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Residual axillary disease in Node-Positive Breast Cancer Patients After Neoadjuvant systemic therapy : A Single center Retrospective Study

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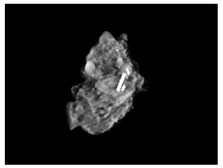
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Introduction

Axillary lymph node status is an integral prognostic factor in breast cancer treatment and steers the decisions on local, regional and systemic treatments. Advances in neoadjuvant chemotherapy has led to de-escalation of axillary surgery in patients with N0-N1 disease.

Axillary lymph node dissection (ALND) has been the standard of care for patients with persistent node-positive (N+) disease after neoadjuvant chemotherapy (NACT). Patients with a good clinical response to NACT, it is appropriate to perform limited axillary surgery to evaluate axillary status, with ALND reserved for those who remain Node positive (N+). Residual disease in patients with triple negative tumours and HER2 overexpression will indicate additional adjuvant treatment with capecitabine or trastuzumab emtansine (TDM1), respectively. This approach leads to concerns regarding false negative rate (FNR). To minimise the FNR, localisation of the biopsied node (Targeted axillary dissection- TAD/Sentinel lymph node biopsy-SLNB) has proved an efficient technique.

We investigated the risk of additional metastases in the axilla when the lymph nodes are removed by targeted axillary dissection (TAD) that harboured metastases after NACT. We aimed to identify histological subgroups suitable for de-escalated axillary treatment.



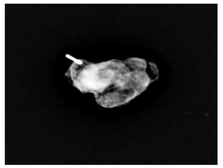


Figure 1. TAD specimen x-ray , Magseed® and tissue marker in the node

Methods and Materials

We conducted a retrospective audit of 82 consecutive patients that underwent targeted axillary dissection post neoadjuvant chemotherapy at our centre from January 2019 to December 2023. We included all patients who became clinically and radiologically node- negative (N0) after NACT. All underwent TAD, involving SLNB combined with removal of the previously clipped metastatic node. The data was extracted from patient electronic medical records following patient confidentiality and data protection guidelines. The study has been approved by the trust's governance team. Data management and statistical analysis were performed using SPSS version 23.. P-values < 0.05 were considered significant.

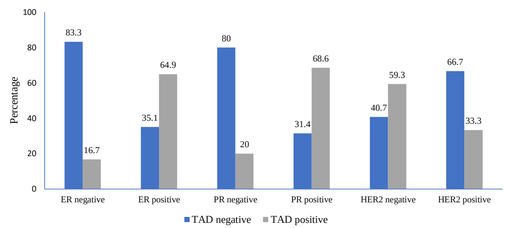
Results

A total of 82 patients underwent targeted axillary dissection (TAD) following neoadjuvant chemotherapy (NACT). Among the 81 patients with a successful TADs, 40 (48.8%) had negative TAD and 41 (51.2%) demonstrated residual nodal disease. Baseline demographics- including age (p = 0.412), menopausal status (p = 0.23), and tumour type (p = 1) did not differ significantly between the TAD positive and TAD negative groups. In contrast, tumour biology showed strong associations with TAD positivity. Patients with hormone-receptor–positive, HER2-negative disease were significantly more likely to have positive TAD nodes (70.7% vs. 22.5%, p < 0.001), while ER- and PR-negative tumours were more common among TAD-negative patients (both p < 0.001). HER2-positive disease was also more frequent in the TAD-negative group (45% vs. 22%, p = 0.028), and triple-negative tumours demonstrated the highest rates of node negativity (25% vs. 4.9%, p = 0.011). The results indicate complete pathological response strongly correlates with TAD status, with 65% of TAD-negative patients achieving pCR compared to only 7.3% of TAD-positive cases (p < 0.001).

Table 1. Patient and Tumour Characteristics Stratified by TAD Status.

