Original Article

False-positive MRI Findings in Breast Cancer After Neoadjuvant Chemotherapy and Correlation Between Tumor Response Patterns and HER2 Status

Meme Kanserinde Neoadjuvan Kemoterapi Sonrası Yanlış-Pozitif MRG Bulguları ve Tümör Yanıt Paternleri ile HER2 Durumu Arasındaki Korelasyon

Aydan Avdan Aslan[1], Servet Erdemli[2], İbrahim Halil Erdoğdu[3], Serap Gültekin[1], Cihan Uras[4], Fatma Tokat[5], Ali Arıcan[6], Leyla Özer[6], Kemal Behzatoğlu[5], Nezih Meydan[7], Füsun Taşkın[2]

[1]Department of Radiology, Gazi University, Ankara, Turkey.
[2]Department of Radiology, Acıbadem M.A.A. University, İstanbul, Turkey.
[3]Department of Pathology, Adnan Menderes University School of Medicine, Aydın, Turkey
[4]Department of General Surgery, Acıbadem M.A.A. University, Istanbul, Turkey
[5]Department of Pathology, Acıbadem M.A.A. University, Istanbul, Turkey
[6]Department of Medical Oncology, Acıbadem M.A.A. University, Istanbul, Turkey
[7]Department of Medical Oncology, Adnan Menderes University, Aydın, Turkey

ABSTRACT

Objective: To demonstrate false-positive MRI findings after neoadjuvant chemotherapy (NAC) in patients with pathologic complete response (pCR) and investigate the correlation between post-NAC MRI findings and tumor response patterns based on human epidermal growth factor receptor 2 (HER2) status.

Methods: This retrospective multicenter study enrolled 118 patients with breast cancer who received NAC and achieved pCR. Tumors were evaluated with MRI pre- and post-NAC. MRI evaluation included lesion characteristics, kinetic curve analysis, background parenchymal enhancement (BPE), and post-NAC changes of MRI features. Tumor response patterns were also assessed and categorized based on MRI findings. Tumor response patterns and post-NAC MRI findings were correlated with HER2 status.

Results: The residual MRI findings following NAC differed significantly between HER2+ and HER2− groups (p=0.02). The most frequent false-positive MRI finding was focus and foci in HER2+ tumors, whereas non-mass enhancement (NME) in HER2− group. The presence of ductal carcinoma in situ (DCIS) and fibrosis in surgical pathology is significantly associated with NME on post-NAC MRI (p<0.001). Axillary pCR was achieved significantly higher in the HER2+ group (p=0.04).

Conclusion: Although MRI is considered the most reliable method for evaluating tumor response after NAC, over and underestimation is still possible. This study revealed that tumor response patterns and post-NAC MRI findings differ according to HER2 status. The diagnostic accuracy of post-NAC MRI is evolving by understanding the underlying mechanisms and tumor biology.

Keywords: neoadjuvant chemotherapy, magnetic resonance imaging, breast cancer, pathologic complete response

ÖZET

Amaç: Bu çalışmada patolojik tam yanıtlı (pTY) meme kanseri hastalarında neoadjuvan kemoterapi (NAK) sonrası yanlış-pozitif MRG bulgularını ortaya koymayı ve tümör yanıt paternleri ile insan epidermal büyüme faktörü reseptörü 2 (HER2) pozitifliği ile arasındaki ilişkiyi değerlendirmeyi amaçladık.

Gereç ve Yöntem: Bu retrospektif çok merkezli çalışmaya, Ocak 2016 ile Eylül 2020 tarihleri arasında NAK alan ve pTY elde eden meme kanseri tanılı118 hasta dahil edildi. Hastaların NAK öncesi ve sonrası MRG bulguları kayıt edildi. Tümör yanıt paternleri kategorilere ayrıldı. HER2 pozitifliği ile post-NAK MRG bulguları ve tümör yanıt paternleri arasındaki ilişki istatistiksel olarak analiz edildi.

