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Original Article

Can We Predict Triple Negative Breast Cancer with Magnetic Resonance Imaging Findings?

Eda Cingöz[1], Rana Günöz Cömert[2], Zuhal Bayramoğlu[1], Neslihan Cabıoğlu[3], Ravza Yılmaz[1]

[1]Department of Radiology, İstanbul University, Faculty of Medicine, İstanbul, Turkey
[2]Department of Radiology,Turhal Hospital, Tokat, Turkey
[3]Department of General Surgery, İstanbul University, Faculty of Medicine, İstanbul, Turkey

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Corresponding author: Eda Cingöz, e-mail: edacanipek@gmail.com

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Abstract

Objective: Triple-negative breast cancer comprises a small percentage of all breast cancers. However, they are accountable for a high percentage of the loss of lives. Being able to predict triple-negative breast cancer by imaging may play a pivotal role in earlier management and the planning of the treatment. We scrutinized imaging features for 64 patients diagnosed with triple-negative breast cancer on magnetic resonance imaging to define the characteristic findings in imaging. An additional objective was to define the spectrum of imaging findings concerning triple-negative breast cancer in mammography as well as ultrasonography.

Methods: In this descriptive study, between 2018 and 2022, 64 patients diagnosed with triple-negative breast cancer and underwent magnetic resonance imaging were enrolled in our present study. Imaging findings were evaluated based on the (Breast Imaging Reporting and Data System) (BI-RADS) Atlas, fifth edition.

Results: Triple-negative breast cancer was more often localized posteriorly in 29 patients (45%). Fifty-five (86%) of the 64 lesions revealed mass enhancement. The internal enhancement patterns were mostly in the rim (36%) and heterogeneous pattern (42%). Masses were commonly round/oval-shaped (63.6%) with irregular margins (51%). It was seen unifocally in 40 (63%) of the patients. The early enhancement was average in 25 (39%) and rapid in 22 (34%) patients, with washout delay enhancement in 24 of 55 cases. Intratumoral copiously high signal occurred in 22 (34%) and high signal intensity in 20 (31%) on T2-weighted images. Round/oval-shaped masses with indistinct margins were common findings in mammography and ultrasonography.

Conclusion: Our results show that triple-negative breast cancer is typically seen as a round/oval-shaped mass with irregular margins and rim-heterogeneous enhancement. Also, triple-negative breast cancer is most commonly related to a very high T2 signal intensity, and they are usually found as unifocal lesions.

Keywords: Breast, carcinoma, magnetic resonance imaging

INTRODUCTION

Breast cancer is one of the complicated morbidities with varied morphological, biological, and molecular characteristics.[1] Triple-negative breast cancer (TNBC) comprises approximately 10-20% of all breast cancers that do not express human epidermal growth factor receptor 2 (HER2), estrogen receptors (ER), or progesterone receptors (PR).[2-4] It is defined by different molecular, histological, and clinical findings inclusive of an especially negative prognosis. Triple-negative breast cancers and basal-like breast cancers are closely related but are not synonymous or interchangeable. Basal-like cancers are frequently related to the high histologic grade, mutation of the TP53 gene, suppressed BRCA1 function, and a bad prognostic result. These are known as aggressive features.[5] Magnetic resonance imaging (MRI) is the most sensitive imaging technique for the diagnosis of breast cancer and that is why it is specified prior to operation to show the scope of the disease. Magnetic resonance imaging can provide significant data not only on the shape of the masses but also on the pathology represented by the signal intensity features and on the dynamic evaluation of contrast medium uptake. Had it been possible to predict TNBC based on MRI features, these findings would provide both pretreatment planning and prognostic information. There have been a few studies on the relationship between TNBC and MRI features.[6-8] The goal of our work was to define the MRI features of TNBC and to reveal whether the diagnostic abilities of MRI could be used to credibly estimate the status of TNBC prior to tissue biopsy results becoming obtainable. An additional aim was to describe the characteristics of imaging features regarding triple-negative cancers on both mammography (MG) and ultrasonography (US).

