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Relationship Between Axillary Metastasis and Tumoral Response and Biomarkers in Breast Cancer Patients Who Received Neoadjuvant Chemotherapy

Neoadjuvan Kemoterapi Almış Meme Kanseri Hastalarında Aksiller Metastaz ve Tümöral Yanıtın Biyobelirteçlerle İlişkisi

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ABSTRACT

Introduction: The molecular subtype of the disease is related to the patient's clinical course, response to chemotherapy, and pathological response rates.
Objective: The molecular subtype of the disease is related to the patient's clinical course, response to chemotherapy, and pathological response rates. This research aimed to elucidate the relationship between neoadjuvant chemotherapy and treatment response in breast cancer patients who received neoadjuvant therapy and were evaluated with axillary lymph nodes after surgery.
Method: This retrospective analysis investigated the relationship between axillary metastasis status, tumoral and pathological complete response status, and molecular subtypes in 103 patients who received neoadjuvant chemotherapy for breast cancer and whose axillary lymph nodes were evaluated. Patients' age, menopause status, type of surgery, tumor side, axillary involvement, nodal involvement, T staging, histopathological type and subtypes, tumor receptors, perineural invasion, lymphovascular invasion, and tumor necrosis data were obtained from hospital records.
Results: A total of 103 female patients were included in the study. Histopathologically, the most common subtype was invasive ductal carcinoma (89.3%), and hormone receptor status was determined as ER-positive (73.8%) and PR positive (63.1%). Molecular subtypes were defined as Luminal B (36.9%) and Luminal A (34%), and the most common tumor grade was grade 2 (57.3%). The most common surgical method after neoadjuvant chemotherapy was radical mastectomy (97.1%). Among the cancer subgroups evaluated after neoadjuvant therapy, the most frequent subgroups with tumoral complete response were HER2 positive (47.4%), and triple-negative (45.5%) groups, the most frequent groups showing nodal complete response were HER2 positive (47.4%) and triple negative (63.6%) groups. The most frequent subgroups showing pathological complete response were HER2 positive (21.1%) and triple negative (36.4%) groups.
Conclusion: Breast cancer genetic subgroups are associated with treatment responses following neoadjuvant chemotherapy. Among breast cancer subgroups, the subgroups that provide the best tumoral, nodal, and pathological complete response to neoadjuvant chemotherapy are HER2-positive breast cancers and triple-negative breast cancer types.

Keywords: Breast Cancer, Neoadjuvant Chemotherapy, Tumor Subtype, Tumor Biology, Pathological Response.

ÖZET

Giriş: Hastalığın moleküler alt tipi hastanın klinik seyri, kemoterapiye yanıtı ve patolojik yanıt oranları ile ilişkilidir.
Amaç: Bu araştırma, neoadjuvan tedavi alan ve ameliyattan sonra aksiller lenf nodları ile değerlendirilen meme kanseri hastalarında neoadjuvan kemoterapi ile tedavi yanıtı arasındaki ilişkiyi açıklamayı amaçlamaktadır.
Yöntem: Bu retrospektif analiz, meme kanseri için neoadjuvan kemoterapi alan ve aksiller lenf nodları değerlendirilen 103 hastada aksiller metastaz durumu, tümöral ve patolojik tam yanıt durumu ve moleküler alt tipler arasındaki ilişkiyi araştırmıştır. Hastaların yaşı, menopoz durumu, ameliyat türü, tümör tarafı, aksiller tutulum, nodal tutulum, T evrelemesi, histopatolojik tip ve alt tipler, tümör reseptörleri, perinöral invazyon, lenfovasküler invazyon ve tümör nekrozu verileri hastane kayıtlarından elde edildi.
Bulgular: Çalışmaya toplam 103 kadın hasta dahil edildi. Histopatolojik olarak en sık görülen alt tip invaziv duktal karsinom (%89.3) iken, hormon reseptör durumu ER-pozitif (%73.8) ve PR pozitif (%63.1) olarak belirlendi. Moleküler alt tipler Luminal B (%36.9) ve Luminal A (%34) olarak tanımlandı ve en sık görülen tümör derecesi 2 (%57.3) olarak belirlendi. Neoadjuvan kemoterapi sonrası en sık uygulanan cerrahi yöntem radikal mastektomi (%97.1) idi. Neoadjuvan tedavi sonrası değerlendirilen kanser alt grupları arasında tümöral tam yanıt gösteren en sık alt gruplar HER2 pozitif (%47.4) ve üçlü negatif (%45.5) gruplardı, nodal tam yanıt gösteren en sık gruplar HER2 pozitif (%47.4) ve üçlü negatif (%63.6) gruplardı. Patolojik tam yanıt gösteren en sık alt gruplar HER2 pozitif (%21.1) ve üçlü negatif (%36.4) gruplardı.