First Received: 13.11.2022, Accepted: 23.12.2022 doi: 10.5505/aot.2023.60973

Bulgular: Post-NAK MRG bulguları HER2+ ve HER2− grupları arasında istatistiksel olarak anlamlı farklılık gösterdi (p=0.02). HER2+ tümörlerinde en sık yanlış-pozitif MRG bulgusu odak kontrast tutulumu iken, HER2− grubunda kitle dışı kontrastlanma (KDK) idi. Cerrahi patolojide duktal karsinoma in situ (DKİS) ve fibrozis varlığı ile post-NAK MRG'de KDK anlamlı olarak ilişkili bulundu (p<0,001). Aksiller pTY, HER2+ grubunda anlamlı derecede daha yüksek elde edildi (p=0.04).
Sonuç: MRG, NAK sonrası tümör yanıtını değerlendirmede en güvenilir yöntem olarak kabul edilse de, yanlış-pozitif ve yanlış-negatif sonuçlar elde edilebilmektedir. Bu çalışma, tümör yanıt paternlerinin HER2 durumuna göre farklılık gösterdiğini ortaya koymuştur. Bu alanda yapılacak yeni çalışmaların tümör biyolojisini anlamaya yardımcı olacağı ve NAK sonrası MRG'nin tanısal doğruluğunu arttırmaya yardımcı olacağı düşünülmektedir.

Anahtar Kelimeler: neoadjuvan kemoterapi, manyetik rezonans görüntüleme, meme kanseri, patolojik tam yanıt

Introduction

Neoadjuvant chemotherapy (NAC) has become the standard treatment in locally advanced breast cancer, and its use has been increasing recently [1]. NAC has also gained acceptance as an alternative therapeutic option in early-stage breast cancer, considering the studies reported no significant difference in survival rates and disease progression between patients who received neoadjuvant and adjuvant chemotherapy [2].

NAC enables breast-conserving surgery with a better surgical outcome in patients with large tumors by downstaging both primary tumor and axillary nodes. As pathologic complete response (pCR) is associated with better disease-free and overall survival, NAC provides valuable prognostic information in patients who achieved pCR [3, 4]. Other potential advantages of NAC over adjuvant chemotherapy include the ability to evaluate the efficacy of selected systematic therapy in vivo.

Accurate ascertainment after NAC is vital to evaluate tumor response and appropriate surgical planning. In the current medical practice, clinical examination and radiological modalities (mammography, ultrasound, and/or magnetic resonance imaging (MRI)) cannot exclude the presence of a residual tumor and surgical treatment must be applied even in the patients with clinical and radiological complete response [5]. As dynamic-contrast enhanced MRI provides information about morphology and function of the tumor, it has been shown that MRI is the most accurate imaging modality to assess tumor response to NAC [6].

Even though MRI is considered the most reliable method in evaluating tumor response following NAC, over and underestimating residual tumor is still possible. Several studies have shown that post-chemotherapy changes in the breast is the major cause of the discordance between pathology and MRI [7, 8]. Besides, tumor response patterns post-NAC are heterogenous and varies depending on subtype and Ki-67 index. Studies have shown that the diagnostic performance of MRI following NAC is better in human epidermal growth factor 2 (HER2) positive tumors with a high Ki-67 index [9-11]. Ballesio et al. evaluated the relation between molecular subtypes and tumor response patterns and demonstrated that concentric pattern is significantly correlated with HER2+ tumors [12]. To our knowledge, no study has investigated false-positive MRI findings following NAC.

Based upon the limited body of knowledge, we aimed to demonstrate false-positive MRI findings after NAC in patients with pCR and investigate the correlation between post-NAC MRI findings and tumor response patterns based on HER2 status.

Materials and Methods

Study population

From January 2016 to September 2020, a total of 292 consecutive women with breast cancer treated with NAC and achieved pCR were reviewed. Inclusion criteria were as follows:

(1), invasive breast cancer histologically proven with image-guided core needle biopsy before NAC; (2), underwent breast MRI pre- and post-NAC; (3), presence of residual contrast enhancement in tumor bed at MRI after NAC; (4), underwent surgery (breast-conserving or modified radical mastectomy) following NAC. According to these eligibility criteria, 118 patients were included in this study. This retrospective study involving three centers was approved by Local Ethics Committee and informed consent was waived (2021-01/07).

Treatment protocol

The NAC regimen included a combination of epirubicin/adriamycin and cyclophosphamide (4 cycles) and taxanes (4 to 12 cycles). Pertuzumab or Transtuzumab was also administered in HER2+ patients. Carboplatin was also applied in patients with BRCA mutation.

