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Diagnostic performance of breast imaging with ultrasonography, magnetic resonance and mammography in the assessment of residual tumor after neoadjuvant chemotherapy in breast cancer patients

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Ethics Committee Approval
Approval for this study was granted from Gaziosmanpasa Training and Research Hospital Ethics Committee for Clinical Studies in July 2020 (reg:215)
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

Conflict of Interest
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Abstract

Background/Aim: Following the administration of neoadjuvant chemotherapy (NAC), a complete pathological response (pCR) is seen at rates of up to 50-70% in breast cancer patients, especially in triple-negative (TNBC) and HER-2 enriched subgroups and related to increased pCR rates, studies to predict the pathological response with preoperative evaluation are ongoing. The aim of this study was to investigate the correlation of preoperative imaging in breast cancer patients receiving NAC with the pathological response.

Methods: The study, organized as a retrospective cohort study, included 129 breast patients who underwent surgery after NAC between April 2014 and February 2020. The demographic data of the patients, the clinical and radiological findings before and after NAC, operation findings, and the histopathological evaluation results were collected retrospectively from the patient files. The radiological images of the patients were examined by separating into groups of patients with ultrasonography (US), magnetic resonance imaging (MRI), US+MRI, and mammography (MG)+US. The NAC response on preoperative breast US and MG was evaluated according to the RECIST-1.1 system, and the NAC response on MRI with the Goorts et al grading system. In the histopathological examination of operation material, the Miller Payne grading system for breast tissue was used in the determination of NAC response.

Results: The mean age of the patients in the study was 49.17 (11.00) years. The vast majority of the patients (87.6%) were diagnosed with invasive ductal cancer, with 27.13% in luminal A, 35.65% in luminal B, 31.0% in HER-2 enriched, and 6.2% in TNBC subgroups. A statistically significant correlation was determined between the pathological response and the US+MRI, MRI, and US+MG groups, with agreement at a moderate level (Kappa: 0.653, $P<0.001$; Kappa: 0.443, $P<0.001$; Kappa: 0.481, $P=0.005$, respectively). Within all the groups, the group with the highest sensitivity and accuracy were seen to be the patients evaluated with US+MRI (66.67%, 90.91%, respectively).

Conclusion: The results of this study demonstrated that there is a correlation between the pathological response and US+MRI, MRI, and US+MG evaluation after NAC. The US+MRI group was found to have the highest sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. When possible, the use of these two imaging methods together in the preoperative evaluation of patients is a successful method in the prediction of pathological response.

Keywords: Breast cancer, Neoadjuvant chemotherapy, Complete pathological response, Complete radiologic response

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Introduction

Neoadjuvant chemotherapy (NAC) in locally advanced-stage breast cancer enable initially inoperable patients to become suitable for surgery by shrinking the tumor and increasing the applicability of breast-sparing surgery. By starting treatment with NAC, depending on the molecular subtype in early-stage tumors, the chemosensitivity of the tumor and the in vivo response can be evaluated. In studies comparing NAC with adjuvant chemotherapy, no difference has been determined regarding mean survival and disease-free survival. However, the prognosis is better in patients with a complete pathological response after NAC [1, 2].

Although the NAC response varies according to molecular subtype, the response is better in human epidermal growth factor receptor-2 (Her-2) enriched and triple-negative breast cancer (TNBC) subgroups, which constitute 20-25% of all breast cancers [3-5]. However, progression in the tumor during NAC or non-response may be seen. Early identification of these patients can help reorganize chemotherapy, reduce complications associated with treatment, and admit for early surgical treatment. The most preferred imaging methods are breast ultrasound (US), mammography (MG) and magnetic resonance imaging (MRI). The size of the tumor, distance to the skin, nipple, and pectoral muscle, border characteristics, additional focus, and continuing microcalcifications are of guidance to the surgeon for the operating technique to be selected. In the evaluation of breast masses, sensitivity in the determination of malignant lesions has been reported to be 75.0%-93.9% for the US, 56.2%-77.3% for MG, and 81%-89% for MRI [6-8].

Just as preoperative evaluation of the tumor after NAC helps the surgeon to select the operating technique, it can also save time in patients showing progression. In addition to shrinking the size, the tumor response is evaluated radiologically from the presence of fibrosis or necrosis, but differentiation of necrosis and fibrous hyperplasia from residual cancer cannot be made well with traditional US [9].