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Sonuç: Meme kanseri genetik alt grupları neoadjuvan kemoterapi sonrası tedavi yanıtlarıyla ilişkilidir. Meme kanseri alt grupları arasında, neoadjuvan kemoterapiye en iyi tümöral, nodal ve patolojik tam yanıtı sağlayan alt gruplar HER2 pozitif meme kanserleri ve üçlü negatif meme kanseri tipleridir.

Anahtar Kelimeler: Meme Kanseri, Neoadjuvan Kemoterapi, Tümör Alt Tipi, Tümör Biyolojisi, Patolojik Yanıt.

INTRODUCTION

According to the World Health Organization (WHO) data, it is stated that cancer is the second cause of death over the globe. Lung cancer in men and breast cancer in women are the most common cancer types, and breast cancer is the fifth most common type of cancer among all cancer deaths (1). In Turkey, breast cancer is seen at a frequency of 20/100.000 in our eastern region and 40-50/100.000 in our western region. It is stated that factors such as excessive hormone replacement therapy, shorter lactation periods, differences in nutritional habits, and adopting a Western lifestyle are influential in this situation. According to the National Breast Cancer Database, the incidence of breast cancer in women in Turkey was reported as 26% in 2020, which was consistent with the rest of the world (2).

Most patients diagnosed with operable breast cancer and indicated for chemotherapy are given chemotherapy before surgery. Neoadjuvant chemotherapy aims to reduce the tumor burden and size before surgical resection, to reduce the axillary metastasis burden, and to eliminate possible small-scale systemic metastasis foci. The reduction of tissue to be resected offers the patient the chance of breast-conserving surgery. In addition to the tumor-reducing effect of neoadjuvant therapy, it can convert local lymph node positivity into node-negative disease. Although the focal response varies according to the subtype and genetics of the cancer, it has been reported that neoadjuvant chemotherapy (CT) can result in a complete nodal response, thus determining the patient's life expectancy (3). In the initial treatment planning, knowing the tumor subgroup and marker load is essential in choosing the most personalized and effective treatment type. Breast cancers are divided into subtypes that vary in their behavioral characteristics, response to treatment, and prognosis (4).

Although molecular subtyping is the most accurate classification, it is often classified according to the status of hormone receptors and human epidermal growth factor receptor-2 in clinical practice. The molecular subtype of the disease is related to the patient's clinical course, response to chemotherapy, and pathological response rates. Within the scope of this research, we aimed to elucidate the relationship between neoadjuvant chemotherapy and treatment response (tumoral, nodal, pathological, and complete response) in breast cancer patients who received neoadjuvant therapy and were evaluated with axillary lymph nodes after surgery.

METHOD

This retrospective analysis investigated the relationship between axillary metastasis status, tumoral and pathological complete response status, and molecular subtypes in 103 patients who received neoadjuvant chemotherapy for breast cancer and whose axillary lymph nodes were evaluated. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution with protocol number 1608, and informed consent has been obtained from all participants.

The patients (n=103) who underwent axillary dissection after neoadjuvant chemotherapy were selected from a decade between 01.01.2010 and 01.01.2020. Patients' age, menopause status, type of surgery, tumor side, axillary involvement, nodal involvement, T staging, histopathological type and subtypes, tumor receptors, perineural invasion, lymphovascular invasion, and tumor necrosis data were obtained from hospital records.

Inclusion Criteria

The inclusion criteria for the study were patients aged 18 years and over who had undergone surgery, who had female breast cancer, who had received neoadjuvant chemotherapy, who had undergone axillary dissection, and who had no deficiencies in their treatment and file records.

