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Original Article

Our Axilla Approach Following Neoadjuvant Chemotherapy in Breast Cancer Patients with Axillary Involvement

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Keywords: Axillary dissection; breast cancer; neoadjuvant chemotherapy; sentinel lymph node.

ABSTRACT

Objective: In this study, we aim to determine the condition of the breast cancer patient's axilla after neoadjuvant chemotherapy (NACT) with PET/CT, evaluate our approach to the axilla after sentinel lymph node biopsy (SLNB), and examine the axillary lymph node dissection (ALND) and its results in the light of the literature.

Methods: In Kartal Dr. Lütfi Kırdar City Hospital, 100 women patients who were diagnosed with breast cancer and operated after NACT between 2016 and 2019 were evaluated retrospectively. Patients were evaluated in terms of tumor size, stage, presence or absence of axillary involvement before and after NACT, age, the operation performed, follow-up time, recurrence, pathological status of the axilla, and mass.

Results: In this study, the mean age was 53.4±11 years (26–75 years). The mean tumor diameter was 29.06±13 mm (10–80 mm) before NACT and 13.42±17 mm (0–80 mm) ($p<0.001$) after NACT. The mean tumor diameter in the pathogen specimen was 14.91±19 mm (0–80 mm). Before NACT, 36 of our patients were stage III and 64 were stage II. After NACT, 79 of our patients were downstage ($p<0.001$), 18 patients did not change in stage, and 3 patients progressed from stage II to III. Pathological complete response was obtained in a total of 34 patients (38%). Before NACT, all patients had axillary lymph node (LN) positivity clinically and visually. SLNB was negative in 51 of 100 patients who underwent SLNB and positive in the remaining 49 patients. After ALND of positive patients, it was seen that the positive LNs of 25 patients were removed by SLNB. Metastasis to other LNs was also detected in 24 patients.

Conclusion: We concluded that it would be appropriate to consider NACT for breast cancer and it would be appropriate to make a surgical decision for axilla after SLNB.

INTRODUCTION

Breast cancer is acommon disease in women. It is reported that the incidence of breast cancer and other cancers increases year by year.[1] Breast cancer incidence and mortality rates remain high worldwide.[2,3] With the increase in knowledge and experience about breast cancer and the rapid development of adjuvant therapies, there have been great changes in breast cancer surgery in the last three decades. Methods using radical surgery have been replaced by more patient-centered conservative treatment by adding multimodality.[4] One of them is the increasing use of neoadjuvant chemotherapy(NACT). NACT is used with increasing frequency in breast cancer for.[5,6]

The National Comprehensive Cancer Network underlined that NACT is a preferable approach in breast cancer.[7]

Applying chemotherapy to the patient before the operation causes the tumor to shrink, facilitating its resectability and negative surgical margin. Based on the PET/CT results, the tumor's response to NACT can be seen;therefore, the prognosis of the patient can be predicted and the patient's treatment can be arranged.[8,9] Thus, it enables breast-conserving surgery (BCS) to be performed by preventing mastectomy.[10] In addition, axillary node-positive patients also may have significant negative axilla after NACT.[11] In this situation, less invasive axillary therapy is applied to these patients who have clinically N0 after NACT. Unnecessary complicatedinterventions were avoided by evaluating using sentinel lymph node biopsy (SLNB) instead of axillary lymph node dissection (ALND).[12,13]

In this study,our aim is to determine the condition of the patient's axilla especially after NACT with PET/CT, examine our approach to the axilla after SLNB in our clinic,

and examine the avoidance of ALND in the light of the literature.

MATERIALS AND METHODS

A total of 100 women patients, who were diagnosed with breast cancer and operated after NACT between 2016 and 2019, were retrospectively evaluated. The data were obtained from the hospital archive. Patients were evaluated in terms of tumor size, stage, presence or absence of axillary involvement before and after NAC, age, the operation performed, follow-up time, recurrence, pathological status of the axilla, and mass.

Ethical approval was obtained (Decision number: 2020/514/179/38; Date: June 11, 2020).

All patients underwent trucut biopsy without ultrasound (palpable masses) or with ultrasound guidance. In the first examination, the tumor size and LN status of each patient were evaluated by ultrasound and PET/CT, and the results were recorded. Immunohistochemistry subtypes were determined according to estrogen and progesterone, Ki-67 level, and HER2 status.

