

Evaluation of Clinical, Radiological, and Pathological Efficacy Regarding Neoadjuvant Chemotherapy in Breast Cancer

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ABSTRACT

Objective: The aim of this study was to evaluate the radiological, clinical, and pathological responses before and after neoadjuvant chemotherapy (NAC) in patients with breast cancer, to examine the reliability of imaging modalities, and to compare treatment responses according to pathological subtypes.

Materials and Methods: Forty breast cancer patients who underwent neoadjuvant chemotherapy followed by surgery between June 2020 and 2025 were retrospectively analyzed. Tumor diameters before and after treatment were measured using positron emission tomography-computed tomography (PET-CT). Axillary lymph node metastases were compared clinically, radiologically, and pathologically. In addition, treatment responses were analyzed according to pathological subtypes.

Results: A significant reduction in tumor size was observed following NAC ($p<0.001$). Among the 20 patients who demonstrated a complete response on PET-CT, only 8 had a complete pathological response. The sensitivity, specificity, positive predictive value, and negative predictive value of PET-CT in detecting complete response were 100%, 62.5%, 40%, and 100%, respectively. A statistically significant downstaging after NAC was observed ($p<0.001$). Higher response rates were found in human epidermal growth factor receptor 2 (HER2)-positive and triple-negative subtypes.

Conclusion: Neoadjuvant chemotherapy significantly reduces tumor size and axillary involvement, enabling more conservative surgical approaches. Although PET-CT has high sensitivity in detecting complete response, its low positive predictive value highlights the need for complementary evaluation methods. Pathological subtypes are predictive of treatment response and should be taken into account during treatment planning.

Keywords: Breast cancer, HER2, neoadjuvant therapy, positron emission tomography-computed tomography

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INTRODUCTION

Breast cancer is one of the most commonly encountered cancers worldwide. Early-stage breast cancer can be treated curatively by surgery. In locally advanced and inoperable breast cancer cases, neoadjuvant chemotherapy (NAC) has significant clinical value, as shown by many trials.^[1] NAC is effective in locally advanced or metastatic breast cancer cases by either downstaging or causing shrinkage of the tumor, allowing breast-conserving surgery (BCS) instead of mastectomy.^[2,3] Moreover, NAC is effective in cases with axillary lymph node involvement by downstaging, making it possible to avoid axillary dissection and its complications.^[4-6]

Pathological complete response (pCR) after NAC is an important prognostic factor. Therefore, early evaluation of post-NAC response is important for verifying treatment efficacy as well as identifying non-responders to plan alternative treatment options.^[7,8] For these reasons, evaluation after NAC is performed using mammography and ultrasonography, generally combined with magnetic resonance imaging (MRI) and/or positron emission tomography (PET-CT).

Some studies have reported that patients, especially those with triple-negative and HER2-positive tumors, who achieve a complete pathological response to NAC have longer overall and disease-free survival.^[9-11] In earlier periods, NAC had a



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limited role; however, its use in early breast cancer has recently been debated.^[12] Moreover, some studies suggest avoiding surgical treatment in patients with pCR.^[13,14] Therefore, it is important to identify patients expected to have the best response and understand the long-term advantages of NAC.

In this study, we evaluated the radiological, clinical, and pathological responses to NAC in 40 breast cancer patients retrospectively.

MATERIALS and METHODS

In this retrospective study, data of 129 patients operated for breast cancer between June 2020 and June 2025 in Istanbul Aydın University Medical Faculty, Department of General Surgery, were evaluated. Forty patients subject to NAC were included in the study. Treatment strategy was decided by the Oncology Council, consisting of doctors from the general surgery, medical oncology, radiation oncology, nuclear medicine, and radiology departments. The NAC decision was taken regarding clinical and radiological staging in light of PET-CT. All of the tumors were marked by metallic clips before NAC. After NAC, the surgical technique was decided based on the latest clinical and radiological findings. All of the surgical operations were performed by the same surgical team. The surgical technique was either breast-conserving surgery or mastectomy.

Sentinel lymph node biopsy (SLNB) was performed with methylene blue and evaluated with frozen section in the operating room. In patients with metastasis and failed dye sampling in SLNB, axillary dissection was performed. Pathological diagnosis was performed by the same pathology team both in frozen section and postoperative evaluation.