After completing NAC, surgery was performed for all patients.

MRI Acquisition and Evaluation

MRI scan was performed in three tertiary referral centers using 1.5T (Achieva, Philips Medical Systems, The Netherlands or Magnetom Aera, Siemens Healthinieers, Erlangen, Germany) or 3T (Skyra, Siemens Healthinieers, Erlangen, Germany) MRI systems with a dedicated 7- or 16-channel bilateral breast coil. Breast MRI protocol comprised high-resolution precontrast and dynamic contrast-enhanced imaging in axial plane including one pre-contrast and five or six post-contrast image sets after administration of gadolinium-based contrast agent. MRI scans were performed prior to NAC therapy and immediately before the surgery. MRI studies were evaluated using fifth edition of BI-RADS lexicon by four breast radiologists with 4 to 20 years of experience in breast imaging. For the patients with multifocal and multicentric disease largest tumor was accepted as index lesion. Largest diameter of tumor at peak enhancement was accepted as tumor size. Tumor response pattern following NAC was grouped according to the classification suggested by Kim et al [13].

Histopathological Evaluation

Before NAC, all patients underwent US-guided core needle biopsy procedure and invasive breast cancer diagnosis was confirmed histologically. Tumor histology and Ki-67 index were assessed using core biopsy samples. Ki-67 index was classified into three groups; ≤15%, 16-39% and ≥40% [14]. Estrogen receptor (ER) and progesterone receptor (PR) were assessed as negative if there was <10% nuclear staining. Human epidermal growth factor receptor 2 (HER2) was considered as positive if there was 3+ staining and negative if the staining score was 0 or 1+. In case of 2+ score, HER2 gene amplification testing was performed using fluorescent in situ hybridization. Patients were grouped into four categories according to hormone receptor (HR) and HER2 status: HR+/HER2−, HR+/HER2+, HR−/HER2+ and HR−/HER2−.

After NAC, surgery was performed for all patients and surgical specimen was evaluated for pCR. pCR was defined as absence of invasive cancer regardless of ductal carcinoma in situ or metastatic lymph node presence.

Statistical Analysis

Statistical analysis was performed using SPSS version 22 (version 22; IBM, USA). The categorical variables were expressed as counts and percentages, and the continous variables were expressed as means and ranges. Categorical variables were compared based on HER2+ status using Chi-square or Fisher's exact test. P values <0.05 were considered statistically significant.

Results

Study population and pre-NAC clinico-pathologic characteristics

This study included 118 breast cancer patients who received NAC consecutively. The median age was 47.0 (range: 27-85). The majority (66.7%) of the patients were premenopausal. Regarding molecular

subtype, 43 (36.5%) tumors were HR+ HER2+, 34 tumors (28.8%) were HR− HER2+, 24 tumors (20.3%) were HR+ HER2−, and the remaining 17 (14.4%) were triple-negative. The mean tumor size by MRI before NAC was 30.4 mm (range:9-78 mm). Twelve patients (10.1%) had multifocal carcinoma, and one patient (0.8%) had bilateral invasive breast cancer. The histopathological analysis of surgical specimen revealed 103 (87.3%) invasive ductal carcinoma, seven (5.9%) invasive lobular carcinoma, three (2.5%) invasive ductal and lobular carcinoma, two (1.7%) invasive medullary carcinoma and one (0.8%) invasive mucinous. The majority of the patients (78.8%) were axillary node positive at presentation. The baseline clinico-pathological characteristics of patients were summarized in Table 1.

Table 1. Baseline clinicopathological characteristics of patients (n=118)

	All patients (n=118)
Median age, years (range)	47.0 (27-85)
Menopausal status	
Premenapausal	80(67.8)
Postmenapausal	38(32.2)
Basal MRI mean tumor size, mm (range)	30.4 (9-78)
Histologic type	
IDC	103(87.3)
ILC	7(5.9)
IDC+ILC	3(2.5)
Medullary carcinoma	2(1.7)
Mucinous carcinoma	1(0.8)
Other	2(1.6)
Molecular subtype	
HR+/HER2-	24(20.3)
HR+/HER2+	43(36.4)
HR-/HER2+	34(28.8)
HR-/HER2-	17(14.4)
Ki-67 index	
≤15%	5(4.2)
16-39%	57(48.3)
≥40%	56(47.5)
Node status at presentation	
Negative	25(21.2)
Positive	93(78.8)