Exclusion Criteria

Exclusion criteria for the study were patients with incomplete files, patients who did not continue their follow-up, male patients under 18 years of age, and patients who did not undergo axillary dissection or core needle biopsy.

Statistical Analysis

Patient data collected within the scope of the study were analyzed with the IBM Statistical Package for the Social Sciences (SPSS) for Windows 26.0 (IBM Corp., Armonk, NY) package program. Frequency and percentage for categorical data and mean and standard deviation for continuous data were given as descriptive values. For comparisons between groups, the "Independent Sample T-test" was used for two groups, and the "Pearson Chi-Square Test" was used to compare categorical variables. The results were considered statistically significant when the p-value was less than 0.05.

RESULTS

This analysis included 103 patients who underwent axillary dissection after neoadjuvant CT between 2010 and 2020. All patients were female; their mean age was 55±11.8 (Min 26, Max 89 years). It was determined that 24 (23.3%) patients were in menopause. No statistically significant relationship was found between tumoral response, nodal response, and complete pathological response regarding menopausal status (p>0.05).

Table 1. Histopathology Results of Core Needle Biopsy Performed Before Neoadjuvant LT

	N	%
lnvazive Ductal Carcinoma	92	89.3
Invazive Lobular Carcinoma	7	6.8
Medullary Carcinoma	2	1.9
Mucinous Carcinoma	2	1.9
Total	103	100.0

Table 2 examines preoperative tumor location and staging. It determined that 58.3% of the patients had left breast involvement, 93.2% had axillary involvement, 48.5% had T2 involvement, and 59.2% had I involvement. The number of patients with negative lymph node scores before neoadjuvant administration was 7 (Table 2). There was no statistically significant relationship between tumoral response, nodal response, and pathological complete response regarding the side of the tumor (p>0.05).

Invasive ductal carcinoma was detected (89.3%) in the thick needle biopsy performed before neoadjuvant CT (Table 1). Estrogen receptor positivity (ER +) was detected in 73.8%, and progesterone receptor positivity (PR +) in 63.1%. The most commonly detected thick needle biopsy was a Grade 2 tumor (Table 2). The KI-67 of the patients was 27.4 ± 21.6 in the preoperative biopsy.

In the subtype calculations, KI-67 was 20% and above positive. The most common tumor subtype was Luminal B (36%), followed by Luminal A (34%). The distribution of other subtypes is given in Table 3. After neoadjuvant KT, 97.1% of the patients underwent modified radical mastectomy. The mean number of dissected lymph nodes in the patients was 17.5±66 (median: 17, min: 5, max: 39). The mean positivity in the obtained lymph nodes was 2.9±4.5 (median: 1, min: 0, max: 21).

Table 2. Histopathology Results and Receptor Status of Bone Needle Biopsy Performed Before Neoadjuvant KT

		N	%
ER	Negative	27	26,2
	Positive	76	73,8
PR	Negative	38	36,9
	Positive	65	63,1
C-ERB2	Negative	64	62,1
	Positive	39	37,9
Tumor Necrosis	Negative	84	81,6
	Positive	19	18,4
Lymphovascular Invasion	Negative	56	54,4
	Positive	47	45,6
Perineural Invasion	Negative	91	88,3
	Positive	12	11,7
Tumor Grade	I	7	6,8
	II	59	57,3
	III	37	35,9

**ER: Estrogen Receptor, PR: Progesterone Receptor, C-ERB2: protein involved in normal cell growth.*

Table 3. Subtype Result Distribution of Core Needle Biopsy Performed Before Neoadjuvant KT

	N	%
Luminal A	35	34
Luminal B	38	36,9
HER-2 (+)	19	18,4
TRIPPLE (-)	11	10,7
TOTAL	103	100

***HER-2: human epidermal growth factor receptor 2.*

Table 4. Histopathological Features and Receptor Status of Thick Needle Biopsies Before Neoadjuvant LT Distribution of Tumoral, Nodal, and Pathological Diagnosis After Treatment