Complete response was accepted in cases with complete remission in breast tumor, axillary metastatic lymph node, or distant metastasis with radiologic evaluation and PET-CT after NAC. Tumor shrinkage by 25% in diameter and/or decrease in metastatic lymph node involvement or disappearance was accepted as partial response. No change in tumor size or lymph node involvement, less than 25% shrinkage in tumor diameter, or less than 20% increase in tumor size was accepted as stable disease. More than 20% increase in tumor size and/or increased axillary lymph node involvement was accepted as progressive disease.

Statistical Analysis

Statistical analyses were performed using SPSS Statistics version 15.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics, including mean, standard deviation (SD), and percentages, were calculated. Continuous variables are presented as

mean±standard error of the mean (SEM) with ranges, unless otherwise specified. For categorical variables, comparisons were made using the Chi-square test or Fisher's exact test, as appropriate. The distribution of continuous data was assessed using the Kolmogorov–Smirnov test. Normally distributed variables were analyzed with the Student's t-test, while non-normally distributed variables were analyzed with the Mann–Whitney U test. A p-value of <0.05 was considered statistically significant.

AI-Assisted Figure Generation

Graphical visualizations illustrating the distribution of clinical and pathological responses according to molecular subtypes in patients receiving neoadjuvant chemotherapy for breast cancer were generated using the artificial intelligence tool ChatGPT (GPT-5, OpenAI, August 2025 version). Aggregated, anonymized study data were provided to the AI system without any patient-identifiable information. The prompts included detailed instructions specifying the type of figure (e.g., bar chart, pie chart), axis labeling, color coding for molecular subtypes, and legend formatting. The generated figures were reviewed and finalized by the authors to ensure accuracy and consistency with the study results.

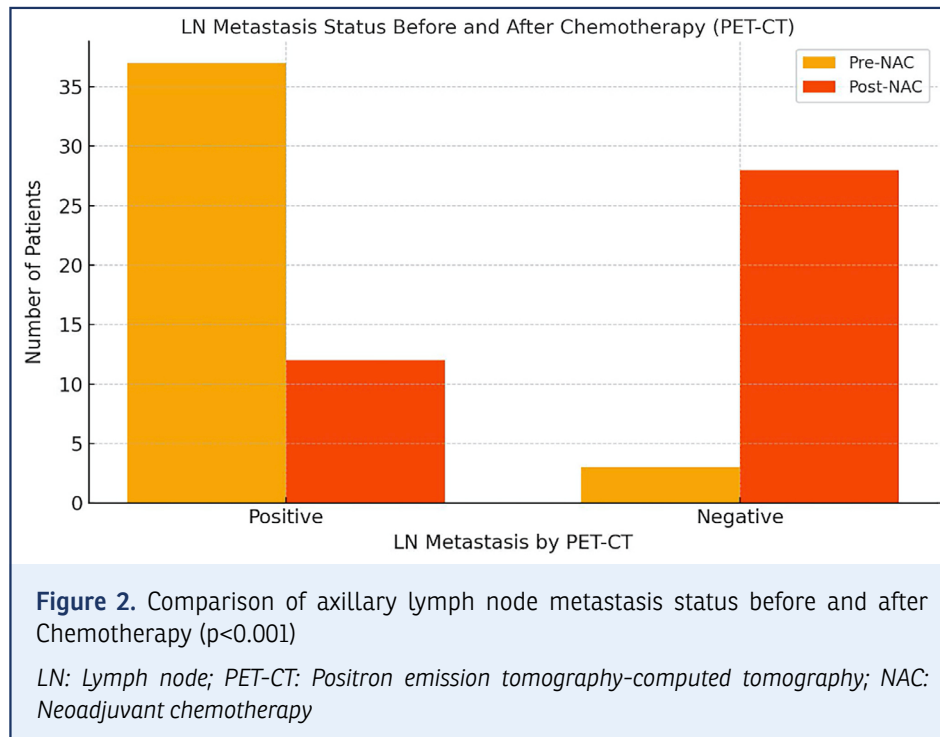
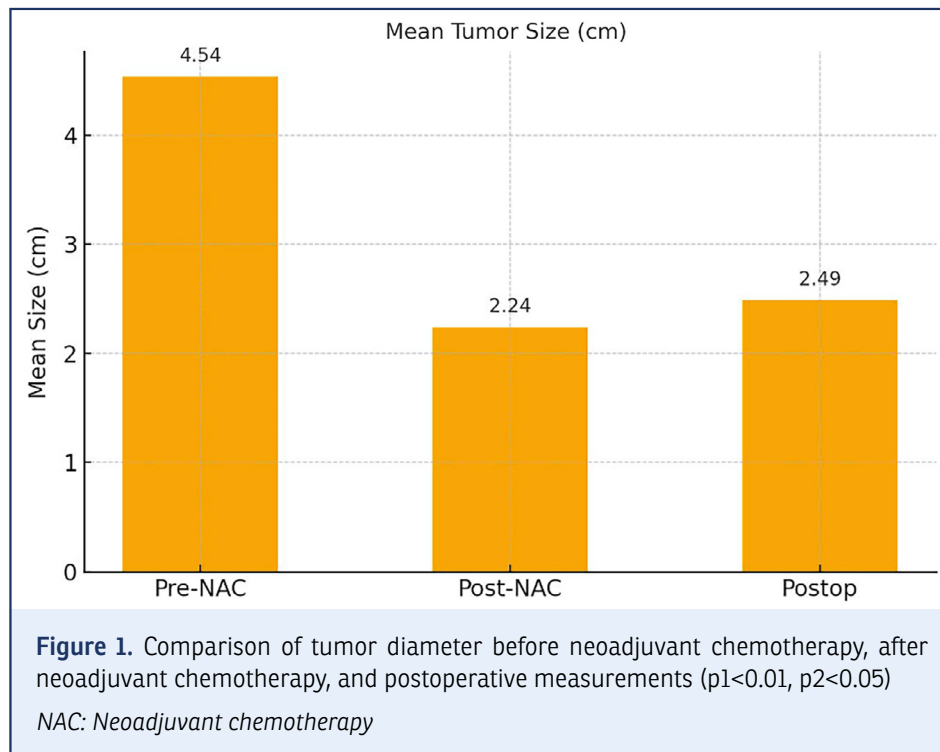
Ethics Committee Approval