Age presented as median (range) and tumor size presented as mean (range). All other variables are numbers of patients (percentages). MRI=Magnetic resonance imaging, IDC=Invasive ductal carcinoma, ILC=Invasive lobular carcinoma, HR=Hormone receptor, HER2=Human epidermal growth factor receptor 2

MRI findings of tumors before and after NAC

The mean tumor size by MRI after NAC was 9.9 mm (range:3-55 mm). The most frequent MRI findings at presentation were mass and non-mass enhancement (NME) in HER2+ and HER2− groups. The MRI findings following NAC differed significantly between HER2+ and HER2− groups (p=0.02). The most frequent false positive MRI finding was focus and foci in HER2+ tumors, whereas NME in HER2− group (Figure 1). In pre-NAC MRI peritumoral edema was significantly associated with HER2+ tumors (p=0.04). Pre- and post-NAC, the presence of the metastatic lymph nodes by MRI was similar in both groups (p>0.05). The most frequent enhancement curve pattern was type 3 at presentation, whereas the majority of tumors presented type 1 and type 2 enhancement curve pattern after NAC in both groups (p>0.05). Pre- and post-NAC MRI findings of tumors based on HER2 status were summarized in Table-2.

Changes of MRI features and pathologic findings after NAC

The majority of post-NAC tumor size by MRI was smaller than tumor size at presentation. Following NAC, three tumors (7.3%) in HER2− group and one tumor (1.3%) in HER2+ group showed increase in size. The post-NAC MRI finding was NME in all tumors that increased in size. Regarding the tumor size pre- and post-NAC, ≥50% reduction in size was significantly associated with HER2+ tumors (p<0.001). In pathologic evaluation, fibrosis in tumor bed was found more often in the HER2− group without significant difference (p=0.10). Presence of DCIS and fibrosis in surgical pathology was significantly associated with NME on post-NAC MRI (p<0.001). A high-risk lesion with atypia in the surgical specimen was found more likely in the HER2+ group, whereas failed to reach a significant difference (p=0.06). Axillary pCR was achieved significantly higher in the HER2+ group (p=0.04). There was no significant difference

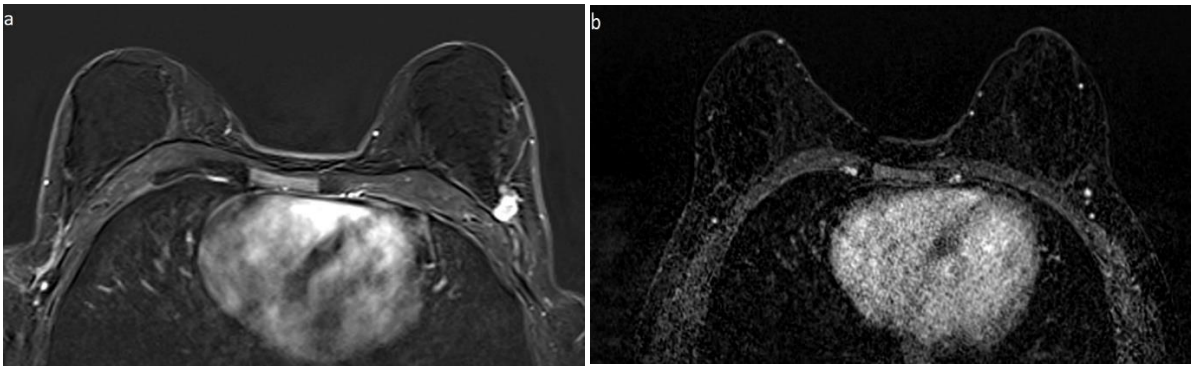

Figure 1. 36-year-old woman with invasive ductal carcinoma (hormone receptor-positive and HER2-positive)
(a) Axial substracted postcontrast T1-weighted image shows an irregular enhancing mass of left breast before chemotherapy.
(b) After completion of neoadjuvant chemotherapy, axial subtracted postcontrast T1-weighted image shows an enhancing focus at the original tumor site, which turned out to be a false-positive finding. No tumor or fibrosis was detected in the specimen after surgery.