		TAD negative n = 40 (%)	TAD positive n = 41 (%)	P value
Age (years)	Mean ± SD	50.7 ± 9.6	49 ± 9.0	0.412
Menopausal status	premenopausal	20 (50.0)	26 (63.4)	0.223
	postmenopausal	20 (50.0)	15 (36.6)	
Type	Infiltrating duct carcinoma	38 (95.0)	39 (95.1)	1.000
	Lobular carcinoma	2 (5.0)	2 (4.9)	
Grade	Low grade (grades 1-2)	)5.42 (17	27 (65.9)	0.035
	High grade (grade 3)	23 (57.5)	14 (34.1)	
Triple negative breast cancer (TNBC)	Not TNBC	30 (75.0)	39 (95.1)	0.011
	TNBC	10 (25.0)	2 (4.9)	
ER&PR positive Her 2 negative	ERPR positive Her2 negative	9 (22.5)	29 (70.7)	< 0.001
	other	31 (77.5)	12 (29.3)	
HER 2	negative	22 (55.0)	32 (78.0)	0.028
	positive	18 (45.0)	9 (22.0)	
Complete pathological response in breast	No	14 (35.0)	38 (92.7)	< 0.001
	Yes	26 (65.0)	3 (7.3)	

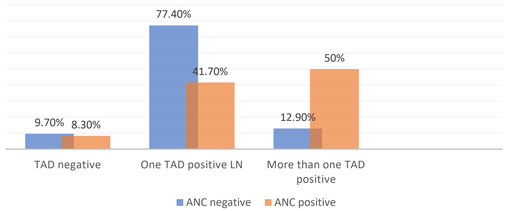
Chart 1. Distribution of receptors status across TAD classes



Results

Axillary node clearance (ANC) was performed in 43 patients, enabling correlation of TAD findings with the true axillary burden. ANC-positive patients were significantly more likely to harbour multiple positive TAD nodes (50% vs. 12.9%), whereas ANC-negative patients more often had only one positive TAD node (77.4% vs. 41.7%) (p = 0.022). This demonstrates a clear step-wise relationship between increasing TAD tumour burden and likelihood of residual disease in the axilla. Conversely, neither complete pathological response (p = 0.658) nor radiological breast or axillary response on MRI (p = 0.945 and p = 0.526, respectively) showed significant association with ANC involvement. Together, these findings highlight that TAD status—particularly the number of positive TAD nodes—is a more accurate predictor of residual axillary disease than MRI response or breast pCR, and that hormone-receptor–positive, HER2-negative tumours represent the group most likely to harbour residual nodal metastases.

Chart 2: Correlation of TAD burden with residual axillary disease identified in the ANC.



Discussion

Our study indicates that patients with ER/PR-positive, HER2-negative breast cancer have a significantly higher likelihood of residual nodal disease following neoadjuvant chemotherapy compared to other molecular subtypes. This suggests a lower chemosensitivity within this subgroup, consistent with existing evidence that luminal tumours respond less to systemic treatment than triple-negative or HER2-positive cancers. Despite the observed association between this subtype and positive TAD findings, omitting targeted axillary dissection in ER/PR-positive, HER2-negative patients may risk inaccurate estimation of residual nodal disease. Therefore, TAD remains an important staging and management tool in this population, ensuring accurate axillary assessment and guiding subsequent surgical and adjuvant treatment decisions.

The strong association between ANC positivity and the number of positive TAD nodes indicates that the extent of nodal involvement detected by TAD may serve as a reliable predictor of residual axillary disease burden. Specifically, the finding that patients with multiple positive TAD nodes are more likely to have residual disease on axillary clearance supports the concept of using TAD as a surrogate marker for axillary status. Conversely, the lack of correlation between ANC involvement and MRI or breast pathological response suggests that imaging and breast response alone are insufficient for accurate axillary assessment. These results reinforce the clinical value of performing TAD, particularly in patients at higher risk for nodal involvement, to optimize axillary staging and guide further management.

Overall, our study indicates the clinical utility of TAD in accurately identifying residual nodal disease, particularly in histologically less chemosensitive subtypes. Incorporating TAD into axillary management pathways may therefore optimize staging accuracy, minimize overtreatment, and tailor adjuvant therapy more effectively. However, the study is limited by its relatively small sample size and the need for longer follow-up to fully assess long-term oncological outcomes, which may influence the interpretation and generalisability of these findings.

Conclusions

Patients with ER/PR-positive, HER2-negative breast cancer are the most likely to harbour residual nodal disease after neoadjuvant therapy, reinforcing the importance of targeted axillary dissection for accurate staging in this subgroup. Overall, TAD—particularly the number of positive TAD nodes—outperforms MRI and breast pCR in predicting true axillary burden and should remain integral to guiding axillary management.

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