In evaluations made with MRI after NAC, the residual tumor is determined in the evaluation of operation material in 30%-50% of patients showing complete radiological response (rCR), and complete pathological response (pCR) is seen in 20% of patients with residual clinical disease [10, 11].

Therefore, the histopathological evaluation of operation material continues to be the gold standard in evaluating pathological response.

This study aimed to evaluate to what extent the NAC response can be predicted with preoperative imaging in patients applied with NAC after a breast cancer diagnosis in our hospital and investigate which tumor characteristics were more determinative of the prediction.

Materials and methods

Data collection

In this retrospective cohort study, ethics committee approval, (approval number: 215 and date: 30/12/2020), was obtained from the Gaziosmanpasa Training and Research Hospital Ethics Committee, to which our hospital is affiliated. Patient informed consent was not required due to the retrospective use of anonymous administrative data. All the female patients who underwent surgery after NAC because of breast cancer in our hospital between April 2014 and February 2020 were included in the study. After excluding patients determined with distant metastasis before treatment (n:3), patients who did not complete chemotherapy (n:2), and patients who refused surgical treatment after chemotherapy, the study was completed with 129 patients. The medical records were reviewed retrospectively regarding age, physical examination findings, medical history, drugs used in NAC, the breast US, MG, and MRI findings before and after NAC, and the tru-cut biopsy and pathology results.

Histopathological assessment

The pathological examination of the tru-cut biopsy and operation material was evaluated regarding histopathological diagnosis, histological-nuclear grade, Ki-67 level, hormone receptor, and Her-2 neu status. The Bloom-Richardson grading system was used in histological grading [12].

In the hormone receptor evaluation, a nuclear reaction >1% for estrogen receptor (ER) and progesterone receptor (PR) was accepted as positive. In the Her-2 evaluation, score 0 (<10% incomplete reaction) and score 1 (<10% incomplete reaction) were accepted as unfavorable, and score 3 (>10% strong reaction) was accepted as positive. Materials with a score of 2 (>10% moderately severe reaction ≤ 10% strong reaction) were re-evaluated with fluorescent in situ hybridization (FISH) analysis.

Clinicopathological definitions of breast cancer subtypes were made as follows [13].

Luminal A like: ER-positive, PR positive (>20%), Ki-67 low, Her-2 negative

Luminal B like: ER-positive, PR low (<20%), or ER-positive, Her-2 neu positive, any PR. Ki-67 value or low PR may be used to distinguish between Luminal A like, and Luminal B like.

Her-2 enriched (non-luminal): ER and PR negative, Her-2 neu positive

TNBC: ER, PR and Her-2 neu negative

US technique and image interpretation

The two experienced radiologists (NU and YK) conducted the US examinations using Toshiba Aplio 500 software version 6.0 (Toshiba Corporation, Tokyo, Japan) ultrasound scanner with a 5–14 MHz linear-array transducer.

MG technique and image interpretation

Mammographic images from two planes (mediolateral oblique and craniocaudal) were obtained using a digital mammography unit (Giotto Image MC, IMS, Italy). The images were evaluated according to the ACR 2013 lexicon, and the final BIRADS assessment category was determined.

MRI technique and image interpretation

MR imaging studies were performed using a 1.5 Tesla unit (GE Signa HDx, GE Medical Systems, USA) using 8-channel phased-array breast surface coil. All MR images were reviewed by two radiologists with 10 years of experience in interpreting breast MR imaging (NU and YK), on a PACS imaging workstation (Infinitt PACS; Infinitt Healthcare, Seoul, Korea).

Chemoradiotherapy and surgery

All the patients included in the study were applied with anthracycline-based therapy with 4AC+T (doxorubicin plus cyclophosphamide followed by paclitaxel) as the NAC regimen. In addition, Transtuzumab was added to the treatment of patients in the Her-2-positive group. Surgical treatment was applied as breast-conserving surgery, subcutaneous mastectomy, or mastectomy. Sentinel lymph node biopsy was performed with excision of at least three lymph nodes in patients with clinically negative axilla, and axillary lymph node dissection was performed in patients with sentinel lymph node biopsy positivity and those with N2-3 before NAC.

Assessing the chemotherapy response according to the radiographic results

The lesions were evaluated radiologically twice, at the time of diagnosis and after NAC with US, MRI, and MG. The Response Evolution Criteria in Solid Tumors (RECIST1.1) criteria were used to measure the NAC response of lesions on US and MG. The largest single diameter, or in multifocal, multicentric lesions, the total of the long axes of all the target lesions were used in the measurements [14].