Table 2. MRI findings based on HER2 status before and after NAC

	Before NAC			After NAC		
	HER2+(n=77) (65.2%)	HER2−(n=41) (34.7%)	p	HER2+(n=77) (65.2%)	HER2−(n=41) (34.7%)	p
BPE						
Minimal	21(27.3)	6(14.6)	0.36	39(50.6)	12(29.3)	0.04*
Mild	37(48.1)	20(48.8)		30(39.0)	20(48.8)	
Moderate	17(22.1)	13(31.7)		7(9.1)	9(22.0)	
Marked	2(2.6)	2(4.9)		1(1.3)	0(0)	
MRI finding						
Mass	41(53.2)	22(53.7)	1.0	11(14.3)	2(4.9)	0.02*
NME	1(1.3)	0(0)		32(41.6)	25(61.0)	
Mass+NME	35(45.5)	19(46.3)		1(1.3)	3(7.3)	
Focus	0(0)	0(0)		33(42.9)	11(26.8)	
Peritumoral edema						
Present	37(48.1)	12(29.3)	0.04*	4(5.2)	2(4.9)	1.0
Absent	40(51.9)	29(70.7)		73(94.8)	39(95.1)	
Axillary LAP						
Present	61(79.2)	32(78.0)	0.88	14(18.2)	9(22.0)	0.62
Absent	16(20.8)	9(22.0)		63(81.8)	32(78.0)	
Kinetic curve type						
1	1(1.3)	0(0)	1.0	47(61.0)	25(61.0)	1.0
2	20(26.0)	11(26.8)		29(37.7)	16(39.0)	
3	56(72.7)	30(73.2)		1(1.3)	0(0)	

Data are presented as n(%).
*p values less than 0.05 regarded as statistically significant.
BPE=Background parenchymal enhancement, NAC=Neoadjuvant chemotheraphy, HER2=Human epidermal growth factor receptor 2, NME=Non-mass enhancement, LAP=Lymphadenopathy

Table 3. Changes of MRI features and pathologic findings based on HER2 status after NAC

	HER2+(n=77)	HER2−(n=41)	p
Tumor size difference in MRI			
≥50% reduction	68(88.3)	22(53.7)	<0.001*
<50% reduction	8(10.4)	16(39.0)	
Increase	1(1.3)	3(7.3)	
Tumor response pattern			
Concentric shrinkage	14(18.2)	4(9.8)	0.10
Crumble	6(7.8)	3(7.3)	
Focus or NME	48(62.3)	22(53.7)	
Diffuse enhancement	9(11.7)	12(29.3)	
BPE decrease (in categories)			
0	50(64.9)	28(68.3)	0.88
1	24(31.2)	11(26.8)	
2	3(3.9)	2(4.9)	
Tumor bed; fibrosis			
Present	28(36.4)	9(22.0)	0.10
Absent	49(63.6)	32(78.0)	
Tumor bed; DCIS			
Present	13(16.9)	10(24.4)	0.32
Absent	64(83.1)	31(75.6)	
Lesion with atypia in surgical specimen			
Present	21(27.3)	5(12.2)	0.06
Absent	56(72.7)	36(87.8)	
Axillary pathologic response			
Complete response	65(84.4)	28(68.3)	0.04*
Partial response	12(15.6)	13(31.7)	

Data are presented as n(%).
**p* values less than 0.05 regarded as statistically significant.
HER2=Human epidermal growth factor receptor 2, BPE=Background parenchymal enhancement, NME=Non-mass enhancement, DCIS=Ductal carcinoma in situ

regarding the frequency of residual in situ component in the surgical specimen and the degree of BPE reduction at MRI between groups. Changes in MRI features and pathologic findings following NAC were summarized in Table 3.

Discussion

In recent years, the use of NAC in breast cancer has become widespread. MRI is considered the most accurate method for evaluating tumor response after NAC; however, post-NAC MRI assessment may be challenging due to the heterogeneity of tumor response and the possibility of over and underestimation. To our knowledge, this study is the first study reporting false-positive MRI findings post-NAC and tumor response patterns based on molecular subtypes in breast cancer patients who achieved pCR. Our results revealed that residual MRI findings differ according to HER2 status. HER2+ tumors mostly present with focus or foci after NAC whereas non-mass enhancement more likely found in HER2− tumors.