This study was approved by the Ethics Committee of Istanbul Aydın University (approval number: 165/2025). It was conducted in accordance with the ethical standards of the institutional and national research committees and with the 1964 Declaration of Helsinki and its later amendments. Due to the retrospective nature of the study, the requirement for individual informed consent was waived by the ethics committee. No intervention or modification was made in patient care within the scope of this research.

RESULTS

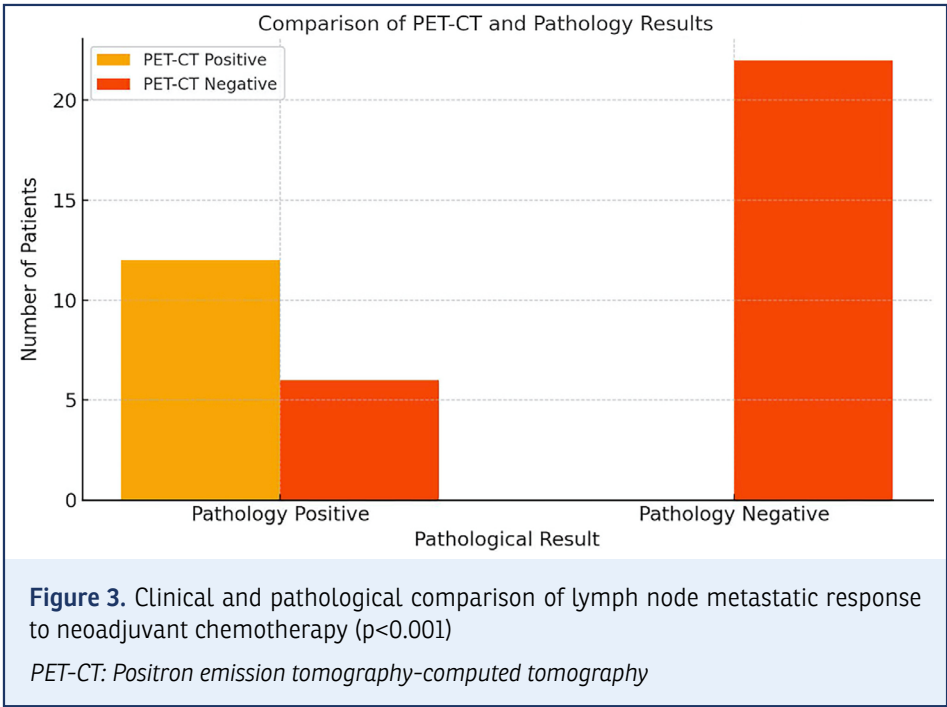
The mean age of the patients at the time of NAC was 59.2±11.0 years (31–70). Regarding the core biopsy results, 35 (87.5%) had invasive ductal carcinoma, 2 (5%) had invasive lobular carcinoma, 1 (2.5%) had inflammatory carcinoma, 1 (2.5%) had metaplastic carcinoma, and 1 (2.5%) had mucinous carcinoma.

