grading system was uniformly applied across all specimens to ensure consistency in tumor characterization.

Hormone receptor status for estrogen receptor (ER) and progesterone receptor (PR) was assessed by immunohistochemistry using commercially available antibodies (DakoCytomation, Kyoto, Japan). A threshold of>10% nuclear staining was used to define receptor positivity. Immunostaining was performed only in cases for which hormone receptor evaluation was clinically indicated. Based on receptor status, tumour grade, lymph node involvement, patient age, and tumour size, the St. Gallen risk stratification was applied to categorize patients into minimal-low-risk or average/high-risk groups.

Ten-year survival predictions were generated using Adjuvant! Online Version 8.0, utilizing individualized clinicopathological data including age, comorbidities, ER status, tumour size, tumour grade, and nodal status.[6] All collected data were entered into Microsoft Excel and analyzed using SPSS version 16.0. Statistical analyses included frequencies and means, chi-square tests for categorical variables, and ANOVA for quantitative variables; p-values <0.05 were considered statistically significant.

RESULTS

A total of 150 cases of infiltrating duct carcinoma were evaluated in this study. Marginal adipose tissue invasionwas identified in 92 cases (61.3%), while 58 cases (38.7%) showed no evidence of ATI. Lymphovascular invasion was observed in 60 cases (40%), with the remaining 90 cases (60%) being LVI-negative. The study population consisted predominantly of females (149 cases; 99.3%), with only one male patient. Age distribution analysis showed no statistically significant difference between cases with and without ATI. Most ATI-positive patients belonged to the 41–60 years age group (61 cases, 66.3%).

Tumour grade distribution did not differ significantly between ATI groups ($p = 0.45$). Grade II tumours formed the majority in both ATI-positive (56 cases; 60.9%) and ATI-negative (37 cases; 63.8%) subsets. However, a statistically significant association was observed between ATI and lymph node metastasis ($p = 0.0001$). ATI-positive cases showed markedly higher rates of nodal involvement, with 50% of patients demonstrating ≥5 metastatic nodes compared with only 10.3% among ATI-negative cases. Tumour size distribution did not differ significantly by ATI status ($p > 0.05$), with 2–5 cm tumours comprising the largest proportion of cases in both groups (76.1% of ATI-positive and 63.8% of ATI-negative patients).

Hormone receptor status analysis revealed a significant association between ATI and estrogen receptor (ER) positivity ($p = 0.025$), with ATI-positive tumours showing higher ER positivity (63.6%) than ATI-negative tumours (38.2%). Progesterone receptor (PR) status, however, showed no significant correlation with ATI ($p > 0.05$), although PR negativity predominated among ATI-positive cases (54.5%). St. Gallen risk stratification demonstrated that all ATI-positive cases fell into the average/high-risk category, though this association did not reach statistical significance ($p = 0.364$).

Survival prediction analysis using the Adjuvant! Online tool showed a lower predicted 10-year survival in ATI-positive patients (57.6%) compared with ATI-negative patients (61.6%), although this difference was not statistically significant ($p > 0.05$). In contrast, lymphovascular invasion showed a significant negative impact on predicted survival, with LVI-positive cases demonstrating a markedly lower 10-year survival estimate (54.3%) compared with LVI-negative cases (62.4%) ($p = 0.0099$).

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Table1: Clinico-pathological characteristics of the study population based on adipose tissue invasion

Parameters	AT1+ (n=92)	AT1– (n=58)	P value
Lymph node metastasis			
Present	61	18	0.0001
Absent	31	40	
Mean ± SD age (years)	52.3 ± 10.3	54.8 ± 11.8	0.183
Tumour size(Mean)	3.5 ± 1.4	3.3 ± 1.7	0.464
Lymphatic vessel invasion			
Present	39	21	0.560
Absent	53	37	
Histologic grade			
Grade 1	18	7	0.450
Grade 2	56	37	
Grade 3	18	14	
Estrogen receptor			
Positive	28	13	0.025
Negative	16	21	
Progesterone receptor			
Positive	20	9	0.086
Negative	24	5	
St. Gallen risk stratification			
Average–high risk	44	32	0.364
Minimum–low risk	0	2	
Adjuvant Predicted 10-year survival rate	57.6%	61.7%	0.202

DISCUSSION

In this study, 150 cases of invasive ductal carcinoma were evaluated to determine the clinicopathological significance of marginal adipose tissue invasion (ATI), lymphovascular invasion (LVI), and lymph node metastasis. The distribution of ATI, LVI, tumour grade, age, and hormone receptor status largely reflected patterns described in earlier literature. The majority of patients were in the 40–60-year age group, consistent with the age-related increase in breast cancer incidence.[7,8] Although no significant association was observed between ATI and patient age, the tendency for ATI-positive cases to cluster in the middle-age group parallels findings from Yamaguchi et al., who proposed a possible age-related influence on adipose tissue invasion.[4]

Tumour grade distribution in the present study was similar to earlier observations, with most cases falling under grade II according to the modified Bloom–Richardson system. While 56.2% of ATI-positive cases showed nodal metastasis, the association between tumour grade and ATI was not statistically significant.

However, ATI showed a strong positive correlation with lymph node metastasis, supporting previous findings by Woo et al, who reported a similar relationship and additionally linked nodal involvement to reduced 12-year survival.[9] The pattern suggests that ATI may represent a morphological marker of aggressive tumour behaviour, reflecting the ability of tumour cells to infiltrate loosely cohesive adipose tissue, thereby facilitating lymphatic or vascular intravasation.

A significant association was noted between ATI and estrogen receptor status, with 63.6% of ATI-positive tumours being ER-positive. This aligns with the findings of Kimijima et al, who demonstrated a link between breast tissue invasion and ER positivity in older patients.[10] No significant differences, however, were observed in progesterone receptor status, tumour size, or LVI between ATI-positive and negative groups, findings that correspond to the trends reported by Yamaguchi et al.and others.[4] Although all ATI-positive cases belonged to the St. Gallen intermediate–high-risk category, the association was not statistically significant, implying that ATI may complement but not replace existing risk stratification tools.

Survival prediction using Adjuvant! Online suggested a lower mean estimated 10-year survival for ATI-positive cases (57.6%) compared with ATI-negative cases (61.6%), though the difference was not statistically significant. In contrast, LVI showed a clear correlation with poorer predicted survival, consistent with the work of Cornwell et al. , who demonstrated a significant relationship between LVI and nodal metastasis.[11] The combined presence of ATI and peritumoral LVI showed even higher frequencies of nodal metastasis, echoing the findings of Yamaguchi et al.[4] These results collectively suggest that while ATI alone may not independently predict survival, its coexistence with LVI significantly enhances its prognostic relevance, especially in cases where lymph node sampling is limited or inconclusive.[12,13]

CONCLUSION

Marginal adipose tissue invasion in invasive ductal carcinoma of the breast is associated with higher rates of lymph node metastasis, indicating its role as a marker of aggressive tumour behaviour. Although ATI did not independently correlate with tumour grade or survival prediction, its significant association with estrogen receptor status suggests biological relevance. The coexistence of ATI with lymphovascular invasion further amplifies its prognostic significance. ATI may therefore serve as a helpful adjunct parameter in assessing tumour

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aggressiveness, particularly when lymph node sampling is limited or inadequate.

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