The efficacy of NAC in breast cancer varies according to molecular subtypes. Studies have shown that HER2+ and triple-negative tumors are more responsive to chemotherapeutics due to their high cellular proliferation [15, 16]. Targetted agents used in the HER2+ group also increase this effectiveness. In agreement with the previous results, the majority of our study population (79.6%) consist of HER2+ and triple-negative breast cancer.

In a multicenter study, the overall accuracy of MRI after NAC was reported as 74% [17]. In a retrospective study with 98 patients, Choi et al. reported false positive rate of post-NAC MRI as 47% [18]. Confounding factors in radiology-pathology discordance should be taken into consideration to avoid inappropriate surgical planning. Post-chemotherapy changes including fibrosis, inflammation, and necrosis can mimic

residual tumor and thereby may cause false-positive results on imaging. Molecular subtype, tumor size and chemotherapy regimen are also among the factors that influence the diagnostic performance of MRI. Studies have shown that the diagnostic accuracy of MRI was higher in HER2+ and triple negative tumors than hormone receptor-positive breast cancer. MRI-pathology discordance was also higher in tumors with >5 cm size and in tumors with low Ki-67 index [19]. Tumors presented with non-mass enhancement (NME) at pre-NAC MRI were also associated with lower diagnostic performance [20]. Furthermore, a decrease in contrast enhancement at post-NAC MRI resulting from the antiangiogenetic effect of taxanes may cause underestimation of residual tumor.

Another challenge in evaluating the post-NAC residual tumor is the heterogeneity of the tumor response patterns. Ballesio et al. evaluated MRI-based tumor shrinkage patterns (concentric, nodular and mixed pattern) and investigated its relationship between pCR rates and molecular subtypes. Results showed that concentric pattern is significantly associated with pCR and HER2+ subtype. However, mixed pattern is significantly associated with Luminal A tumors and non-pCR [12]. In our study, foci and NME was the most frequent response pattern post-NAC without significant difference according to HER2 status. This discrepancy may be attributable to the difference in the study populations and that only patients who achieved pCR were included in our study. Moreover, Lee et al. revealed that tumor response patterns differ histopathologically according to molecular subtypes [21]. According to this study, fibrosis within tumor bed was found more frequently in HR+ tumors which is in line with our results.

Imaging biomarkers based on MRI can be used in order to increase the diagnostic accuracy of post-NAC MRI. Studies have shown that decrease in background parenchymal enhancement (BPE) after NAC is correlated with pCR [22, 23]. Oh et al. also revealed that no significant correlation between post-NAC BPE decrease and molecular subtypes, which is consistent with our results [22]. In a retrospective study, Kim et al. used lesion-to-background parenchymal signal enhancement ratio (SER) on MRI in ≤ 5 mm lesions, and their results indicate that SER≤1.6 criterion significantly improves specificity to distinguish pCR from a residual tumor [24]. In regard to apparent diffusion coefficients (ADC), high ADC values post-NAC is associated with pCR. Santamaria et al. reported that pre- and post-NAC ADC ratio was >1.5 in 86% of patients who achieved pCR [25].

Our study has some limitations. First, this was a multi-center study thus MRI scans were performed with different MRI systems which could affect MRI assessment. Second, interobserver variability was not assessed even though MRI evaluation was made by two radiologists to reach consensus in ambiguous cases. At last, the definition of pCR may have an influence on MRI accuracy, and pCR was defined as the absence of invasive tumor regardless of DCIS presence in this study. However, Santamaria et al. revealed that pCR definition has no significant effect on the post-NAC MRI accuracy [26].

In conclusion, each breast tumor shows different response characteristics to NAC, and the diagnostic accuracy of MRI following NAC is evolving by understanding the underlying mechanisms and tumor biology. Our study revealed that tumor response patterns and post-NAC MRI findings differ according to HER2 status. It should be noted that focus and foci are the most frequent false-positive MRI finding in patients with pCR, particularly in HER2+ cases. With the help of further information in this field, avoidance of post-NAC surgery might be possible with an accurate prediction of pCR.