Evaluation of clinical and radiological responses was done before and after NACT. All patients underwent PET/CT before and after NACT. The tumor was evaluated according to the TNM system.

The decision for surgery was made after evaluating the results following NACT. The treatment decision was made mainly according to the patient's request and the patient's age, response to NACT, and breast and tumor size.

ALND was done based on the SLNB result.

Chi-squared and Kaplan–Meier analyses were used for statistical evaluation.

Exclusion criteria: Male sex, age under 18 and above 80 years, pregnant women, patients who previouslyunderwent breast surgery, patients with other oncological diseases, patients who were lost to follow up, ASA4 patients, patients for whom PET/CT could not be reached before and after the NACT.

RESULTS

In our study, our youngest patient was 26 years old, and our oldest patient was 75 years old. The mean age was 53.4±11 years. The tumor was located in the left breast in 58 of our patients and in the upper outer quadrant in 31 patients. Of the 100 patients, 72 were postmenopausal and 28 were premenopausal. Forty-eight of our patients underwent modified radical mastectomy (MRM), 18 mastectomy, 27 BCS, and 7 underwent BCS and axillary dissection (since SLNB was positive) (Table 1).

The mean tumor diameter of our patients was 29.06±13 mm (10–80 mm) before NACT and 13.42±17 mm (0–80 mm) after NACT. The mean tumor diameter in the pathogen specimen was 14.91±19 mm (0–80 mm). Of our patients, 91% were diagnosed with invasive carcinoma, 6% lobular carcinoma, 2% mucinous carcinoma, and 1% neuroendocrine carcinoma. Before NACT, 36 of our patients were in stage III and 64 were in stage II. After NACT, 30 patients were evaluated as stage I and 37 patients asstage 0 (Table 2). Thirty-eight patients had complete remission according to PET/CT image. Six of these patients did not have pathological complete remission (pCR). pCR was obtained in 2 patients in whom complete remission images could not be obtained on PET/CT. In total, 34 patients (38%) had pCR.

Table 1. Clinicopathological characteristics of the patients

Features	Result
Age	
Median	53±11
Interval	26–75
Menstrual statu	
Premenopausal	28
Postmenopausal	72
Breast	
Right	42
Left	58
Quadran	
Upper outer	59
Lower outer	18
Upper inner	10
Lower inner	9
Areola	5
Surgery	
MRM	48
Mastectomy	18
BPS	27
BPS+ALND	7
Follow up time	
Median	17.80±13
Interval	8–50 month

BPS: Breast protection surgery; MRM: Modify radical mastectomy; ALND: Axillary lymph node dissection.

Table 2. Stage

Before NACT		After NACT	
Stage II	64 patients	Stage 0	27 patients
Stage I	22 patients		
Stage II	12 patients		
Stage III	3 patients		
Stage III	36 patients	Stage 0	11 patients
Stage I	7 patients		
Stage 2	12 patients		
Stage III	6 patients		
Total	100	Total	100

NACT: Neoadjuvant chemotherapy.

Table 3. Distribution of pathological complet response by receptors

Receptors state	pCR
Hormone(+)/HER2(+)	14 (14/25)
Hormone(-)/HER2(+)	8 (8/9)
Hormone(+)/HER2(-)	10 (10/56)
Trible negative	2 (2/10)
Total	34 (34/100)

pCR: Pathological complet response.

Table 4. Receptors state

Receptors	Patients
Hormone(+)/HER2(-)	56
Hormone(-)/HER2(+)	9
Hormone(+)/HER2(+)	25
Triple negative	10
Total	100

Table 5. Pathologic remission status after NACT

Number of patients	Remission
31	No
35	Partial
34	Complete
100	Total

NACT: Neoadjuvant chemotherapy.

Before NACT, all patients had axillary LN positivity clinically and visually. LN positivity was detected in 25 patients (25%) after NACT. Other patients were also evaluated as LN visually and clinically negative. Twenty-five patients with LN positive on PET/CT imaging who underwent SLNB were positive in 24 except one. We detected 25 (33%) positivity in SLNB of 75 patients whose axilla was evaluated visually as negative. Of the 100 patients who underwent SLNB, 51 patients were negative and 49 patients were positive. After the axillary dissection of the positive patients, it was observed that the positive LNs of 25 patients were removed by SLNB. In 24 patients, there was also spread to other LNs.