According to these criteria, radiological determination has been defined as follows;

Complete response (rCR): Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have a reduction in short axis to <10 mm.

Partial response (rPR): At least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

Progressive Disease (rPD): At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on the study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. (Note: the appearance of one or more new lesions is also considered progression).

Stable disease (rSD: Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest total diameters in the examination [15].

The response to NAC on MRI was evaluated according to the Goorts et al. Classification;

Type 0: complete radiologic response (rCR);

Type 1: concentric shrinkage > 3 mm without surrounding lesions;

Type 2: crumbling: shrinkage with residual multinodular lesions;

Type 3 diffuse contrast enhancement in whole quadrants;

Type 4: stable disease (rSD), i.e. no response, shrinkage <3 mm or increase <3 mm

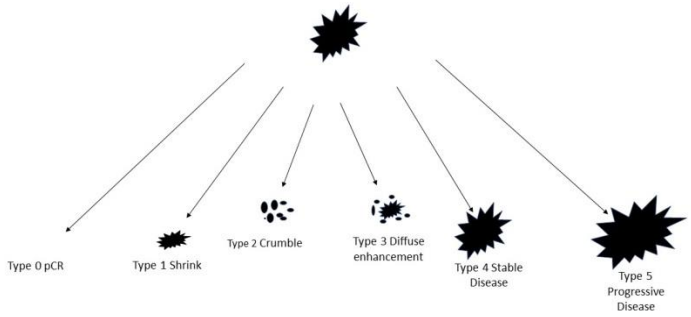
Type 5: progressive disease (rPD), i.e. increase in tumor size >3 mm or new lesions.

Types 1, 2, and 3 on MRI were accepted as a partial radiological response (rPR), and Types 4 and 5 as radiological no response (rNR) [16, 17]. The responses on MRI after NAC in breast cancer are shown in Figure 1.

Assessing the chemotherapy response according to the histopathological evaluation

The NAC response in breast tissue was evaluated using the Miller Payne grading system [18]. According to this pathological system, evaluation has been defined as following: Grade 1, no reduction in overall cellularity (pathological no response, pNR); Grade 2, a minor loss of tumor cells (up to 30% loss); Grade 3, an estimated reduction between 30% and 90% in tumor cells; Grade 4, marked the disappearance of tumor cells (more than 90% loss); and Grade 5 is defined as no identifiable malignant cells, although ductal carcinoma in situ may be present (complete pathological response, pCR). The statistical evaluations made comparisons of Miller Payne Grade 5 pCR, Grades 2, 3, 4 (partial pathological response -pPR) and Grade 1 (pathological no response -pNR).

Figure 1: MRI-based response patterns of breast carcinomas [17]. (Permission to present this figure is granted by Copyright Clearance Center)



Statistical analysis

Data obtained in the study were analyzed statistically using IBM SPSS Statistics 21.0 and medCalc version 20.015 software. In the comparison of continuous variables between groups, One-Way ANOVA was used. The Chi-square test was applied to categorical variables. In the evaluation of the agreement between pathological response and radiological response, Kappa coefficients were calculated. A value of $P<0.05$ was accepted as statistically significant. According to the pathological response status, the predictive values of radiological response were evaluated with diagnostic tests (sensitivity, specificity, positive predicted value, negative predicted value, accuracy). The terminology was defined as follows:

Sensitivity = True positive/(True positive + False negative)
Specificity = True negative/(True negative + False positive)
PPV = True positive/(False positive + True positive)
NPV = True negative/(False negative + True negative)
Accuracy = True positive + True negative/Total number of cases [19].

Results

Patients' demographics

The evaluation was made of 129 female patients who underwent surgery following NAC because of breast cancer. The mean age of the patients was 49.17 (11.00) years.

The mean tumor size was 35.09 (17.93) mm before treatment and 15.92 (19.22) mm after treatment (Tumor diameter was measured by US in the US and US+MG groups, while the measurement was made with MRI in the MR and MRI+US groups). The mean time from the last chemotherapy session to surgery was 22.41 (14.67) days. The diagnosis was of invasive ductal cancer in 112 (87.6%) patients, invasive lobular cancer in 13 (10.07%), and other tumor types in 3 (2.33%) (1 medullar, two metaplastic). The subgroups were determined as 35 (27.13%) luminal A, 46 (35.56%) luminal B, 40 (31.0%) Her-2 enriched, and 8 (6.2%) TBNC. Pre and post-treatment radiological evaluation was made with US in 42 patients, US+MRI in 22, MRI in 46, and US+MG in 19. The clinicopathological data of the patients are shown in Table 1.