REFERENCES

1. Mathew J, Asgeirsson KS, Cheung KL, Chan S, Dahda A, Robertson JF. Neoadjuvant chemotherapy for locally advanced breast cancer: a review of the literature and future directions. Eur J Surg Oncol. 2009; 35(2): 113-122.
2. Mauri D, Pavlidis N, Ioannidis JP. Neoadjuvant versus adjuvant systemic treatment in breast cancer: a meta-analysis. J Natl Cancer Inst. 2005; 97(3): 188-194.
3. Montagna E, Bagnardi V, Rotmensz N, Viale G, Pruneri G, Veronesi P, et al. Pathological complete response after preoperative systemic therapy and outcome: relevance of clinical and biologic baseline features. Breast Cancer Res Treat. 2010; 124(3): 689-699.
4. Von Minckwitz G, Untch M, Blohmer JU, Costa SD, Eidtmann H, Fasching PA, et al. Definition and impact of pathologic complete response on prognosis after neoadjuvant chemotherapy in various intrinsic breast cancer subtypes. J Clin Oncol. 2012; 30(15): 1796-1804.
5. Hayashi N, Tsunoda H, Namura M, Ochi T, Suzuki K, Yamauchi H, et al. Magnetic Resonance Imaging Combined with Second-look Ultra-sonography in Predicting Pathologic Complete Response After Neoadjuvant Chemotherapy in Primary Breast Cancer Patients. Clin Breast Cancer. 2019; 19(1): 71-77.
6. Lobbes MB, Prevos R, Smidt M, Tjan-Heijnen VC, Van Goethem M, Schipper R, et al. The role of magnetic resonance imaging in assessing residual disease and pathologic complete response in breast cancer patients receiving neoadjuvant chemotherapy: a systematic review. Insights Imaging. 2013; 4(2): 163-175.
7. Partridge SC, Gibbs JE, Lu Y, Esserman LJ, Sudilovsky D, Hylton NM. Accuracy of MR imaging for revealing residual breast cancer in patients who have undergone neoadjuvant chemo-therapy. AJR Am J Roentgenol. 2002; 179(5): 1193-1199.
8. Rieber A, Brambs HJ, Gabelmann A, Heilmann V, Kreienberg R, Kuhn T. Breast MRI for monitoring response of primary breast cancer to neo-adjuvant chemotherapy. Eur Radiol. 2002; 12(7): 1711-1719.
9. Chen JH, Bahri S, Mehta RS, Kuzucan A, Yu HJ, Carpenter PM, et al. Breast cancer: evaluation of response to neoadjuvant chemotherapy with 3.0-T MR imaging. Radiology. 2011; 261(3): 735-743.
10. Kuzucan A, Chen JH, Bahri S, Mehta RS, Carpenter PM, Fwu PT, et al. Diagnostic performance of magnetic resonance imaging for assessing tumor response in patients with HER2-negative breast cancer receiving neoadjuvant chemotherapy is associated with molecular biomarker profile. Clin Breast Cancer. 2012; 12(2): 110-118.
11. Mukhtar RA, Yau C, Rosen M, Tandon VJ, I-Spy T, Investigators A, et al. Clinically meaningful tumor reduction rates vary by prechemotherapy MRI phenotype and tumor subtype in the I-SPY 1 TRIAL (CALGB 150007/150012; ACRIN 6657). Ann Surg Oncol. 2013; 20(12): 3823-3830.
12. Ballesio L, Gigli S, Di Pastena F, Giraldi G, Manganaro L, Anastasi E, et al. Magnetic resonance imaging tumor regression shrinkage patterns after neoadjuvant chemotherapy in patients with locally advanced breast cancer: Correlation with tumor biological subtypes and pathological response after therapy. Tumour Biol. 2017; 39(3): 1010428317694540.
13. Kim TH, Kang DK, Yim H, Jung YS, Kim KS, Kang SY. Magnetic resonance imaging patterns of tumor regression after neoadjuvant chemotherapy in breast cancer patients: correlation with pathological response grading system based on tumor cellularity. J Comput Assist Tomogr. 2012; 36(2): 200-206.
14. Zhang X, Wang D, Liu Z, Wang Z, Li Q, Xu H, et al. The diagnostic accuracy of magnetic resonance imaging in predicting pathologic complete response after neoadjuvant chemotherapy in patients with different molecular subtypes of breast cancer. Quant Imaging Med Surg. 2020; 10(1): 197-210.
15. Loo CE, Straver ME, Rodenhuis S, Muller SH, Wesseling J, Vrancken Peeters MJ, et al. Magnetic resonance imaging response monitoring of breast cancer during neoadjuvant chemotherapy: relevance of breast cancer subtype. J Clin Oncol. 2011; 29(6): 660-666.
16. Colleoni M, Bonetti M, Coates AS, Castiglione-Gertsch M, Gelber RD, Price K, et al. Early start of adjuvant chemotherapy may improve treatment outcome for premenopausal breast cancer patients with tumors not expressing estrogen receptors. The International Breast Cancer Study Group. J Clin Oncol. 2000; 18(3): 584-590.
17. De Los Santos JF, Cantor A, Amos KD, Forero A, Golshan M, Horton JK, et al. Magnetic resonance imaging as a predictor of pathologic response in patients treated with neoadjuvant systemic treatment for operable breast cancer. Translational Breast Cancer Research Consortium trial 017. Cancer. 2013; 119(10): 1776-1783.
18. Choi BB, Kim SH. Effective factors to raise diagnostic performance of breast MRI for diagnosing pathologic complete response in breast cancer patients after neoadjuvant chemotherapy. Acta Radiol. 2015;56(7):790-797.
19. Bouzon A, Acea B, Soler R, Iglesias A, Santiago P, Mosquera J, et al. Diagnostic accuracy of MRI to evaluate tumour response and residual tumour size after neoadjuvant chemotherapy in breast cancer patients. Radiol Oncol. 2016; 50(1): 73-79.
20. Negrao EMS, Souza JA, Marques EF, Bitencourt AGV. Breast cancer phenotype influences MRI response evaluation after neoadjuvant chemotherapy. Eur J Radiol. 2019; 120: 108701.

