Section: General Surgery

Original Research Article

# A STUDY OF EVALUATION OF CLINICAL, RADIOLOGICAL AND PATHOLOGICAL RESPONSE FOLLOWING NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED BREAST CANCER

**Vijayshankar.R[1], R. Nandha Kumar[2], M. Saraswathy[3]**

[1]Assistant Professor, Department of General Surgery, Coimbatore Medical College and Hospital, Tamilnadu, India
Assistant Surgeon, Department of General Surgery, Government Hospital, Mathur, Krishnagiri, Tamilnadu, India
Assistant Professor, Department of General Surgery, Coimbatore Medical College and Hospital, Tamilnadu, India.

*Received* : 12/06/2024
*Received in revised form* : 01/08/2024
*Accepted* : 16/08/2024

*Keywords:*
*FAC regimen, PACLITAXEL regimen, Oncologic safety, TNM staging, Breast carcinoma.*

Corresponding Author:
**Dr. M. Saraswathy,**
Email: drsaraswathyms@gmail.com

DOI: 10.47009/jamp.2024.6.4.104

Source of Support: Nil,
Conflict of Interest: None declared

*Int J Acad Med Pharm*
2024; 6 (4); 530-534

## Abstract

**Background:** Neoadjuvant chemotherapy (NACT) is pivotal for the treatment of breast cancer. This study delves into the clinical and pathological responses after NACT in locally advanced breast cancer, examining their impact on surgical outcomes. **Aim:** This study aimed to analyse the clinical, radiological, and pathological response rates of locally advanced breast cancer following neoadjuvant chemotherapy. **Materials and Methods:** This study was conducted on 30 patients aged > 25 years who presented at the general surgery OPD in Coimbatore Medical College Hospital with locally advanced breast carcinoma between October 2021 and September 2022. The diagnosis was confirmed through core needle biopsy, and grade and metastatic workups were performed. The clinical responses were assessed before and after neoadjuvant chemotherapy. Descriptive statistics and chi-square tests ($p < 0.05$) were used to compare the TNM stage distributions before and after treatment. **Results:** Predominantly perimenopausal (54%), 63% presented tumours larger than 5 cm pre-chemotherapy. Post-treatment, 36% of the patients had T2 tumours, and 33% had T3 tumours. Nodal involvement decreased in 43% of N1 cases and 20% of N2 cases. The TNM staging showed comparable results. Miller Payne Grading indicated that 13% of respondents were complete respondents. The TNM stage before and after neoadjuvant treatment exhibited no discernible differences ($p=0.07$). **Conclusion:** Individualised treatment is important, considering patient age, tumour size, and staging. The analysis showed no difference in the TNM stage before and after therapy, supporting its effectiveness in reducing tumour size. These findings offer insights for clinicians to tailor treatment strategies.

## INTRODUCTION

Breast cancer surgery has undergone numerous paradigm shifts over the past 100 years.[1] While axillary lymph node dissection (ALND) and (radical) mastectomy have been the mainstay of therapy. Most women with early-stage breast cancer are now advised to undergo specialised and less invasive techniques, including breast-conserving surgery and sentinel lymph node biopsy (SLNB), integrated into multimodal therapy approaches (surgery, systemic treatment, and radiation). Before a definitive surgical procedure, a systemic medication called neoadjuvant chemotherapy (NACT) is administered.[2] NACT was developed to downstage locally progressed or inflammatory (inoperable) disease, making it operable as the treatment for breast cancer.[3] NACT is currently used for operable breast cancer due to its advantages, which include higher rates of breast-conserving surgery and the ability to monitor early in vivo response to systemic chemotherapy.