METHODS

Patients

All TNBCs between May 2012 and December 2016 were reviewed, and 64 (56 invasive ductal carcinomas, 7 metaplastic carcinomas, and 1 invasive lobular carcinoma) patients who received MRI in our institution were taken into this study after informed consents were provided from all of the participants. Immunohistochemical analysis of ER, PR, and HER2 status had been performed on breast tissue materials attained from surgery and ER and PR's status was considered to be negative if the expression was less than 10%. The histopathological preparations were tested

for HER2 gene expression using a validated dual-probe fluorescence in situ hybridization. Triple-negative breast cancers are defined by the lack of the 3 predictive/prognostic markers: ER, PR, and HER2. The study was approved by the ethics committee of Istanbul University (Date: July 29, 2022, Decision no: 2022/1296).

Ultrasonography and Mammography

Two radiologists experienced in breast imaging (1 with 7 years and the other with 4 years of experience) evaluated all images and evaluated the images according to the BI-RADS (Breast Imaging Reporting and Data System) Atlas, fifth edition Radiology.[9] Ultrasonography (Acuson Antares; Siemens, Germany) was performed on all patients via a high-resolution linear probe with a 12 MHz frequency. Women underwent MG by bilateral 2-view full-field digital MG (Giotto; Bologna, Italy).

Magnetic Resonance Imaging

Studies were exerted at 1.5-T on an MRI unit (Achieva; Philips Medical Systems, Best, The Netherlands). A dedicated 4-channel phased-array breast coil was used in the prone position. Each MRI examination included a T1-weighted (T1-W) sequence (TR [Time of Repetition]/TE [Time of Excitation]: 495/8 ms; FOV (Field of View), 340 × 400 mm; NEX (Number of Excitation), 2; slice thickness, 2 mm; matrix, 272 × 267) in the axial plane and fat-saturated T2-weighted (T2-W) images in the axial plane using turbo spin-echo sequence (TR/TE: 4130/118 ms; FOV, 340 × 340mm; NEX, 3; slice thickness, 2 mm; matrix, 272 × 224) were performed. In the T1-W turbo field-echo 3-dimensional sequences (TR/TE, 6.8/3.3 ms; NEX, 3; FOV, 340 × 340 mm; matrix, 340 × 338), dynamic images were taken once before and 5 times following the injection of the contrast agent including 0.1 mmol/kg gadolinium. Lesions of the time-signal intensity curves were plotted and commented. In patients with multifocal tumors, we assessed only the index mass in order to perform a statistical analysis of the correlation between the histological and the MRI findings. Lesions were divided into 3 categories: focus, mass, and non-mass enhancement. Masses were scrutinized with regard to shape (irregular, round, or oval), margin (smooth, spiculated, or irregular), and characteristic features of internal enhancement pattern (heterogeneous, homogeneous, or rim enhancement). Non-mass enhancement was described in terms of distribution (focal, linear, segmental, regional/multiple regional, or diffuse) and internal enhancement (heterogeneous, homogeneous, clumped, or clustered ring). The initial contrast uptake and late contrast enhancement-time intensity curve images were obtained by post-processing with MRI software. We evaluated MRI kinetics in terms of the most suspicious kinetics pattern. Background parenchymal enhancement obtained with the second contrast-enhanced sequence is categorized as minimal, mild, moderate, or marked, and also either symmetric or asymmetric was described. The amount of fibroglandular tissue, the long and short diameters of the tumor, the intensity of mass, and parenchyma edema on the T2-W image were documented. Skin retraction-thickening-invasion and nipple retraction-invasion and invasion to pectoral muscle, presence of cyst, and distortion were detected. The tumor locations were classified as quadrant locations and antero-posterior localization (1/3 anterior, 1/3 middle, 1/3 posterior, and extensive). The type of the disease was categorized as 1 of 3 types. The unifocal type was described when just 1 single malignant focus was encountered, the multifocal type was described when more than 1 malignant focus was encountered in the same quadrant, and the multicentric type was described when more than 1 malignant focus was revealed in more than 1 quadrant. In multifocal and multicentric cases, in addition to the index lesion, at least 1 biopsy was performed from a malignant focus. The biopsy results were exactly compatible with the analyzed lesion on MRI. The study was conducted in a descriptive fashion. Mean ± standard deviation and median with range data are presented. The frequencies of the findings of magnetic resonance studies were also evaluated.