		Tumor Response		Complete Nodal Response		Complete Pathologic Response	
		N	%	N	%	N	%
ER	Negative	12	38,7	15	36,6	7	39
	Positive	19	61,3	26	63,4	11	61
PR	Negative	17	54,8	20	**48,8**	9	50
	Positive	14	45,2	21	51,2	9	50
C-**ERB2**	Negative	13	41,9	23	56,1	9	50
	Positive	18	58,1	18	43,9	9	50
Tumor Necrosis	Negative	27	87,1	33	80,5	14	78
	Positive	4	12,9	8	19,5	4	**22**
Lymphovascular Invasion	Negative	19	61,3	26	63,4	12	67
	Positive	12	**38,7**	15	36,6	6	33
Perineural Invasion	Negative	30	96,8	37	90,2	18	100
	Positive	1	3,2	4	9,8	0	0
Tumor Grade	I	2	6,5	2	4,9	1	5,6
	II	21	67,7	14	58,5	12	67
	III	8	25,8	15	36,6	5	28

**ER: Estrogen Receptor, PR: Progesterone Receptor, C-ERB2: protein involved in normal cell growth.*

The mean follow-up period of the patients was 21.6±10.1 months. The number of patients with surgical smear positivity was 0%. No patient was surgically positive. While the mean preoperative tumor size was 30.0±17.5 mm, the mean tumor size in the final specimen was 20.9±22.7. This difference in tumor size was statistically significant ($p<0.05$).

Complete Response (CR)

The mean age of 31 patients (30.1%) who showed a complete response (CR) was 51.5±10.7, while the mean age of 72 patients who did not show a complete response was 57.6±11.8 with a statistically significant difference (p=0.0l6). No statistically significant relationship was found between tumor grade, ER (+), number of removed lymph nodes, tumoral necrosis, lymphovascular invasion, and perineural invasion (p>0.05) (Table 4). No statistical significance was found between ER (+), C-ERB (+), tumor grade, tumoral necrosis, KI-67, lymphovascular invasion, and perineural invasion (p>0.05). However, PR (-) was statistically significant in nodal complete response (p=0.042). The PR (-) (p=0.013) and C-ERB2 (+) (p=0.011) were statistically significant in tumoral complete response (Table 4). There was no statistically significant difference in ER (+), PR (+), C-ERB2 (+), tumor necrosis, or lymphovascular invasion (p>0.05). Perineural invasion (p=0.026) and KI-67 (+) (p=0.045) were statistically significant in pathological complete response. The number of removed lymph nodes was 1±1.82 in the group with tumoral complete response, while it was 3.76±4.98 in the group without complete response (p=0.002).

Nodal Complete Response

The mean age of the 41 (39.8%) patients with nodal complete response was 54.39±11.14, while the mean age of the group with no nodal complete response was 56.7±12.21 (p=0.03). No statistically significant difference was found between nodal complete response and histopathological distribution in the breast (p>0.05). Nodal complete response was the least in luminal A (28.6%), while it was most common in TRIPLE (-) patients.

Pathological Complete Response

The mean age of the 18 (17.4%) patients with pathological complete response was 51.33±11.57, while the mean age of the group without pathological complete response was 56.72±11.69. Although the age of the group with a pathological complete response was lower, this difference was not statistically significant (p=0.078). No statistically significant difference was found between pathological complete response and histopathological distribution in the breast (p>0.05). Tumoral complete response was detected at least in luminal A (20%), while it was most frequently detected in HER-2 (+) and TR.IPPLE (-) (47.4%, 45.5%), respectively. The tumor complete response rate was higher in patients with KI-672 than in patients with lower KI-67 values, which was statistically significant (p=0.042) (Table 3).

Pathological complete response was 11.42% (n=4) in luminal A and 15.78% (n=6) in luminal B. It was 21% (n=4) in HER2 and 36.6% in the TRIPPLE (-) group. For all groups, the number of axillary (+) lymph nodes detected in the TRIPPLE (-) group was 3.2±4.6, while the mean number of positive lymph nodes in other subtype groups was 0.5±0.8 (p=0.021).