Postoperative pathological examinations revealed complete regression in 8 (20%) patients. Remaining patients had pathological results similar to the pre-NAC results. Mean tumor size with PET-CT evaluation before NAC was 4.54±0.72 cm (mean ± SEM; range: 1–26 cm), whereas mean tumor size after NAC was 2.24±0.77 cm (mean±SEM; range: 0–25 cm).



There was a statistically significant regression in the tumor size ($p<0.001$). However, mean tumor size after NAC within the surgical specimens was 2.49 ± 0.71 cm (mean $\pm$ SEM; range: 0–25 cm), which was statistically significantly higher than the PET-CT results ($p<0.05$) (Fig. 1).

In 37 (92.5%) patients, clinical and radiological lymph node involvement was present, with 3 (7.5%) free of axillary involvement. After NAC, 12 (30%) patients had persistent axillary lymph node involvement ($p<0.001$) (Fig. 2). After NAC, 25 of 37 patients had radiological regression in lymph node involve-



ment. There was a statistically significant difference between pre-NAC and post-NAC involvement radiologically ($p<0.001$). Twelve patients with both pre-NAC and post-NAC axillary lymph node positivity had axillary dissection, and all of these patients were proven to be metastatic in the pathological examination. The remaining 28 patients had SLNB, in which 3 of them had additional axillary dissection due to positivity of SLNB, and pathological examination also confirmed metastasis. In another 3 patients, SLNB failed to stain the lymph nodes; therefore, additional axillary dissection was performed, and no metastatic lymph node was detected in the dissection specimen. In 3 of the SLNB-negative patients, micrometastasis was revealed perioperatively in the paraffin section, but no additional operation was performed. As a result, post-NAC radiological examination revealed 12 positive cases, whereas in post-surgical specimens, 18 patients had metastasis (3 of them with micrometastasis) (Fig. 3). There was a statistically significant difference regarding these results ($p<0.001$).