From the perspective of breast surgery, the development of neoadjuvant systemic treatment (NACT) comprising chemotherapy and targeted antibody therapy has long been viewed as a double-edged sword. On the one hand, NACT frequently causes the tumour to shrink before surgery, enabling surgical downstaging and less invasive breast-conserving procedures to spare patients substantial treatment-associated morbidity.[4] However, because studies had demonstrated equal oncologic safety in


ISSN (O): 2687-5365; ISSN (P): 2753-6556

an adjuvant therapy environment, which may not be applicable for the neoadjuvant setting, the oncologic safety of less invasive breast-conserving surgery and SLNB following NACT has been unclear for a long time.[5] Later research, however, revealed that in terms of oncologic outcomes, both SLNB and breast-conserving surgery following NACT are comparable to ALND and mastectomy.[6]

The underlying tumour's clinical response to NACT can vary from a mild response to a pathological Complete Response (pCR), and the underlying tumour's clinical response to NACT can vary.[7] pCR is defined differently in different studies. The three most frequently used definitions of pCR are the absence of invasive cancer and in situ cancer in the breast and axillary nodes-ypT0 ypN0, absence of invasive cancer in the breast and axillary nodes regardless of ductal carcinoma in situ ypT0/is ypN0, and absence of invasive cancer in the breast. Methods used to assess tumour neoadjuvant treatment response include physical examination, mammographic imaging of the breast, and US. Using callipers to measure the size of the tumour is usually carried out monthly, if not with each chemotherapeutic cycle.[8] The precision of clinical breast imaging assessment to determine pCR in those who have locally advanced breast cancer following neoadjuvant hormonal therapy or chemotherapy is only 57%, which is less than ideal. US (79%), and mammography (74%). Conventional breast imaging was performed before the initiation of neoadjuvant treatment. A diagnostic full-field mammography should be performed. The mediolateral oblique and craniocaudal views included spot views and mediolateral views with compression or magnification at the location of the tumour and full-field mediolateral and craniocaudal oblique perspectives of the opposite, regardless of ductal carcinoma in situ or nodal involvement-ypT0.

**Aim**

This study aimed to analyse the rates of clinical, radiological, and pathological responses to neoadjuvant chemotherapy for locally advanced breast cancer.

## MATERIALS AND METHODS

This study was conducted on 30 patients aged > 25 years who presented at the general surgery OPD in Coimbatore Medical College Hospital with locally advanced breast carcinoma between October 2021 and September 2022.

**Inclusion Criteria**

Patients diagnosed with locally advanced breast cancer and those aged > 25 years were included in the study.

**Exclusion Criteria**

Patients with a history of breast surgery or those presenting with metastatic disease were excluded.

Patients aged > 25 years who presented with a malignant breast lump were evaluated. The diagnosis was confirmed through core needle biopsy, and grade and metastatic workups were performed. Thirty eligible patients met the inclusion criteria underwent neoadjuvant chemotherapy (FAC/PACLITAXEL REGIMEN). The clinical responses were assessed before and after neoadjuvant chemotherapy. Modified radical mastectomy was performed, and the specimens were analysed for pathological responses with subsequent observations.

**Statistical Analysis**

Demographic and clinical characteristics were summarised using descriptive statistics for statistical analysis. The distribution of tumour characteristics before and after neoadjuvant chemotherapy was presented as a percentage. The TNM stage before and after treatment was compared using the chi-square test, with statistical significance determined by a p-value of < 0.05.

## RESULTS

The age distribution of the population was as follows: < 30 years (3%), 31-40 years (12%),41-50 years (24%), 51-60 years (30%), and > 60 years (30%). [Table 1]

The population distribution based on tumour size was as follows: 37% had 2-5 cm tumours, while 63% had tumours larger than 5 cm. Regarding the T stage, 37% were classified as T2, 53% as T3, and 10% as T4b. Regarding the N stage, 3% were N0, 66% were N1, and 30% were N2, whereas there were no cases of N3.

After NACT, the distribution of the T stage was 13% T0, 10% T1, 36% T2, 33% T3, and 6% T4b. Regarding the N stage, 33% were N0, 43% were N1, 20% were N2, and 3% were N3. Only 13% of patients achieved a Miller Payne score of 5, indicative of a complete response, while 27% scored 3-4, signifying a partial response. 60% scored 1-2, indicating non-response. [Table 1]

The distribution of TNM stages Before NACT was 3% T2N0M0, 33% T2N1M0, 30% T3N1M0, 23% T3N2M0, 3% T4bN1M0, and 6% T4bN2M0.