The pCR status (Table 3) was mostly (88%) in the hormone negative and HER2 positive patient group. According to the receptor status, 10 patients were triple negative, 56 patients were HER2 negative, and 34 patients were HER2 positive (Table 4).

Our mean Ki-67 value was 35.04±19.36 (1–80). The mean follow-up time of the patients was 15.30±10.73 months (8–50 months). The pathological response of NACT was complete in 34 patients, unresponsive in 31 patients, and partial in 35 patients (Table 5).

DISCUSSION

In the last 20 years, the management of breast cancer patients has turned toward less invasive axillary surgery. Two main strategies contributed to this situation: the development of SLNB[14] and the implementation of the NACT.[15] Effective chemotherapy regimens, radiotherapy (RT), and endocrine treatment have affected breast cancer operation models in a way that moves away from radical methods.[16] Preoperative treatments significantly increased compared with the previous decade, which increased operability rate, BCS rate, and pCR rate.[17] Individual medical practice and breast cancers that respond to selected NACT regimens led to a negative node of 40% of node positive.[18] In our study, the LN turned negative in 51% of patients after applying NACT. NACT is currently applied widely in breast cancer to convert an inoperable tumor to operable or to convert an operable tumor to BCS.[19,20] It has been observed that 40–60% of patients with clinically positive nodes benefit from NACT with a pCR.[21] Acquisition of axilla pCR has a strong correlation with prognosis, whether or not there is a residual tumor in the breast.[17] In our study, we found that 51 of 100 patients were SLNB negative after NACT. Our complete remission rate in the axilla was 51%, which is consistent with the literature. Again, our tumor diameters decreased after NACT (from 29.06±13 mm to 13.42±17 mm) ($p<0.001$). Before NACT, 36 of our patients were stage III and 64 were stage II. After NACT, 79 of our patients were downstage ($p<0.001$), 18 patients did not change in stage, and 3 patients progressed from stage II to III (Table 2).

As there was not enough information about whether preoperative LNs were fixed and conglomerate and their numbers in our patients, subgroups could not be specified in clinical TNM staging. Therefore, subgroups were not taken into consideration in pathological staging as there was no difference in preoperative and postoperative stage evaluation. This is a limitation of our study.

Again, the pCR status according to the receptor status was the most (88%) in the hormone negative and HER2 positive patient group in accordance with the literature (Table 3).[6]

In the last two decades, SLNB has become the standard approach for surgical staging, replacing excessive morbidity of ALND in clinically node-negative primary surgery.

SLNB high negative predictive value indicates that patients with node negative have no additional axillary node involvement. As a result, these patients are not exposed to ALND and their morbidity decreases.[22] At the same time, ALND was overtreatment even in SLNB with micrometastases and had no effect on disease-free survival.[23]

Previous studies have also stated that performing SLNB after NACT accurately shows the condition of the axilla.[24]

However, there is controversy about the evaluation of ALN status after NACT among patients with initial node metastasis.[25] The St. Gallen International Exper Consensus Conference recommended SLNB to evaluate the axilla

after NACT in patients with axilla node positive before NACT. They also reported that the reliability of SLNB in patients was dependent on the number of LNs removed.[16] In our study, we applied SLNB to all patients. If there was no clinical suspicion, ALND was not applied to those who were negative.The number of LNs removed was 3 or more(86%).OneLN in 2 patients andtwoLNs in 12 patients were removed.

If we look at the operations performed in our study, we see that MRM is excessive. This is due to the fact that even a small suspicion is directed to MRM since patients receive NACT and the tumor is not clipped before NACT. When we retrospectively evaluate the operations performed, we see that the metastatic LNs were removed during SLNB in most patients (51%) (25 patients/49 patients) who underwent ALND, and that the subsequent LNs were clean. Only 24 patients had involvement in other LNs.

Involvement of other LNs was detected in only 24 of 49 patients with positive SLNB. In other words, ALND was unnecessarily applied to 25 patients.