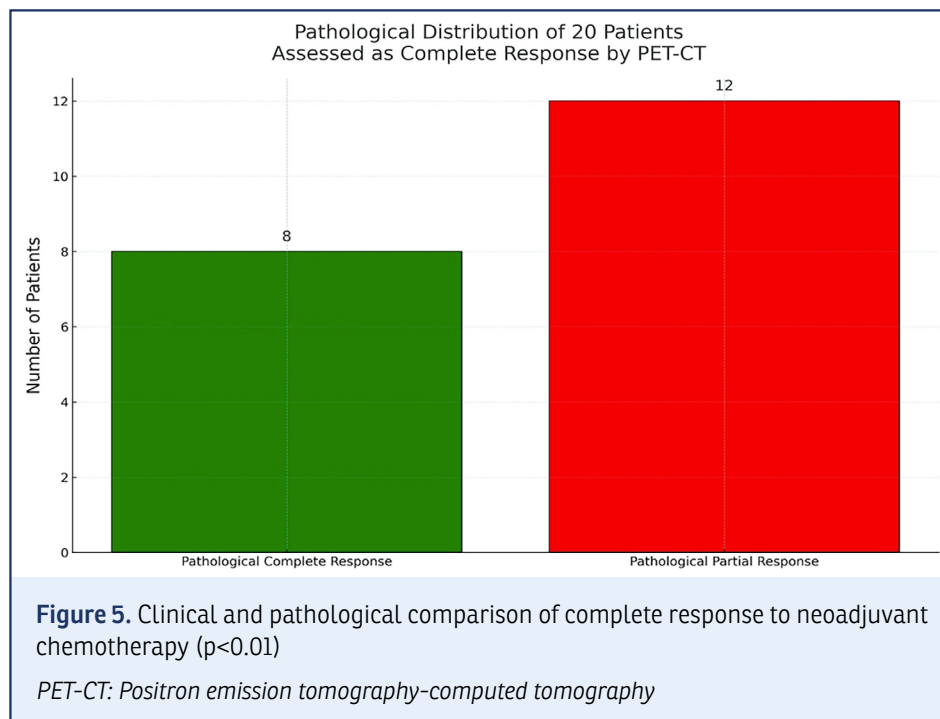
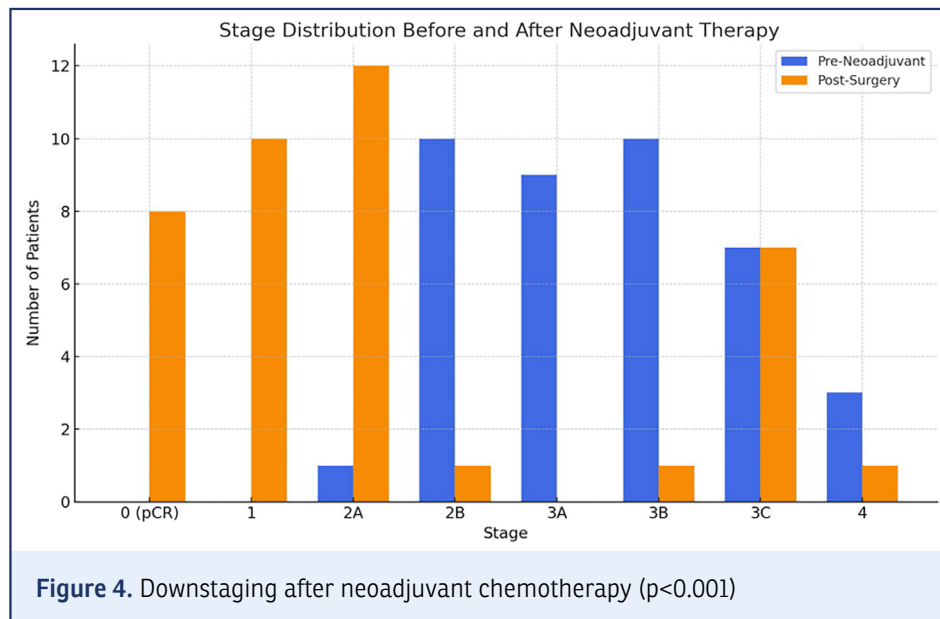
During surgery, 20 patients had mastectomy (50%) and 20 (50%) had BCS. In the mastectomy group, 3 patients were suitable for BCS after NAC but preferred mastectomy.

Clinical and radiological examinations regarding TNM classification revealed that 1 patient (2.5%) had Stage 2A, 10 (25%) had Stage 2B, 9 (22.5%) had Stage 3A, 10 (25%) had Stage 3B, 7 (17.5%) had Stage 3C, and 3 (7.5%) had Stage 4 disease. None of the NAC patients had Stage 1 disease. Post-surgical pathological examination revealed that 10 patients (25%) had

Stage 1, 12 (30%) had Stage 2A, 1 (2.5%) had Stage 2B, 1 (2.5%) had Stage 3B, 7 (17.5%) had Stage 3C, and 1 (2.5%) had Stage 4. In 8 patients (20%), pathological complete response was achieved. These results showed that NAC significantly ensured downstaging. Stages of our patients statistically significantly decreased clinically and radiologically ($p<0.001$) (Fig. 4).

