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Breast Tumor Response & Axillary Clearance After Neoadjuvant Chemotherapy

Mahdis Bayat [1], Hossein Hatami [2,*], Mohammad Esmaeil Akbari [3,**]

[1] Department of Public Health, School of Public Health and Safety, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2] Department of Public Health, Safety and Environmental and Occupational Hazards Control Research Center, School of Public Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3] Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran

[*] ***Corresponding Author:*** Department of Public Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Email: hatami@sbmu.ac.ir
[**] ***Corresponding Author:*** Cancer Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. P.O. Box: 15179/64311, Email: profmeakbari@gmail.com

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Abstract

Background and Objective: Neoadjuvant chemotherapy (NAC) is widely used in the management of breast cancer (BC) and provides an opportunity to evaluate treatment response in both the primary tumor and axillary lymph nodes (LNs). Understanding the relationship between breast tumor response and axillary clearance may inform surgical decision-making and prognostication.

Methods: In this retrospective study, patients with histologically confirmed BC who received NAC followed by definitive breast and axillary surgery at a tertiary referral center between 1987 and 1990 were included. Exclusion criteria were male sex and incomplete pathological data regarding breast tumor response, axillary LN status, or immunohistochemical profile. Chi-square test (χ^2) and odds ratio (OR) with 95% confidence intervals (CI) were used for statistical analysis.

Results: A total of 375 patients with BC treated with NAC were evaluated for breast tumor response and axillary LN response at definitive surgery. A strong association was observed between breast tumor response and axillary LN response, with patients demonstrating a favorable breast tumor response showing significantly higher odds of axillary clearance (OR 5.18, 95% CI 3.07 - 8.75; $P < 0.001$). In addition, breast tumor response was significantly associated with non-luminal immunohistochemical status (OR 1.76, CI95% 1.02 - 3.03; $P = 0.03$), as was axillary LN response (OR 2.43, 95% CI 1.48 - 3.99; $P < 0.001$).

Conclusions: Breast tumor response following NAC is strongly correlated with axillary LN response and is associated with tumor biology. These findings support the potential role of response-based stratification in guiding individualized management strategies for patients with BC.

Keywords: Breast Tumor, Axillary Clearance, Neoadjuvant Chemotherapy

1. Background

Breast cancer (BC) remains one of the most prevalent malignancies among women worldwide, and neoadjuvant chemotherapy (NAC) has become an essential component of treatment for patients with locally advanced disease as well as selected cases of early-stage cancer (1, 2). Beyond its established role in tumor size reduction and facilitating surgical management, NAC offers a unique clinical opportunity to assess in vivo tumor sensitivity to systemic therapy (3).

Previous research has shown that axillary and margin clearance are associated with improved disease-free and overall survival in patients with BC, largely reflecting favorable tumor biology and effective systemic treatment (4-6). In addition, pathologic complete response (pCR) in the primary breast tumor after NAC has consistently been associated with improved patient survival, particularly among biologically aggressive subtypes such as HER2-enriched

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and triple-negative BC (7, 8). However, despite the favorable prognostic implications of tumor pCR, some studies have reported discrepancies between breast pCR and axillary lymph node (LN) pCR rates in patients with clinically node-positive disease, suggesting tumor heterogeneity as a key biological factor underlying differential responses between the primary tumor and metastatic LNs (9-11). As a result, response assessment following NAC has gained increasing importance not only for prognostic stratification but also for guiding subsequent surgical and adjuvant treatment decisions (12).

In this regard, understanding the relationship between treatment response in the primary tumor and in the axillary LNs is of considerable clinical relevance (13).

2. Objectives

The present study was designed to evaluate the correlation between breast tumor response and axillary LN clearance following NAC.