DISCUSSION

Neoadjuvant therapy refers to systemic treatment of breast cancer before surgical treatment. Neoadjuvant chemotherapy (NACT) aims to reduce tumor size in locally advanced breast cancers, to provide the patient with a chance of breast cancer surgery (BCS), and to prevent micrometastatic foci while awaiting surgery. Neoadjuvant chemotherapy can eliminate disease in regional lymph nodes and convert node-positive disease into node-negative disease, reducing the size of primary tumors (5). Knowing the subtype of the disease affects the choice of chemotherapeutic agent, response to chemotherapy, and the risk of recurrence. Some studies have shown nodal pathological complete response rates of approximately 40% after NACT, and it has been demonstrated that the tumor molecular subtype is associated with the level of response (6). However, 20% of known cases do not receive the necessary response to neoadjuvant chemotherapy, and this patient group is delayed with ineffective treatment options, exposed to unnecessary chemotherapeutic toxicity burden, and loses the chance of

early surgery (7). This situation requires a detailed examination of the tumor group in which NACT treatment is sufficiently compelling to make personalized treatment plans.

In our clinic, 103 patients underwent neoadjuvant chemotherapy and then breast surgery in 10 years. The current study was conducted to determine whether the molecular structure of the tumor affects the type of breast surgery and to what extent tumor histopathology and tumor subtypes are related to the response to treatment after AKT. To investigate the effectiveness of neoadjuvant chemotherapy, we examined the patients' tumoral response, nodal response, and pathological complete response levels.

Factors that give an idea about the risk of disease recurrence independent of the treatment are prognostic factors, among which axillary node involvement status, tumor diameter, histological grade, and age are the most essential factors. In this study, patients with histopathologically proven clinical stage T0-T4 0-N2 M0 who received neoadjuvant treatment before surgery were examined. The mean age of these patients, all women, was determined to be 55 years. It was determined that a smaller portion of the patients included in the study (23.3%) were in menopause. The age and menopause status of our patients in the survey were unrelated to tumoral, nodal, and pathological complete responses. According to our study, age and menopause status were not found to be independent factors affecting the response of the disease to ACT. In our study, the mean age showed a significant difference only in patients who showed tumoral complete response; the mean age of patients who showed tumoral complete response (TCR) was 51 and 57 in those who did not show TCR, respectively.

As is known from the literature, the incidence of breast cancer is up to 4 times higher in women over 50 years of age than in younger women (8,9). Although it has been reported that younger patients may respond better to neoadjuvant therapy because proliferative tumors are frequently seen (10), studies also show that age is not related to response but inversely related (9). In addition to variable reports of results regarding response to treatment, studies on the effects of age and menopausal status on clinical course and prognosis are also variable; some studies fail to show a relationship between age and response, and publications suggest an inverse relationship (9). It is seen that large-scale meta-analyses are needed to standardize information regarding parameters such as age, menopausal status, breast cancer clinical course, prognosis, and response to neoadjuvant therapy.

It was observed that most of the patients in our study presented with left breast involvement. It was observed that the side of the disease was not related to the treatment response and was not a factor affecting the treatment. At the time of presentation, it was observed that all cases, except 6.7%, presented with non-involvement. The tumor size of the patients included in the study was 30 mm on average. The tumor size decreased to 20 mm after surgery and was found to be significantly different from the pre-surgery one. It was shown that the tumor diameter, clinical T stage, and clinical non-involvement stage (N I and N2) of the patients before neoadjuvant therapy were similarly distributed in the tumor subtypes. Second-degree tumors and I involvement were more frequent in number, although not significant. It can be suggested that this difference is not essential due to the relatively small number of our study patients. Similarly, it has been shown in the literature that in patients diagnosed with locally invasive breast cancer, the side of the breast affected by the disease is not related to the prognosis. Still, the disease burden, tumor size, and axillary node involvement have predictive value (10,11). In their study, Mamounas et al. reported that age, clinical features of the tumor, and initial lymph node involvement were factors affecting treatment success and locoregional recurrence after neoadjuvant CT (12).