Table 1: Clinicopathologic data of the patients in four groups

Characteristic	US(n:42) Mean(SD)		MRI(n:46) mean(SD)		US+MRI(n:22) mean(SD)		US+MG(n:19) mean(SD)		Total(n:129) mean(SD)		*P*-value[1]
Age (year)	50.49(11.43)		47.72(11.24)		48.41(9.67)		50.74(11.21)		49.17(11.00)		0.602
Before treatment tumor size (mm)	34.68(17.2)		34.11(18.42)		41.32(19.84)		31.33(16.11)		35.09(17.93)		0.364
Post-surgery tumor size (mm)	16.52(18.62)		15.77(20.24)		17.59(21.84)		12.83(15.52)		15.92(19.22)		0.882
Last imaging-operation period (day)	22.15(14.65)		22.9(15.78)		20.55(12.95)		23.79(14.76)		22.41(14.67)		0.910
Last imaging-chemotherapy period (day)	30(10.97)		29.83(9.6)		28.81(8.65)		32.4(13.37)		30.11(10.43)		0.806
	n	%	n	%	n	%	n	%	n	%	P-value[2]
Pathology											
Invasive ductal cancer	37	88.09	40	86.96	17	77.27	19	100.0	113	87.6	0.556
Invasive lobular cancer	4	9.53	5	10.87	4	18.18	0	0.0	13	10.07	
Other tumor types	1	2.28	1	2.17	1	4.45	0	0.0	3	2.33	
Tumor subtype											
Luminal A	12	28.57	14	30.43	6	27.27	3	15.78	35	27.13	0.984
Luminal B	16	38.09	15	32.6	7	31.81	8	42.1	46	35.65	
Her-2 enriched	12	28.57	14	30.43	7	31.81	7	36.84	40	31.0	
TNBC	2	4.76	3	6.52	2	9.09	1	5.26	8	6.2	
ER											
Present	5	11.9	6	13.04	3	13.63	5	26.31	19	14.72	0.489
Absent	37	88.1	40	89.96	19	86.37	14	73.69	110	85.28	
PR											
Present	9	21.42	11	23.91	5	22.72	8	42.1	33	25.58	0.352
Absent	33	78.58	35	76.09	17	77.28	11	57.9	96	74.42	
Her-2											
Present	27	64.28	30	65.21	13	59.1	12	63.16	82	63.56	0.968
Absent	15	35.72	16	34.79	9	40.9	7	36.84	47	36.44	
Grade											
1	0	0.0	1	2.17	0	0.0	0	0.0	1	0.78	0.513
2	29	69.06	23	50.0	14	63.63	10	52.63	76	58.91	
3	13	30.94	22	47.83	8	36.37	9	47.37	52	40.31	
Miller Payne											
1 (pNR)	3	7.14	4	8.69	1	4.54	2	10.52	10	7.75	0.943
2 (pPR)	7	16.66	4	8.69	3	13.63	4	21.05	18	13.95	
3 (pPR)	15	35.71	17	37.0	9	40.9	3	15.78	44	34.1	
4 (pPR)	6	14.28	6	13.0	3	13.63	3	15.78	18	13.95	
5 (pCR)*	11	26.19	15	32.6	6	27.27	7	36.84	39	30.23	

[1]: One-Way ANOVA, [2]: Chi-Square test, US: ultrasonography, MRI: Magnetic resonance imaging, MG: Mammography TNBC: Triple negative breast cancer, ER: Estrogen receptor, PR: Progesterone receptor, Her-2: Human epidermal growth factor receptor-2, pCR: Complete pathological response, pPR: Pathological partial response, pNR: Pathological no response

Table 2: The correlations between radiological imaging methods and pathological response