3. Methods

3.1. Study Design

This retrospective study included patients with histologically confirmed BC who received NAC followed by definitive breast and axillary surgery at a tertiary referral center from 1987 to 1990. Eligible patients had available pathological assessments of both the primary breast tumor and axillary LNs after completion of NAC. From a total of 390 patients, 3 male patients and 12 patients with incomplete pathological data regarding breast tumor response, axillary LN status, or immunohistochemical (IHC) profile were excluded from the analysis.

The ethics committee of Shahid Beheshti University of Medical Sciences approved the study (IR.SBMU.PHNS.REC.1404.001), and all methods were conducted in compliance with applicable guidelines and regulatory standards. Informed consent for publication was obtained from all patients.

3.2. Treatment and Pathological Assessment

All patients received standard NAC regimens in accordance with contemporary institutional protocols, based on tumor stage, receptor status, and clinical guidelines at the time of treatment. Surgical management consisted of breast-conserving surgery (BCS) or modified radical mastectomy (MRM), with axillary evaluation performed using sentinel LN biopsy and/or axillary LN dissection, as clinically indicated.

Data were extracted from pathology reports and institutional records and assessed by experienced pathologists. Breast tumor response was defined based on post-treatment histopathological findings and categorized according to the presence or absence of residual invasive disease. Axillary LN response was determined by the absence or presence of residual metastatic disease in resected LNs. Immunohistochemical analysis included standard evaluation of estrogen receptor, progesterone receptor, and HER2 status, in accordance with established guidelines.

3.3. Variables and Outcome Measures

The primary outcome was the association between breast tumor response and axillary LN response following NAC. The secondary outcome included the relationships between breast tumor response and IHC characteristics, and axillary LN response and IHC characteristics.

3.4. Statistical Analysis

The data were analyzed using IBM SPSS ver. 27. The categorical variables are expressed as proportions and frequencies. Associations between categorical variables were evaluated using the chi-square (χ^2) test, and results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). Statistical significance was defined as a P-value < 0.05.

4. Result

4.1. Patients' Characteristics

In this study, 375 patients who received NAC were evaluated. Table 1. provides the patients' baseline characteristics. The patients were categorized into two groups for axillary LNs and breast tumor response as follows: Pathologic complete response (pCR) without any positive LN/breast tumor remnant in the surgery report, and non-pathologic complete response (N-pCR)

with one or more positive LNs/breast tumor remnants. The mean age of patients was 46.71 ± 11.52.

Table 1. Patient's Characteristics

Variables	No. (%)
Age group	
≤ 50	237 (63.2)
> 50	138 (36.8)
Family history	
Negative	257 (68.5)
Positive	86 (22.9)
Unknown	32 (8.5)
Breast tumor side	
Left	148 (39.5)
Right	174 (46.4)
Unknown	53 (14.1)
Breast tumor size	
T1: 0 - 2 cm	1 (0.3)
T2: 2 - 5 cm	33 (8.8)
T3: > 5 cm	341 (90.9)
Pathology	
IDC	340 (90.6)
ILC	19 (5.1)
Other	16 (4.3)
LVI	
Positive	68 (18.1)
Negative	196 (52.3)
Unknown	111 (29.6)
Grade	
1	20 (5.3)
2	180 (48.0)
3	111 (29.6)
Unknown	64 (17.1)
Ki67%	
≤ 14	98 (26.1)
> 14	45 (12.0)
Unknown	232 (61.9)
IHC	
Luminal A	218 (58.1)
Luminal B	74 (19.7)
HER2-enriched	24 (6.4)
TN	59 (15.7)
Breast surgery	
BCS	174 (46.4)
MRM	161 (30.9)
Unknown	85 (22.7)
Breast tumor response	
pCR	86 (22.9)
N-pCR	289 (77.1)
Axillary clinical status	
1 LNs	10 (2.6)
> 1 LNs	365 (97.4)
Axillary clearance	
pCR	149 (39.7)
N-pCR	226 (60.3)
Radiotherapy	
Yes	296 (78.9)
No	7 (1.9)
Unknown	72 (19.2)
Hormone therapy	
Yes	297 (79.2)
No	71 (18.9)
Unknown	7 (1.9)