In our study, the most common tumor type was invasive ductal carcinoma. Hormone (ER and PR) positivity was the most common receptor positivity in the entire cancer group, and the most common subtypes were Luminal B and Luminal A, respectively. The preoperative mean Ki-67 level was 27%. This information, which is consistent with the widely known general characteristics and distribution rates of locally invasive breast cancers, is consistent with many studies (13,14), as well as the latest data from the Surveillance, Epidemiology, and End Results (SEER) database of the National Cancer Institute

(15). It is known that ER and PR expression (especially ER positivity), as in Luminous A subgroup tumors, is generally associated with a good prognosis in the short term. This receptor status determines whether breast cancer requires adjuvant endocrine therapy (16–18). Knowing the genetic subtypes of cancer is essential for the type of neoadjuvant therapy to be planned. Personalization of breast cancer treatment should form the basis of the treatment strategy. Our study determined the mean value of Ki-67 before neoadjuvant CT to be 27%. TTY was found to be significantly higher in patients with lower Ki-67 positivity. Based on studies correlating Ki-67 expression with poor prognosis, it seems consistent that lower levels of Ki-67 are associated with better TTY response.

In our study, only 2.9% of the patients underwent BCS after neoadjuvant therapy, and the remaining patients underwent radical mastectomy. This result is far below the data in the literature. In one of the most comprehensive prospective clinical studies examining the effect of neoadjuvant therapy on surgery, the American College of Surgeons Oncology Group (ACOSOG) Z1071 study, it was reported that the breast-conserving surgery (BCS) rate after NACT increased to 40% (19). Another survey by Buzdar et al. (20), which examined the effect of subtypes on surgical options after neoadjuvant therapy, reported this rate as 38% in the Z1041 study. In addition, the triple-negative and HER2-positive tumor subtypes were significantly associated with selecting BCS as interventional treatment (19). According to the data obtained from this study, although the treatment success rates according to subgroups after ACT were parallel to the study reports presented by Palmer et al. (19) in 2018, the BCS rate was found to be significantly low in our clinic. The low rate of preventive surgery can be explained by the fact that our study was retrospective, and the preferences depended on the surgeon and patient preferences. We can report that the ongoing surgical treatments in our clinic are changing more in line with the current literature.

In our study, the treatment responses evaluated after neoadjuvant chemotherapy showed that the HER2 positive and triple negative groups showed the most common tumoral complete response, the most common nodal complete response, and the most common pathological complete response among the cancer subgroups. Histopathologically, Medullary carcinoma was the pathological subtype showing the most common tumoral complete response, nodal complete response, and pathological complete response (although not statistically significant). Ki-67 antibody deficiency was associated with pathological diagnosis response.

Our study determined that the molecular subtype in which TIY was most frequently observed in patients whose tumoral response was evaluated was HER2-positive patients. The subgroup with the least TTY response was Luminal A. Our results were consistent with other studies examining breast tissue and regional lymph node responses to AKT; according to ACOSOG 21071 (Alliance) study reports, the breast complete response rate in HER2 patients was determined as 49.8% (54), and according to Gem1an Breast Group reports, it was defined as 32.9% (21).

Ki-67 ratios were also evaluated in patients whose TTY was assessed. It was determined that Ki-67 expression load was lower in 23 patients who were TTY positive and that this was significantly associated with TTY. Although Ki-67 antibody expression is a parameter used in breast cancer follow-up, reports on its reliability vary. The relationship between Ki-67 expression dw-um and prognosis in early-stage breast cancer is being studied extensively. The use of Ki-67 as a prognostic marker in clinical care remains controversial due to the heterogeneity and inconsistency of studies. Azambuya (22) and Stuart-Harris (23) conducted the two most comprehensive meta-analyses.

The axillary lymph node involvement status changes the patient's prognosis and treatment options. To determine the treatment algorithm that minimizes the lymph node metastasis burden among breast cancer subtypes, it is essential to decide on which molecular subtype responds more effectively after ACT. In our study, nodal response was most frequently detected in triple negative patients and least in Luminal A subgroup patients. Among histopathological subtypes, nodal complete response was most