Radiological response category	Pathological response category						Total		*P*-value
	pCR		pPR		pNR				
	n	%	n	%	n	%	n	%	
US									
rCR	4	36.36	3	10.71	0	0	7	16.66	Kappa=0.141
rPR	7	63.63	22	78.57	3	100	32	76.19	*P*=0.246
rNR (rSD)	0	0	3	10.71	0	0	3	7.14	pX^2=0.2
Total	11	100	28	100	3	100	42	100	
US+MRI									
rCR	4	66.66	0	0	0	0	4	18.18	Kappa=0.653
rPR	2	33.33	15	100	1	100	18	81.82	*P*<0.001
Total	6	100	15	100	1	100	22	100	pX^2=*0.001*
MRI									
rCR	8	53.33	1	3.7	0	0	9	19.56	Kappa=0.443
rPR	6	40	24	88.88	3	75	33	71.73	*P*<0.001 pX^2=0.019
Concentric shrinkage	5	33.33	16	59.33	3	75	24	52.17	
Crumbling	1	6.67	7	25.87	0	0	8	17.36	
Diffuse enhancement	0	0	1	3.68	0	0	1	2.2	
rNR	1	6.66	2	7.4	1	25	4	8.69	
rSD	0	0	1	3.7	0	0	1	2.17	
rPD	1	6.66	1	3.7	1	25	3	6.52	
Total	15	100	27	100	4	100	46	100	
US+MG									
rCR	4	57.14	0	0	0	0	4	21.05	Kappa=0.481
rPR	3	42.86	10	100	2	100	15	78.95	*P*=0.005
Total	7	100	10	100	2	100	19	100	pX^2=*0.013*

US: Ultrasonography, MRI: Magnetic resonance imaging, MG: Mammography, pCR: Complete pathological response, pPR: Pathological partial response, pNR: Pathological no response, rCR: Radiological complete response, rPR Radiological partial response, rNR: Radiological no response, rSD: Radiological stable disease rPD: Radiological progressive disease

Table 3: The sensitivity, specificity, PPV, NPV and accuracy of imaging modalities according to pathological response

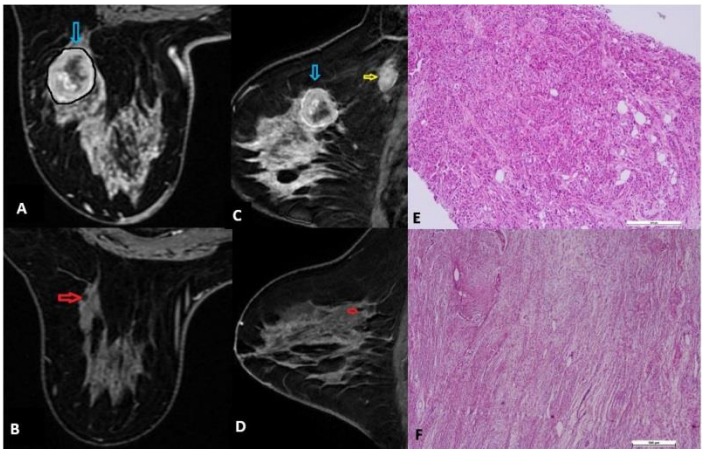
Radiological Response	Complete Pathological Response				
Radiological Complete Response	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
US	36.36 (10.93-69.21)	90.32(74.25-97.96)	57.14(26.08-83.44)	80(71.61-86.39)	76.19(60.55-87.95)
MRI	53.33(26.59-78.73)	96.77(83.30-99.92)	88.89(52.35-98.31)	81.08(71.31-88.08)	82.61(68.58-92.18)
US+MRI	66.67(22.28-95.67)	100(79.41-100)	100	88.89(72.07-96.13)	90.91(70.84-98.89)
US+MG	57.17(18.41-90.10)	100(73.54-100)	100	80(62.97-90.39)	84.21(60.42-96.62)
	Pathological Partial Response				
Radiological Partial Response	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
US	78.57(59.05-91.70)	28.57(8.39-58.10)	68.75(59.98-76.35)	40(18.30-66.49)	61.91(45.64-76.43)
MRI	88.89(70.84-97.65)	52.63(22.86-75.55)	72.73(61.97-81.36)	76.92(51.37-91.32)	73.91(58.87-85.73)
US+MRI	100(78.20-100)	57.14(18.41-90.10)	83.33(68.01-92.16)	100	86.36(65.09-97.09)
US+MG	100(69.15-100)	44.44(13.70-78.80)	66.67(52.72-78.20)	100	73.68(48.80-90.85)
	Pathological No Response				
Radiological No Response	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
US	0(0-70.76)	92.31(79.13-98.39)	0	92.31(91.64-92.93)	85.71(71.46-94.57)
MRI	25(0.63-80.59)	92.86(80.52-98.50)	25(4.25-71.48)	92.86(88.01-95.84)	86.96(73.74-95.06)
US+MRI	0(0-97.5)	100(83.89-100)	-	95.46(95.46-95.46)	95.46(77.16-99.89)
US+MG	0(0-84.19)	100(80.49-100)	-	89.47(89.47-89.47)	89.47(66.86-98.70)