4.2. Correlation of Breast Tumor Response with Axillary Lymph Nodes Response

A total of 375 patients were included in the analysis, of whom 86 (22.9%) achieved breast pCR. A significant association was observed between breast tumor response and axillary LN response following NAC (Table 2). Patients demonstrating a favorable breast tumor response were significantly more likely to achieve axillary clearance, with an OR of 5.18 (95% CI: 3.07 - 8.75; P < 0.001), indicating a strong correlation between primary tumor response and nodal downstaging.

4.3. Correlation of Tumor IHC with Breast Tumor and Axillary Lymph Nodes Responses

Among IHC subtypes, non-luminal tumors were associated with increased odds of achieving pCR in both breast tumors and axillary LNs compared with luminal tumors (Table 2). Tumors with favorable response patterns showed higher odds for non-luminal types, with an OR of 1.76 (95% CI: 1.02 - 3.03; P = 0.03). Similarly, axillary LN response demonstrated a robust association with this IHC status, with an OR of 2.43 (95% CI: 1.48 - 3.99; P < 0.001).

Collectively, these findings underscore the close interrelationship between tumor biology and treatment response in both the breast and axilla.

5. Discussion

The findings of this study demonstrated a strong and clinically meaningful association between breast tumor response and axillary LN clearance following NAC. Patients who achieved a favorable response in the primary breast tumor were significantly more likely to exhibit an axillary nodal response, underscoring the coordinated biological behavior of primary and regional disease compartments under systemic treatment (14). This observation supports the concept that chemosensitivity in the breast is frequently mirrored by treatment effects in the axilla.

The magnitude of the association observed between breast tumor response and axillary LN response was substantial, suggesting that effective eradication of tumor burden in the breast often coincides with nodal downstaging. This observation is consistent with prior reports indicating higher rates of axillary pathologic complete response in patients achieving breast pCR, particularly among biologically aggressive but chemosensitive subtypes (15).

Both breast tumor response and axillary LN response showed significant associations with IHC profiles, highlighting the critical role of tumor biology in determining treatment responsiveness. The findings support the known chemosensitivity of non-luminal tumors. The observed correlations suggest that molecular characteristics not only influence primary tumor shrinkage but also govern nodal sensitivity to

Table 2. Correlations of Breast Tumor and Axillary Lymph Nodes Responses to Neoadjuvant Chemotherapy

Variables	ORs	Confidence Interval 95%	P-Value
Breast tumor response & axillary LNs response	5.18	3.07 - 8.75	< 0.001
Breast tumor response & IHC	1.76	1.02 - 3.03	0.03
Axillary LNs response & IHC	2.43	1.48 - 3.99	< 0.001

Abbreviations: ORs, odds ratio; LNs, lymph nodes.

systemic therapy. These findings align with existing evidence demonstrating differential response patterns across BC subtypes and support the integration of biological markers into predictive models for treatment response and surgical planning (16-18).

Several limitations should be acknowledged. The retrospective design and the large proportion of missing data for some variables may introduce potential bias. Statistical analysis was limited to univariate chi-square tests and unadjusted OR; the lack of adjustment for potential confounders may have affected the observed associations. Additionally, treatment protocols and surgical practices evolved over the study period, which may have influenced response patterns; however, this historical context may offer insight into biologic concordance between breast and axillary responses. Future prospective studies are warranted to validate these findings.

5.1. Conclusions

In summary, this study demonstrates a strong correlation between breast tumor response and axillary LN clearance following NAC, highlighting the coordinated biological response of primary and regional disease to systemic treatment. Both breast and axillary responses were significantly associated with IHC characteristics, underscoring their prognostic relevance. Prospective validation is required to determine how these associations can be safely translated into management protocols without compromising oncologic outcomes.