MAIN POINTS

- While triple-negative breast cancer constitutes a small percentage of all breast cancers, it has an enormous contribution to deaths from breast cancer.
- Certain magnetic resonance imaging findings including round/oval-shape, rim or heterogeneous enhancement, high signal intensity on T2-weighted images, and posterior-prepectoral location could direct the diagnosis to triple-negative breast cancer.
- Triple-negative breast cancer tends to be seen in more dense and heterogeneous breasts.

RESULTS

Mammography and US features of an index tumor were documented in multifocal and multicentric patients. Our study population's MG findings are shown in Table 1. Eight mammograms were normal in TNBC. The most common mammographic finding was mass appearance in 53 (82.7%) patients. Masses without calcification were most common on 41 (64%) mammograms. Ultrasonography revealed masses in all patients, including the 8 cancers determined to be occult on MG. Ultrasonography findings are documented in Table 2. Triple-negative breast cancer mostly showed masses with round/oval shape in 37 cases (57.8%) and indistinct margins in 40 (62.5%). Fifty-one of the TNBCs (79.6%) were hypoechoic and 34 of them (53.1%) had no posterior acoustic features. The mean age was 47.5 years (range 28-72). The mean size of the tumors was short diameter 2.6 cm (range 0.3-10 cm) and long diameter 3.6 cm (range 0.4-11 cm) (Table 3). Superior-outer quadrant represented the most common localization in 40 patients (63%). The amount of fibroglandular tissue was type A in 2 (3%), type B in 15 (23%), type C in 28 (44%), and type D in 19 (30%). Background parenchymal enhancement was minimal in 17 (26%), mild in 28 (44%), moderate in 12 (19%), and marked in 7 (11%). Triple-negative breast cancers were located 1/3 posterior in 29 patients (45%), middle 1/3 segment in 17 (26%), 1/3 anterior in 8 (13%), and both 1/3 posterior and 1/3 middle segment that was classified as extensive in 10 of them (16%). As a result, TNBCs were located posteriorly in 39 of 55 patients (61%). Very high signal intensity was seen in 22 (34%), high signal intensity in 20 (31%), and hypointense/isointense was seen in 22 (34%) patients on T2-W images. Parenchyma edema was

Table 1. Mammographic Features in Triple-Negative Breast Cancer

		Frequency (Percent)
Mammographic findings	Normal	12
	Mass only	64
	Mass with calcification	19
	Calcification	2
	Focal asymmetry	3
Mass shape	Round/oval	55
	Irregular	45
Mass margin	Circumscribed	17
	Microlobulated	13
	Obscured	15
	Indistinct	55

Table 2. Ultrasound Features of Triple-Negative Breast Cancer

		Frequency (Percent)
Mass shape	Round/oval	58
	Irregular	42
Mass margin	Circumscribed	9
	Indistinct	63
	Angular	12
	Microlobulated	16
Echo pattern	Hypoechoic	80
	Complex	12
	Isoechoic	8
Posterior acoustic features	None	53
	Enhancement	31
	Shadowing	6
	Combined	10