21. Lee HJ, Song IH, Seo AN, Lim B, Kim JY, Lee JJ, et al. Correlations between molecular subtypes and pathologic response patterns of breast cancers after neoadjuvant chemotherapy. Ann Surg Oncol. 2015; 22(2): 392-400.
22. Oh SJ, Chae EY, Cha JH, Shin HJ, Choi WJ, Kim HH. Relationship between background parenchymal enhancement on breast MRI and pathological tumor response in breast cancer patients receiving neoadjuvant chemotherapy. Br J Radiol. 2018; 91(1088): 20170550.
23. Preibsch H, Wanner L, Bahrs SD, Wietek BM, Siegmann-Luz KC, Oberlecher E, et al. Background parenchymal enhancement in breast MRI before and after neoadjuvant chemo-therapy: correlation with tumour response. Eur Radiol. 2016; 26(6): 1590-1596.
24. Kim SY, Cho N, Shin SU, Lee HB, Han W, Park IA, et al. Contrast-enhanced MRI after neoadjuvant chemotherapy of breast cancer: lesion-to-background parenchymal signal enhancement ratio for discriminating pathological complete response from minimal residual tumour. Eur Radiol. 2018; 28(7): 2986-2995.
25. Santamaria G, Bargallo X, Fernandez PL, Farrus B, Caparros X, Velasco M. Neoadjuvant Systemic Therapy in Breast Cancer: Association of Contrast-enhanced MR Imaging Findings, Diffusion-weighted Imaging Findings, and Tumor Subtype with Tumor Response. Radiology. 2017; 283(3): 663-672.
26. Santamaria G, Bargallo X, Ganau S, Alonso I, Munoz M, Molla M, et al. Multiparametric MR imaging to assess response following neoadjuvant systemic treatment in various breast cancer subtypes: Comparison between different definitions of pathologic complete response. Eur J Radiol. 2019; 117: 132-139.

Corresponding author e-mail: aydanavdanaslan@gmail.com

Orcid ID:
Aydan Avdan Aslan 0000-0002-7169-5933
Servet Erdemli 0000-0001-5545-768X
İbrahim Halil Erdoğdu 0000-0002-5445-2649
Serap Gültekin 0000-0001-6349-3998
Cihan Uras 0000-0002-6838-2311
Fatma Tokat 0000-0002-6976-1567
Ali Arıcan 0000-0002-6099-2000
Leyla Özer 0000-0001-8763-5268
Kemal Behzatoğlu 0000-0002-9843-9825
Nezih Meydan 0000-0003-4100-5804
Füsun Taşkın 0000-0001-7985-3660

Doi: 10.5505/aot.2023.60973