commonly seen in medullary carcinoma, but it was not statistically significant (2 cases). Another reason focal diagnostic response rates are reported at different rates in the literature is that the degree of nodal involvement of the patients included in the study before neoadjuvant therapy differs (12). In some studies, only node-positive patients were included; in others, as in our research, it is included in O patients. Neoadjuvant chemotherapy is effective in reducing the size of the primary tumor as well as in reducing the disease burden in regional lymph nodes. In our study, the number of lymph nodes removed in axillary dissection was significantly lower in patients who obtained CR after neoadjuvant CT; an average of 1 node was removed in patients with CR, and an average of 4 nodes were removed in those without. As seen in our study, the probability of conversion from node-positive to node-negative disease is higher in women with Tripple-negative breast cancer than in those with hormone receptor-positive disease (24,25). Neoadjuvant chemotherapy offers opportunities to minimize the extent of surgery for both the breast and axilla. With the conversion of OD-positive disease to node-negative, axillary staging with sentinel lymph node surgery allows patients who convert to node-negative to prevent axillary lymph node dissection potentially. In cases where there is a positive sentinel node in breast cancer patients, axillary treatment is also indicated and is most commonly in the form of standard axillary lymph node dissection.

Axillary lymph node dissection provides effective regional control, but it also brings with it many side effects and patient morbidity. The EORTC 10981-22023 AMAROS study, presented in the Lancet Journal 2014, showed that axillary radiotherapy could provide regional control with fewer side effects. Donker et al. have shown that axillary radiotherapy provides effective regional control and results in less morbidity in patients with T1-T2 primary breast disease and no palpable lymphadenopathy. Axillary lymph node dissection should be performed if the axilla is clinically positive or if there is metastasis in SL biopsy after neoadjuvant CT (26,27).

In our study, the tumor subgroup with the most pathological complete response rate was the triple-negative group (36.4%), and the second most was the HER2-positive subgroup (21.1%). However, no significant relationship was found between pathological CR after adjuvant CT and the histopathological distribution of the tumor. This study's response rates to neoadjuvant chemotherapy, including pathological CR rates in patients with triple-negative or HER2-positive disease, are consistent with previous studies. Treatment response rates for triple-negative tumors in the breast and axilla have been reported as 35.8% in the German Breast Group analysis, 35% in the SPY 1 study (28), and 38% in the report from the US MD Anderson Cancer Center (25). In addition, all patients in Z1071 had node-positive disease. In contrast, in the other studies cited, there was a mixture of clinically node-negative and node-positive disease, explaining some of the differences in the pathological CR rates reported here.

Breast cancer treatment is a complex process with medical treatment, surgical intervention, and axilla management. The aim should be to provide minimally invasive optimal treatment options to control the disease and reduce patient morbidity. It has been reported that neoadjuvant chemotherapy, when given to patients with surgical indications before the intervention, can reduce the burden and size of the primary tumor, reduce axillary lymph node involvement, and even bring the node to a negative stage, thus saving the patient from axilla intervention. In this study, we found that the molecular subtypes of the tumor are associated with the response that develops in the breast tissue and regional lymph nodes after neoadjuvant chemotherapy. Specifically, it was observed that patients with triple-negative or HER2-positive breast cancer have a higher chance of achieving a pathological complete response in both the breast tissue and regional lymph nodes.

CONCLUSION

In this study, breast cancer subtypes were associated with tumoral, nodal, and pathological complete response levels after neoadjuvant treatment. Tumoral, nodal, and pathological complete response rates were higher in triple-negative subgroup patients and HER2-positive patients, respectively. The number

of lymph nodes excised after neoadjuvant chemotherapy was lower in patients with a complete tumor response than in those without a complete tumor response among all subgroups. Regardless of the success of the treatment response, the number of lymph nodes excised after neoadjuvant chemotherapy was highest in the triple-negative subgroup.

DESCRIPTIONS

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AI Statement: The authors used AI and AI-assisted Technologies (Grammarly and MS Word Editor) in the writing process. These technologies improved the readability and language of the work. Still, they did not replace key authoring tasks such as producing scientific or medical insights, drawing scientific conclusions, or providing clinical recommendations. The authors are ultimately responsible and accountable for the contents of the whole work.

Data Availability: The data supporting this study's findings are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Ethical Declaration: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Our institution has granted ethics committee approval. As this was retrospective research, no informed consent was obtained from participants.

Note: Converted from a subspeciality thesis into an article.

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