minimal in 12 (19%) and prominent in 32 (50%) patients. Fifty-five (86%) of the 64 TNBCs revealed as a mass, and the other 9 (14%) had non-mass enhancement. None of the triple-negative cancers was evaluated as a focus. The 55 TNBCs with mass appearance were frequently round/oval-shaped (64%) and irregular-shaped (36%). Mass margins were irregular in 28 (51%), spiculated in 10 (18%), and smooth in 17 (31%) of the masses. The predominant pattern of internal enhancement of mass was founded as rim enhancement which was seen in 20 (36%) of the 55 patients. Heterogeneous enhancement was monitored in 23 of the 55 cases (42%) and homogeneous enhancement was monitored in 12 of them (22%). All metaplastic cancers appeared as masses with rim enhancement. Only 1 case of invasive lobular cancer showed non-mass enhancement with an internal heterogeneous enhancement of diffuse distribution. Magnetic resonance imaging showed 4 only one mass in 40 (63%) of the patients, multifocality in 13 (20%), and multicentricity in 11 (17%). The most common pattern regarding internal enhancement was heterogeneous (56%) in the 9 patients with non-mass enhancement. Three of them reviewed diffuse distribution, 5 of them showed segmental distribution, and only 1 cancer showed multiple regional enhancements. Focus, focal, and linear enhancement patterns were not seen. The early enhancement patterns were mostly medium in 25 (39%) and fast in 22 (34%) of our patients. The delay enhancement patterns were washout, as observed in 24 (38%), and plateau in 23 (36%). A persistent time–intensity pattern was noted in 17 cases (Table 3). Skin changes were seen in 20 patients. Skin retraction-thic kening-invasion were seen in 15, 2, and 3 patients, respectively. No cyst was seen in 48 patients. Distortion accompanying mass was seen in 21 patients (33%). Seven patients had nipple retraction and 3 of them had nipple involvement, and 5 patients had invasion to pectoral muscle and this finding was visualized only on MRI. Necrosis was seen in 26 (41%) patients. Mean value of Ki-67 was 71 with a range of 5-95. Ki67 was positive in 89% of cases (57 of 64), with a cutoff value of 50%.

Table 3. Magnetic Resonance Imaging Features of Triple-Negative Breast Cancer

		Frequency (Percent)
Location	Anterior	8
	Middle	17
	Posterior	29
T2 sequence signal	Hypoisointense	22
	Hyperintense	20
	Very hyperintense	22
Mass/non-mass	Mass	55
	Non-mass	9
Mass shape	Round/oval	64
	Irregular	36
Mass margin	Smooth	31
	Spiculated	18
	Irregular	51
Mass enhancement	Heterogeneous	23
	Rim	20
	Homogeneous	22
Non-mass enhancement	Heterogeneous	56
	Clumped	28
Non-mass distribution	Diffuse	33
	Regional	11
	Segmental	55
Early enhancement	Slow	27
	Medium	39
	Fast	34
Delay enhancement	Persistent	26
	Plateau	36
	Washout	38