TNM stage distribution After NACT includes 13.33% T0N0M0, 3.33% T1N0M0, 6.67% T1N1M0, 10% T2N0M0, 26.67% T2N1M0, 6.67% T3N0M0, 6.67% T3N1M0, 16.67% T3N2M0, 3.33% T3N3M0, 3.33% T4bN1M0, and 3.33% T4bN2M0. The chi-square value was 3.27, and the p-value was 0.07 (>0.05), indicating that the result is statistically insignificant. The null hypothesis was accepted with a p-value of 0.07 (>0.05), suggesting no discernible difference between TNM stages before and after neoadjuvant treatment. [Table 2]


ISSN (O): 2687-5365; ISSN (P): 2753-6556

**Table 1: Age, tumour characteristics, and Miller Payne grading before and after neoadjuvant chemotherapy**

| | | Population (N) | Percentage |
|---|---|---|---|
| Age (years) | <30 | 1 | 3% |
| | 31-40 | 3 | 12% |
| | 41-50 | 7 | 24% |
| | 51-60 | 10 | 30% |
| | >60 | 9 | 30% |
| **Before NACT** | | | |
| Tumour Size | 2-5cm | 11 | 37% |
| | >5cm | 19 | 63% |
| T stage | T2 | 11 | 37% |
| | T3 | 16 | 53% |
| | T4b | 3 | 10% |
| N stage | N0 | 1 | 3% |
| | N1 | 20 | 66% |
| | N2 | 9 | 30% |
| | N3 | 0 | 0% |
| **After NACT** | | | |
| T stage | T0 | 4 | 13% |
| | T1 | 3 | 10% |
| | T2 | 11 | 36% |
| | T3 | 10 | 33% |
| | T4b | 2 | 6% |
| N stage | N0 | 10 | 33% |
| | N1 | 13 | 43% |
| | N2 | 6 | 20% |
| | N3 | 1 | 3% |
| Miller Payne Grading | 1-2 | 18 | 60% |
| | 3-4 | 8 | 27% |
| | 5 | 4 | 13% |

**Table 2: Comparison of TNM stage before and after neoadjuvant chemotherapy**

| TNM Stage | Before chemotherapy, N (%) | After chemotherapy, N (%) |
|---|---|---|
| T0N0M0 | 0(0) | 4(13.33) |
| T1N0M0 | 0(0) | 1(3.33) |
| T1N1M0 | 0(0) | 2(6.67) |
| T2N0M0 | 1(3.33) | 3(10) |
| T2N1M0 | 10(33) | 8(26.67) |
| T3N0M0 | 0(0) | 2(6.67) |
| T3N1M0 | 9(30) | 2(6.67) |
| T3N2M0 | 7(23) | 5(16.67) |
| T3N3M0 | 0(0) | 1(3.33) |
| T4bN1M0 | 1(3.33) | 1(3.33) |
| T4bN2M0 | 2(6.77) | 1(3.33) |

## DISCUSSION

This study presents a meticulous exploration of NACT outcomes in a cohort of patients with locally advanced breast cancer aged > 25 years. The primary outcomes illuminate a diverse landscape, with 13% achieving a complete response, 27% exhibiting a partial response, and 60% categorised as non-responders. An in-depth analysis of tumour characteristics, including size and staging, revealed notable variations before and after treatment; however, the TNM stage remained largely unchanged.