Evaluation of NAC effects regarding PET-CT scans revealed complete response in 20 (50%) patients, partial response in 10 (25%) patients, and stable disease in 10 (25%) patients. Comparison of these results with pathological results showed that complete response was obtained only in 8 (20%) patients, whereas partial response was obtained in 22 (55%) patients, with stable disease in the remaining 10 (25%) patients. According to these findings, specificity and sensitivity of PET-CT in assessment of complete response were 62.5% and 100%, respectively. Positive predictive ratio was 40% and negative predictive ratio was 100%. This suggests that PET-CT does not miss patients with complete response; however, as the tumor diameter and axillary lymph node involvement decrease, patients with partial response are misdiagnosed as complete response, and this was statistically significant ($p<0.01$) (Fig. 5).

According to luminal staging, 5 patients were Luminal A, 14 were Luminal B, 17 were HER2-positive, and 4 were triple-negative. Regarding this classification, response to NAC was 82% in HER2-positive patients, 100% in triple-negative patients, 80% in Luminal A patients, and 57% in Luminal B patients (Fig. 6).

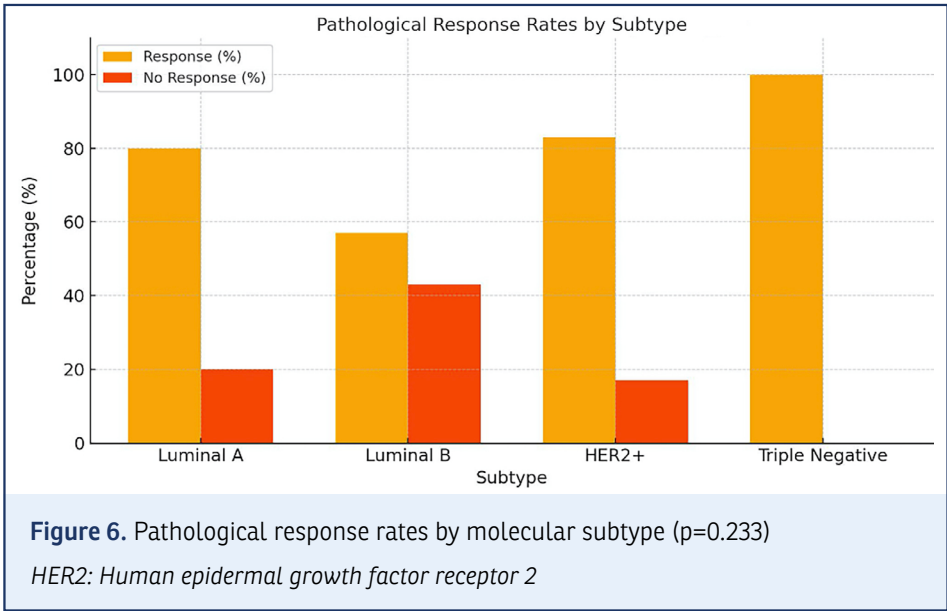


DISCUSSION

Neoadjuvant chemotherapy (NAC) was developed for the treatment of locally advanced breast cancer and is now part of the routine management of biologically aggressive disease, especially for ER-negative and/or HER2-positive cancers. NAC provides survival rates similar to adjuvant chemotherapy.^[7] Moreover, NAC gives an opportunity to perform breast-conserving surgery in patients planned to have mastectomy before NAC, either by disappearance of disease or decreasing tumor

size.^[15] Many studies suggest the possibility of sentinel lymph node biopsy (SLNB) in both node-negative and node-positive patients, thus avoiding unnecessary axillary dissections.^[16–18]

In our study, less aggressive surgical options were possible due to the downstaging effect of NAC. Moreover, 92.5% node positivity before NAC decreased to 30%, allowing avoidance of axillary dissection and its complications in most of them after chemotherapy. However, although PET-CT detected 12 lymph node metastases after NAC, patho-



logical examination revealed macrometastases in 15 patients and micrometastases in 3 patients ($p<0.05$).

Also, mean tumor size was higher in the postoperative pathological evaluation compared to the tumor size measured before NAC ($p<0.05$). These two statistically significant findings suggest to us that as the tumor size and lymph node involvement decrease, detection of tumoral activity in PET-CT decreases. Therefore, SLNB should always be performed in patients with axillary lymph nodal metastasis regression.