US: Ultrasonography, MRI: Magnetic resonance imaging, MG: Mammography, PPV: Positive predictive value, NPV: Negative predictive value

Evaluation of radiological and pathological response

Of the 24 patients with complete radiological response, pCR was seen in 20, and pPR in 4. In the evaluation made with US, rCR was determined in 7 (16.66%) patients, rPR in 32 (76.19%), and the disease had remained stable in 3 (7.14%). In the evaluation made with US+MRI, rCR was determined in 4 (18.18%) patients and rPR in 18 (81.82%). A 51-year-old woman with HER2-positive cancer who demonstrated pathological and radiological complete response shown in Figure 2. In the evaluation of 46 patients with MRI only, rCR was observed in 9 (19.56%), rPR in 33 (71.73%) (24 concentric shrinkage, eight crumbling, 1 diffuse enhancement), and rNR in 4 (8.69%). Of the 19 patients evaluated with MG+US, rCR was determined in 4 (21.05%) and rPR in 15 (78.95%).

Figure 2: 51-year-old woman with HER2-positive cancer who demonstrated pathological and radiological complete response. A-C) On axial and sagittal contrast MRI images show a malignant mass in the left breast before chemotherapy (blue arrow). There is lymphadenopathy in the left axilla (yellow arrow), B-D) No contrast enhancement is observed in the mass after chemotherapy. Axillary lymphadenopathy has regressed. The clip is viewed in post-chemotherapy images (red arrow), E) Before chemotherapy nuclear grade III invasive ductal carcinoma in tru-cut biopsy (H+E stain, x4), F) After chemotherapy pathological complete response in mastectomy (H+E stain, x10)



A statistically significant correlation was determined between the pathological response and US+MRI, MRI, and US+MG evaluations, with agreement at a moderate level (Kappa: 0.653, $P<0.001$; Kappa: 0.443, $P<0.001$; Kappa: 0.481, $P=0.005$, respectively). No significant relationship was seen between US alone and the pathological response ($P=0.246$). Of the patients determined with rCR on US, the residual tumor was present in 42.85% in the examination of operation material. This rate was 12.5% with MRI, and pCR was present in all the patients with rCR in the MRI+US evaluation. In contrast to these findings, the rate of pCR seen in the patients not showing complete response radiologically (rPR and rNR) was 20% with US, 18.91% with MRI, and 11.11% with US+MRI.

There was no statistically significant relationship between tumor subtypes and the radiology-pathology relationship in any group ($P>0.05$). The correlations between the radiological imaging methods and the pathological response are shown in Table 2.

When the imaging methods' sensitivity, specificity, PPV, NPV, and accuracy rates were examined in respect of pCR prediction, the highest sensitivity (66.67%) was determined with US+MRI. The specificity and PPV were found to be 100% for both US+MRI and US+MG. The US+MRI group had NPV of 88.89% and the highest accuracy rate of 90.91%. For pPR, US+MRI and US+MG had 100% sensitivity and NPV, and the highest specificity value of 57.14% was in the US+MRI group. The PPV in the US+MRI group was 83.33% and accuracy was determined to be 86.36%. The findings are shown in Table 3.

Discussion

Since the 1970s, NAC has been an inseparable part of breast cancer treatment, and the treatment of approximately 18% of patients diagnosed with breast cancer starts with NAC [20, 21].

This treatment provides shrinkage in tumor size, regression in axillary nodal disease, and increases the applicability of breast-conserving surgery, which can be evaluated as the efficacy of chemotherapy eradicating potential micrometastatic disease and rendering previously inoperable patients suitable for surgery. In addition, the development of pCR has a positive effect on prognosis. Therefore, histopathological grading systems are the gold standard in the evaluation of response following NAC [22, 23].

In this study, evaluation of chemotherapy response before surgery was applied with breast US, MRI, and/or MG during and after NAC in patients planned to undergo surgery, and the predictive values of these methods were investigated.