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Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

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Conflict of Interests Statement: The authors declare no conflicts of interest.

Data Availability: The datasets utilized and analyzed during the current study are available from the corresponding author upon reasonable request.

Ethical Approval: This study, entitled "Breast Tumor Response and Axillary Clearance After Neoadjuvant Chemotherapy," was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (ethics code: IR.SBMU.PHNS.REC.1404.001).

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References

1. Arzanova E, Mayrovitz HN. Mayrovitz HN, editor. *The Epidemiology of Breast Cancer*. Brisbane (AU); 2022. [PubMed ID: 36122161]. https://doi.org/10.36255/exon-publications-breast-cancer-epidemiology.
2. Mathew J, Asgeirsson KS, Cheung KL, Chan S, Dahda A, Robertson JF. Neoadjuvant chemotherapy for locally advanced breast cancer: a review of the literature and future directions. *Eur J Surg Oncol*.

2009;**35**(2):113-22. [PubMed ID: 18502088]. https://doi.org/10.1016/j.ejso.2008.03.015.

3. Heil J, Kuerer HM, Pfob A, Rauch G, Sinn HP, Golatta M, et al. Eliminating the breast cancer surgery paradigm after neoadjuvant systemic therapy: current evidence and future challenges. *Ann Oncol*. 2020;**31**(1):61-71. [PubMed ID: 31912797]. https://doi.org/10.1016/j.annonc.2019.10.012.
4. Mousavi-Kiasary SMS, Bayat M, Abbasvandi F, Khoundabi B, Mousavi F, Akbari A, et al. Tumor characteristics and survival rate of axillary metastatic breast cancer patients: a three decades retrospective cohort study. *Sci Rep*. 2025;**15**(1):4571. [PubMed ID: 39915527]. [PubMed Central ID: PMC11802794]. https://doi.org/10.1038/s41598-024-84115-7.
5. Abbasvandi F, Mahdavi R, Bayat M, Hajighasemi F, Jahanbakhshi F, Aghaei F, et al. Electrical lymph node scanning (ELS) system for real-time intra-operative detection of involved axillary lymph nodes in adjuvant breast cancer patients. *Sci Rep*. 2024;**14**(1):12900. [PubMed ID: 38839807]. [PubMed Central ID: PMC11153595]. https://doi.org/10.1038/s41598-024-61600-7.
6. Abbasvandi F, Miripour ZS, Bayat M, Mousavi-Kiasary SMS, Shayanfar S, Shojaeian F, et al. Clinical validation on role of cancer diagnostic probe in detecting the involved cavity margins missed in permanent pathology of tumor side in breast cancer surgery. *Diagn Pathol*. 2024;**19**(1):148. [PubMed ID: 39568025]. [PubMed Central ID: PMC11577628]. https://doi.org/10.1186/s13000-024-01574-2.
7. Chica-Parrado MR, Godoy-Ortiz A, Jimenez B, Ribelles N, Barragan I, Alba E. Resistance to Neoadjuvant Treatment in Breast Cancer: Clinicopathological and Molecular Predictors. *Cancers (Basel)*. 2020;**12**(8). [PubMed ID: 32708049]. [PubMed Central ID: PMC7463925]. https://doi.org/10.3390/cancers12082012.
8. Abbasvandi F, Bayat M, Akbari A, Shojaeian F, Zandi A, Rahmani J, et al. Tumor characteristics and survival rate of HER2-low breast cancer patients: a retrospective cohort study. *Sci Rep*. 2023;**13**(1):16719. [PubMed ID: 37794050]. [PubMed Central ID: PMC10550984]. https://doi.org/10.1038/s41598-023-43186-8.