Response to NAC is strongly related to the tumor biology, as especially triple-negative and HER2-positive breast cancers have a better response to NAC, with even subtypes of such tumors differing significantly.^[19]

In our study, of 30 patients with complete or partial response, 14 were HER2-positive and 4 were triple-negative. Although this was not statistically significantly different ($P = 0.233$), our results about outcomes after NAC were compatible with the literature suggesting that NAC is more beneficial in such patients.^[20,21]

In studies investigating the malignant disease response following NAC, certain evaluation criteria previously applied^[22–25] were adapted into a more practical format, and patient responses were assessed using PET-CT. All patients who were found to have a complete pathological response were also evaluated as having a complete response on PET-CT. However, the detection of micrometastases or low-volume metastases in some patients deemed negative on PET-CT has raised concerns regarding the reliability of this imaging modality.

In some previous studies, patients with complete response were not operated on; however, local recurrence rates were

higher in this group. The reason for these recurrences was thought to be due to neglect of local therapies.^[13,14] In another meta-analysis, NAC was shown to be as effective as adjuvant therapy in decreasing distant recurrence and mortality but was associated with a higher incidence of local recurrence than adjuvant chemotherapy.^[12] This may partially explain the higher use of BCS after NAC compared to adjuvant chemotherapy. From our point of view, in patients with complete response, if tumor marking is not performed before NAC, providing safe tumor-free margins in such non-palpable tumors may be the cause of inadequate local control. Therefore, in order to reduce the incidence of local recurrence in patients with complete and partial response after NAC therapy, strategies like precise tumor localization, detailed pathological examination, and appropriate radiotherapy treatment should be taken into consideration.^[12]

The appropriate imaging study after NAC to assess response is still under discussion. There are studies supporting the use of PET-CT, which is currently popular but not considered the primary diagnostic test, as well as studies favoring classical dynamic contrast-enhanced MRI. Some studies suggest PET-CT as the first-line imaging modality, while others recommend MRI, leading to confusion.^[26,27] Some studies report that the sensitivity of MRI for detecting lymph node metastasis is moderate.^[28] To resolve these debates, improvements in MRI or the development of new imaging techniques are necessary.^[29] Recent studies integrating PET-CT with MRI have shown promising results.^[30]

In our study, evaluation of NAC with PET-CT revealed a positive predictive value of 40% and a negative predictive value of 100%,

which is consistent with some reports in the literature, although the limited number of patients may be a study limitation.

CONCLUSION

NAC provides BCS by shrinkage of tumor and improvement of axillary involvement in locally advanced breast cancer cases. In our study, PET-CT is shown to have high sensitivity but limited specificity and low positive predictive value in detection of complete response after NAC. These results suggest that to assess the response to NAC, PET-CT may be supported by conventional imaging studies like MRI to obtain adequate oncological and functional results while planning further treatment modalities like surgery and radiotherapy.

Disclosures

Ethics Committee Approval: The study was approved by the Istanbul Aydın University Non-interventional Clinical Research Ethics Committee (No: 165/2025, Date: 06/08/2025).

Informed Consent: Written informed consent was obtained from all patients.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Use of AI for Writing Assistance: Artificial intelligence was used to generate the figures. Graphical visualizations illustrating the distribution of clinical and pathological responses according to molecular subtypes in patients receiving neoadjuvant chemotherapy for breast cancer were generated using the artificial intelligence tool ChatGPT (GPT-5, OpenAI, August 2025 version). Aggregated, anonymized study data were provided to the AI system without any patient-identifiable information. The prompts included detailed instructions specifying the type of figure (e.g., bar chart, pie chart), axis labeling, color coding for molecular subtypes, and legend formatting. The generated figures were reviewed and finalized by the authors to ensure accuracy and consistency with the study results.

Author Contributions: Concept – S.B., S.K.; Design – S.B., Y.E.A., S.K.; Supervision – S.B., B.K., S.K.; Materials – S.B., C.E.; Data collection and/or processing – S.B., C.E., S.K.; Data analysis and/or interpretation – S.B., Y.E.A., B.K.; Literature search – S.B., Y.E.A., B.K., C.E.; Writing – S.B., C.E., S.K.; Critical review – S.K., Y.E.A., B.K., C.E., S.K.

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