It guides us in evaluating the PET/CT stage before and after NACT and in our approach to the axilla. Its ability to capture dynamic metabolic changes makes PET/CT a powerful element in determining the response of breast cancer under NACT.[26] In our study, the presence of metastatic LN was detected by PET/CT in 25 of 100 patients after NACT, and 24 of them were found to be SLNB positive. Although PET/CT alone stated that LN was not observed in 75 patients, 25 of them were SLNB positive. Therefore, our false-negative rate is above 10%, which is accepted as the upper limit. This may be due to the fact that images that may be slightly suspicious are evaluated as intact.

Whether ALND can be excluded in favor of axillary RT in patients with positive SLNB after NACT is currently being investigated in the ongoing phase III Alliance A011202 study.[27]

We did not detect recurrence in our patients. We attribute this to our short follow-up period.

The limitations of our study are that it is single-centered, the number of cases is low, it is retrospective, and subgroups are not specified in the TNM classification.

CONCLUSION

We evaluated that it would be appropriate to consider NACT in breast cancer and a surgical decision after SLNB for axilla until the results of the ongoing RT studyfor axilla are announced.

Ethics Committee Approval

This study approved by the Kartal Dr. Lutfi Kirdar City Hospital Clinical Research Ethics Committee (Date: 11.06.2020, Decision No: 2020/514/179/38).

Informed Consent

Retrospective study.

Peer-review

Internally peer-reviewed.

Conflict of Interest

None declared.

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AksillaTutulumu Olan Meme Kanseri Hastalarında Neoadjuvant Kemoterapi Sonrası Aksillaya Yaklaşımımız

Amaç: Bu yazının amacı, meme kanseri nedeni ile neoadjuvant kemoterapi (NAKT) gören hastaların aksillalarının durumunu PET/BT ile değerlendirmek ve sentinel lenf nodu biyopsisi (SLNB) ile aksillaya yaklaşımımızı ve aksiler lenf nodu diseksiyonunu ve sonuçlarını literatür eşliğinde irdelemektir.

Gereç ve Yöntem: 2016–2019 yılları arasında Kartal Dr. Lütfi Kırdar Şehir Hastanesinde meme kanseri tanısı alıp NAKT sonrası ameliyat edilen 100 kadın hasta geriye dönük olarak değerlendirildi. Hastalar yaş; NAKT öncesi tümör çapı, evre, aksiler tutulum olup olmaması NAKT sonrası tümör çapı, evresi, aksilla durumu, yapılan ameliyat ve ameliyat sonucu patolojik olarak aksilla ve kitle durumu, takip süresi ve nüks açısından değerlendirildi.

Bulgular: Bu çalışmada, yaş ortalaması 53.4±11 idi (26/75). Hastaların neoadjuvant kemoterapi (NAKT) öncesi tümör çapı ortalaması 29.06±13 mm (10–80 mm), NAKT sonrası tümör çapı 13.42±17 mm (0–80 mm) ($p<0.001$) idi. Patojoli spesmeninde ise tümör çapı ortalamsı 14.91±19 mm (0–80 mm) idi. NAKT öncesi hastaların 36'sı evre III, 64'ü evre II idi. NAKT sonrası; 79 hastanın evresi geriledi ($p<0.001$), 18 hastada evre gerilemesi olmadı, üç hastanın evresi II'den III'e ilerledi. Toplam 34 hastada (%38) patolojik tam yanıt (pCR) elde edildi. NAKT öncesi bütün hastalarda klinik ve görüntüsel olarak aksillar lenf nodu (LN) pozitifliği vardı. NAKT sonrası SLNB yapılan 100 hastanın 51'inde SLNB negatif, 49 hastada pozitif idi. Pozitif gelen hastaların aksiler diseksiyonundan sonra 25 hastanın pozitif lenf nodunun SLNB ile çıkarılmış olduğu görüldü. Yirmi dört hastada ise diğer lenf nodlarında da yayılım vardı.

Sonuç: Meme kanserinde NAKT'nin dikkate alınması ve aksilla için SLNB sonrası cerrahi karar vermenin uygun olacağını değerlendirdik.

Anahtar Sözcükler: Aksiller diseksiyon; meme kanseri; neoadjuvant kemoterapi; sentinel lenf nodu.