In a study by Kenue et al. [24], the predictive value of US and MG for pCR were investigated in patients receiving NAC for breast cancer, and it was concluded that US could more accurately predict residual tumor size following NAC. The sensitivity, specificity, and PPV were found to be 45.8%, 93.8%, and 68.8%, respectively for US, and 54.2%, 86.3%, and 54.2% for MG. There was reported to be no statistically significant difference between the two methods. In the same study, the two methods combined were found to have a sensitivity of 45.8% and specificity of 93.8%.

In a study by Peitinger et al. [25], the use of US and MG together was found to increase accuracy. In predicting pCR with the combined use of the two methods, sensitivity was reported to be 78.6%, specificity 92.5%, and accuracy 88.9%.

Another study evaluated the response to treatment after NAC with US, MG, and tomosynthesis, and reported that the diagnostic power in predicting pCR after NAC was similar between the three imaging modalities [26].

In the current study, the prediction of pCR with US and US+MG after NAC, sensitivity was found to be 36.36% and 57.17%, respectively, specificity 90.32% and 100%, PPV 57.14% and 100%, NPV 80% and 80%, and accuracy 76.19% and 84.21%. Mammography alone was not used in any patient of this study, and the evaluation was made together with US. Of the patients thought to have rCR with US evaluation, the residual tumor was determined in 42.85% on examination of the operation material.

Zhang et al. [27], evaluated US, MG, and MRI in respect of the prediction of pCR after NAC and reported sensitivity, specificity, accuracy, PPV, and NPV to be 36.2%, 90.2%, 71.0%, 67.3%, and 71.9% respectively for US, and 44.4%, 92.9%, 75.6%, 77.7%, and 75.0% for MRI. It was also seen that the accuracy of US was lower for IDC than for other types, and the sensitivity was higher. When the molecular subtypes were examined, sensitivity was highest in the hormone receptor positive and Her-2 positive groups and accuracy was higher in those with hormone receptor positivity. Sensitivity and

PPV were found to be higher in small tumors. When MRI and US were used together, the prediction of pCR was not affected by tumor size, subtype, or histological type.

A study evaluated the MRI prediction of pCR, and reported sensitivity of 97.2%, specificity 44.44%, and accuracy of 84.14%, with the highest sensitivity values obtained in the Her-2 enriched group [28].

In another study by Morrow et al. [29], the efficacy of MRI in the prediction of the response following NAC was examined. They found that MRI doesn't predict pCR with sufficient accuracy with 63.4%PPV and 84.1% NPV.

In a study by Hayashi et al. [30], a patient group was examined in which 26.1% developed pCR after NAC. pCR was determined in 196 of 247 patients with a complete response on MRI and in 154 of 182 patients with a complete response on MRI+US. Sensitivity, specificity, and accuracy were calculated as 84.8%, 95.1%, and 79.4%, respectively for MRI, and 66.6%, 97.3%, and 86.8% for MRI and US together.

In the current study, MRI was found to have a sensitivity of 53.33%, specificity 96.77%, PPV 88.89%, NPV 81.08%, and accuracy 82.61%. If USG added to MRI, we found sensitivity 66.67%, specificity 100%, PPV 100%, NPV 88.89%, and accuracy 90.91%. Thus, the highest accuracy was obtained when these two imaging methods were used together in the MRI+US group. In the histopathological examination of the postoperative specimen, the residual tumor was determined in 12.5% of patients thought to have a complete response on MRI. Histopathologically, the subtypes did not show any effect on sensitivity and specificity.

The limitation of this study was that it was conducted in a single-center, and thus the number of patients was limited. All imaging modalities were performed based on our hospital protocol. Therefore, the results may not be generalizable. In addition, further studies are required to produce similar results to predict the correlation between the radiological response and the pathological response, including more parameters that could affect this correlation.

Conclusions

To sum up, the studies conducted to predict the response following NAC in the preoperative period raise the question of whether a complete response can be known before surgical excision, and can the patient be followed up without surgery. As none of the imaging methods could predict pCR at 100%, the policy of wait and see without surgery does not seem to be an option under current conditions. In most studies evaluating imaging methods, MRI has been advocated as superior to US and MG. However, evaluation with US is a lower-cost and more easily accessible method with fewer contraindications. The current study results demonstrated that MRI+US was the imaging method with the highest sensitivity and accuracy in imaging after NAC. The use of these two methods together provides a better preoperative evaluation.

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