This study demonstrates a notable strength through its inclusive methodology, encompassing a diverse age range and undertaking a comprehensive examination of tumour characteristics. Nevertheless, the study's external validity is potentially compromised by its relatively modest sample size of 30 participants and its singular focus on a single centre. While descriptive statistics and chi-square tests contribute to a foundational understanding, future investigations may benefit from employing more sophisticated analytical methods. The findings of this study are consistent with those of previous studies, affirming the effectiveness of neoadjuvant therapy in reducing tumour size. This concurrence is evident in the studies conducted by Forgia et al. and Giani et al., reinforcing the observed outcomes' robustness.[9,10]

In the absence of a systematic review, this study significantly contributed to advancing our understanding of NACT outcomes in patients with locally advanced breast cancer. The nuanced responses observed underscore the critical necessity of personalised treatment plans tailored to individual patient characteristics. This resonates with the ongoing discourse in the literature, emphasising the imperative for customised approaches to augment treatment efficacy, as articulated by Oshima et al. By offering insights into the diverse responses exhibited by patients, this study enriches our understanding of the evolving landscape of breast cancer treatment. It reinforces the notion that adopting a one-size-fits-all approach may not be


ISSN (O): 2687-5365; ISSN (P): 2753-6556

optimal in the context of locally advanced breast cancer.[11-13]

While offering valuable insights, this study contemplates the generalisability of its findings to other populations. The potential influence of factors, such as ethnicity and socioeconomic status, on treatment responses introduces complexity. Addressing these concerns requires future research with larger and more diverse cohorts.

To improve the external validity of the findings, future investigations should consider enlarging sample sizes and participating in multicentre collaborations. Moreover, delving into the underlying molecular mechanisms influencing treatment responses, as proposed by Tang et al., can offer a more nuanced understanding.[14] Long-term follow-up studies assessing the durability of treatment responses and their consequential effects on overall survival rates are justified. Collaborations that combine knowledge from many research projects will improve our understanding and substantially contribute to the current discussion about breast cancer.[15]

In conclusion, this study contributes to understanding NACT outcomes in locally advanced breast cancers. While confirming the success of neoadjuvant therapy, it also emphasises the importance of individualised and nuanced treatment approaches. By combining lessons from other relevant studies, future research can deepen our understanding, ultimately contributing to more effective and customised treatment methods for locally advanced breast cancer.

**Limitations**

However, there are limitations to consider, such as the relatively small sample size of 30 participants and the concentration at a single centre, which may impact the generalisability of the findings. In terms of interpretation and implications, despite these limitations, the investigation contributes valuable information on neoadjuvant chemotherapy responses in locally advanced breast cancer. These data can assist clinicians in customising treatment strategies, particularly when considering tumour size, staging, and patient age. Potential controversies may arise regarding the applicability of the findings to diverse populations, thus highlighting the need for future research with larger and more diverse samples and multicentre studies.

## CONCLUSION

This study elucidated the varied clinical and pathological reactions to neoadjuvant chemotherapy in cases of breast cancer that have progressed to a locally advanced stage. The results underscore the importance of individualised treatment approaches, considering factors such as patient age, tumour size, and staging. The analysis revealed no substantial disparity in the TNM stage before and after neoadjuvant therapy, thus supporting the effectiveness of this approach in reducing tumour size. Despite certain limitations, such as a relatively small sample size and focus on a single medical centre, the findings offer valuable insights that can assist clinicians in tailoring their treatment strategies. The observed diversity in responses to treatment highlights the necessity for further research involving larger and more diverse sample groups, as well as multicentre studies, to validate and expand upon these discoveries. Ultimately, these insights contribute to the refinement of our understanding of neoadjuvant chemotherapy and the optimisation of patient care in the context of locally advanced breast cancer.