DISCUSSION

Triple-negative breast cancers have no targeted treatment that has been performed effectively. However, they are responsible for a comparatively excessive number of deaths related to breast cancer, often due to aggressive clinical courses.[10] Thus, advanced knowledge of this molecular subtype of breast cancer is required for the proper management of patients. Imaging features are of paramount importance because the more we know about the imaging characteristics of molecular subtypes, the better we can predict the course of the disease. On MG and US, TNBC can mimic lesions with benign morphology.[11-13] Triple-negative breast cancer has been found to be an oval/round mass that is very rarely accompanied by calcification on MG similar to our findings.[7,14] On US, they were likely to be hypoechoic or markedly hypoechoic masses with an irregular or oval/round shape and mostly circumscribed margins in the literature.[15] Against the circumscribed margin of these studies on MG and US, our results suggest TNBCs were mostly oval/round masses but with indistinct margins.[7,14,15] Due to dense breast or benign or unclear MG and ultrasound features, TNBC can be more difficult to diagnose by MG or US.[11-13,16,17] In addition to TNBC, Schrading and Kuhl[18] declared that familial breast cancers tend to occur with benign morphologic features. Magnetic resonance imaging is quite successful in this type of cancer diagnosis compared with conventional methods because of more evident malign findings.[15] Our results show that TNBCs are more frequently mass lesions, round or oval-shaped, irregular margin, and rim or heterogeneous enhancement (Figure 1). Also, MRI findings of TNBC were high signal intensity on T2-W images (65%) and a unifocal lesion (63%) (Figure 2). These features were consistent with typical TNBC features previously repor ted.[6,7,11,14,15] Uematsu et al[6] have reported that a significantly high signal in tumors on T2-W was related to TNBC and also considerably related to necrosis. Twenty-nine (41%) of the TNBC showed necrosis in our study. Respecting enhancement kinetics, features of different delay enhancement patterns have been reported,[6,7] and in our study, 74% of TNBC showed a washout and plateau enhancement pattern. The early enhancement patterns were medium and fast in 73% of our patients, which makes facilitating differentiation between benign and malignant tumors difficult. Multifocal and multicentric disease is frequently encountered in luminal B and HER2 subtypes, compared with luminal A and TNBC.[19,20] Preoperative breast MRI may be very helpful in better defining the extent of disease for patients of luminal B and HER2

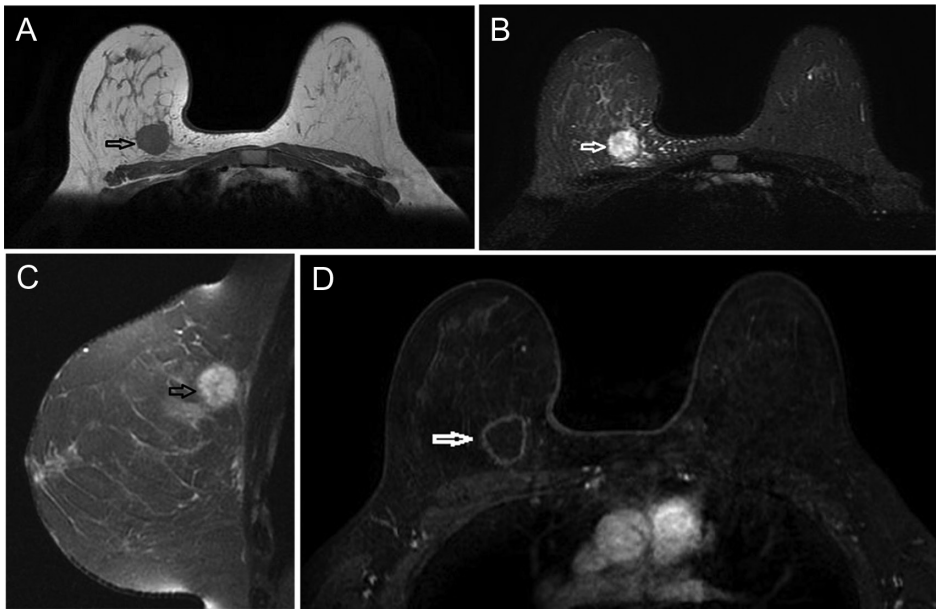

Figure 1. Triple-negative breast cancer is in a 45-year-old woman's right breast. T1-weighted (T1-W) (A) and T2- weighted (T2-W) with fat saturation (B) axial MR images show a 1.5-cm round mass with an irregular margin in the posterior location (black arrow in A and white arrow in B). Very high signal intensity mass and prominent peritumoral edema is seen in fat-saturated T2-W axial image. Hyperintense mass (C) is also seen adjacent to the pectoral muscle (black arrow) in the same sequence at sagittal view. The T1-W subtraction image (D) reveals the mass with rim enhancement (white arrow).