9. Chen SC, Yu CC, Chang HK, Lin YC, Lo YF, Shen SC, et al. Discrepancy of Breast and Axillary Pathologic Complete Response and Outcomes in Different Subtypes of Node-positive Breast Cancer after Neoadjuvant Chemotherapy. *J Cancer*. 2021;**12**(17):5365-74. [PubMed ID: 34335953]. [PubMed Central ID: PMC8317533]. https://doi.org/10.7150/jca.62830.
10. Boughey JC, Ballman KV, McCall LM, Mittendorf EA, Symmans WF, Julian TB, et al. Tumor Biology and Response to Chemotherapy Impact Breast Cancer-specific Survival in Node-positive Breast Cancer Patients Treated With Neoadjuvant Chemotherapy: Long-term Follow-up From ACOSOG Z1071 (Alliance). *Ann Surg*. 2017;**266**(4):667-76. [PubMed ID: 28657941]. [PubMed Central ID: PMC5755619]. https://doi.org/10.1097/SLA.0000000000002373.
11. Bertucci F, Ng CKY, Patsouris A, Droin N, Piscuoglio S, Carbuccia N, et al. Genomic characterization of metastatic breast cancers. *Nature*. 2019;**569**(7757):560-4. [PubMed ID: 31118521]. https://doi.org/10.1038/s41586-019-1056-z.
12. Rubio IT, Sobrido C. Neoadjuvant approach in patients with early breast cancer: patient assessment, staging, and planning. *Breast*. 2022;**62 Suppl 1**(Suppl 1):S17-24. [PubMed ID: 34996668]. [PubMed Central ID: PMC9097809]. https://doi.org/10.1016/j.breast.2021.12.019.
13. Wang Y, Li L, Liu X, Wang Y, Tang Z, Wu Y, et al. Treatment response correlation between primary tumor and axillary lymph nodes after neoadjuvant therapy in breast cancer: a retrospective study based on real-world data. *Gland Surg*. 2021;**10**(2):656-69. [PubMed ID: 33708548]. [PubMed Central ID: PMC7944072]. https://doi.org/10.21037/gs-20-686.
14. Ouldamer L, Chas M, Arbion F, Body G, Cirier J, Ballester M, et al. Risk scoring system for predicting axillary response after neoadjuvant chemotherapy in initially node-positive women with breast cancer. *Surg Oncol*. 2018;**27**(2):158-65. [PubMed ID: 29937166]. https://doi.org/10.1016/j.suronc.2018.02.003.
15. Haque W, Verma V, Hatch S, Suzanne Klimberg V, Brian Butler E, Teh BS. Response rates and pathologic complete response by breast cancer molecular subtype following neoadjuvant chemotherapy. *Breast Cancer Res Treat*. 2018;**170**(3):559-67. [PubMed ID: 29693228]. https://doi.org/10.1007/s10549-018-4801-3.
16. Samiei S, Simons JM, Engelen SM, Beets-Tan RG, Classe J, Smidt ML. Axillary Pathologic Complete Response After Neoadjuvant Systemic Therapy by Breast Cancer Subtype in Patients With Initially Clinically Node-Positive Disease. *JAMA Surgery*. 2021;**156**(6). [PubMed ID: 33881478]. [PubMed Central ID: PMC8060891]. https://doi.org/10.1001/jamasurg.2021.0891.
17. Lim DW, Greene BD, Look Hong NJ. Relationship Between Breast and Axillary Pathologic Complete Response in Women Receiving Neoadjuvant Chemotherapy for Breast Cancer. *Ann Surg Oncol*. 2021;**28**(10):5495-506. [PubMed ID: 34374914]. https://doi.org/10.1245/s10434-021-10519-8.
18. Hong J, Tong Y, He J, Chen X, Shen K. Association between tumor molecular subtype, clinical stage and axillary pathological response in breast cancer patients undergoing complete pathological remission after neoadjuvant chemotherapy: potential implications for de-escalation of axillary surgery. *Ther Adv Med Oncol*. 2021;**13**:1758835921996670. [PubMed ID: 33737963]. [PubMed Central ID: PMC7934036]. https://doi.org/10.1177/1758835921996673.