## REFERENCES


1. Khokhar A. Breast cancer in India: where do we stand and where do we go? Asian Pac J Cancer Prev. 2012;13(10):4861–6. http://dx.doi.org/10.7314/apjcp.2012.13.10.4861.
2. Agarwal G, Ramakant P. Breast cancer care in India: The current scenario and the challenges for the future. Breast Care (Basel). 2008;3(1):21–7. http://dx.doi.org/10.1159/000115288.
3. Huang EH, Tucker SL, Strom EA, McNeese MD, Kuerer HM, Hortobagyi GN, et al. Predictors of locoregional recurrence in patients with locally advanced breast cancer treated with neoadjuvant chemotherapy, mastectomy, and radiotherapy. Int J Radiat Oncol Biol Phys. 2005;62(2):351–7. http://dx.doi.org/10.1016/j.ijrobp.2004.09.056.
4. Haagensen CD. Carcinoma of the breast. J Am Med Assoc. 1948;138(4):279. http://dx.doi.org/10.1001/jama.1948.62900040016005.
5. Haagensen CD, Bodian C. A personal experience with Halsted's radical mastectomy. Ann Surg. 1984;199(2):143–50. http://dx.doi.org/10.1097/00000658-198402000-00002.
6. Garg PK, Prakash G. Current definition of locally advanced breast cancer. Curr Oncol. 2015;22(5):e409-10. http://dx.doi.org/10.3747/co.22.2697.
7. Fisher B, Bryant J, Wolmark N, Mamounas E, Brown A, Fisher ER, et al. Effect of preoperative chemotherapy on the outcome of women with operable breast cancer. J Clin Oncol. 2023;41(10):1795–808. http://dx.doi.org/10.1200/JCO.22.02571.
8. Adams S, Chakravarthy AB, Donach M, Spicer D, Lymberis S, Singh B, et al. Preoperative concurrent paclitaxel-radiation in locally advanced breast cancer: pathologic response correlates with five-year overall survival. Breast Cancer Res Treat. 2010;124(3):723–32. http://dx.doi.org/10.1007/s10549-010-1181-8.
9. Forgia L, Vestito D, Lasciarrea A, Comes M, Diotaiuti MC, Giotta S, et al. Response predictivity to neoadjuvant therapies in breast cancer: a qualitative analysis of background parenchymal enhancement in DCE-MRI. J Pers Med 2021;11(4). https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8065517/.
10. Giani M, Tavella K, Tartarotti RI, Nori E, Vanzi J, Bianchi E, et al. Prognostic Role of Tumor Size Reduction> 50% after Neoadjuvant Chemotherapy for Breast Cancer. J Cancer Sci Clin Ther 2022; 6:349–57. http://dx.doi.org/10.26502/jcsct.5079174.
11. Oshima K, Mitsuyoshi A, Kikumori K, Hori A, Yanagawa T, Shinke G, et al. A Case of Locally Advanced Breast Cancer That Responded to Paclitaxel plus Bevacizumab and Underwent Radical Surgery. Gan to Kagaku Ryoho 2022;49(13):1645–7. https://pubmed.ncbi.nlm.nih.gov/36733163/.
12. Lin Y-H, Chidley P, Admojo L, Jassal S, Zantuck N, Foroudi F, et al. Pathologic complete response and oncologic outcomes in locally advanced breast cancers treated with neoadjuvant radiation therapy: An Australian perspective.




ISSN (O): 2687-5365; ISSN (P): 2753-6556

Pract Radiat Oncol 2023; 13:301–13. https://doi.org/10.1016/j.prro.2022.12.004.
13. Hansen CW, Vogsen M, Kodahl AR. Management and outcomes after neoadjuvant treatment for locally advanced breast cancer in older versus younger women. Acta Oncol. 2022;61(11):1362–8. http://dx.doi.org/10.1080/0284186X.2022.2137844.
14. Tang X, Thompson KJ, Kalari KR, Sinnwell JP, Suman VJ, Vedell PT, et al. Integration of multiomics data shows downregulation of mismatch repair and tubulin pathways in triple-negative chemotherapy-resistant breast tumours. Breast Cancer Res. 2023;25(1):57. http://dx.doi.org/10.1186/s13058-023-01656-x.
15. Joshi S, Chougle Q, Noronha J, Hawaldar R, Nair N, Vanmali V, et al. Determinants of pathological complete response to neoadjuvant chemotherapy in breast cancer: A single-institution experience. Indian J Cancer. 2023. http://dx.doi.org/10.4103/ijc.IJC_813_20.


ISSN (O): 2687-5365; ISSN (P): 2753-6556