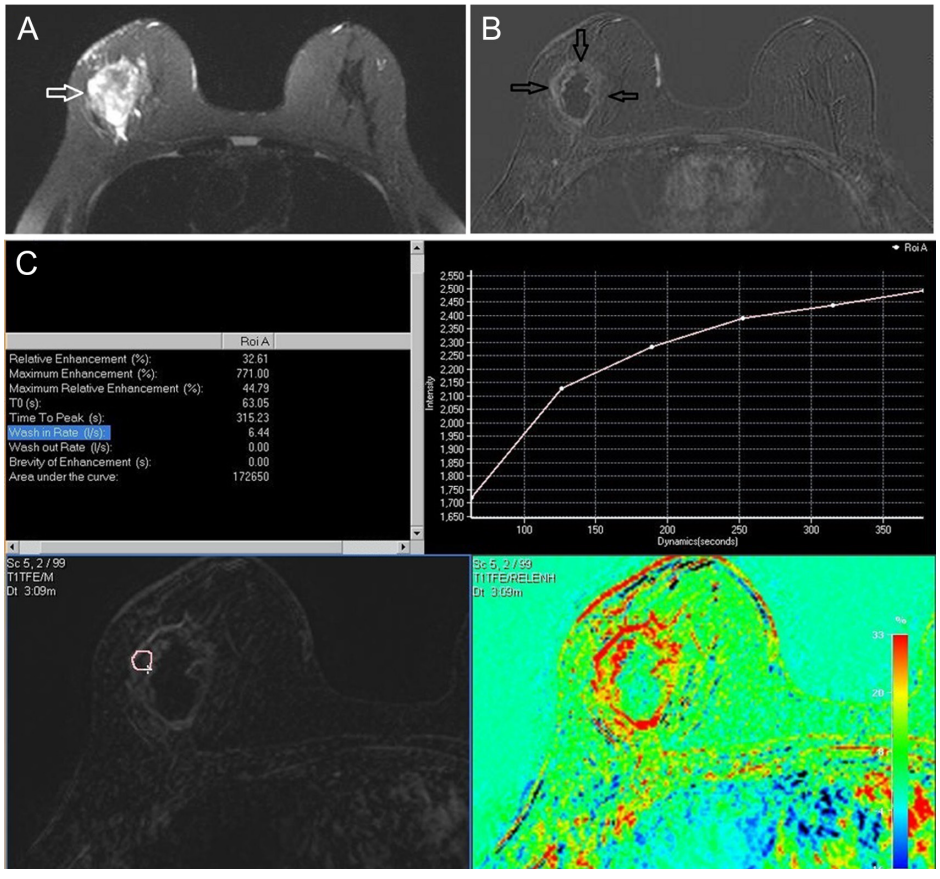

Figure 2. A 43-year-old woman with palpable triple-negative breast cancer of the right breast. T2-weighted with fat saturation image (A) demonstrates a 4.5-cm hyperintense mass with irregular margin and peritumoral edema in both middle and posterior segments (white arrow). Mass with irregular rim enhancement (black arrows) is seen on the postcontrast T1-weighted subtraction image (B). Measurements made from the periphery of the lesion showed a type 1 curve and areas in pink indicate a delayed persistent-type curve following slow early enhancement (C).

subtypes. Triple-negative breast cancer more commonly showed rim enhancement on postcontrast MRI and more high intratumoral signal intensity on T2-W than other tumor subtypes.[15] Besides morphological and kinetic analyses, location is useful for the diagnosis of TNBC. Our findings revealed that 67% of TNBC tend to locate in a posterior or prepectoral region. Breast cancers in familial high-risk women and BRCA1 mutation carriers were located in the posterior or prepectoral region of the breast without analyzing the results according to tumor subtype as observed by Schrading and Kuhl.[18] One study showed that TNBCs were commonly located in the posterior third or prepectoral region of the breast in accordance with our study.[21] Mammography and US may be insufficient to detect this type of breast cancer. It can be skipped in MG, especially when combined with dense parenchyma and may be difficult to visualize deep plans in breasts with a heterogeneous background with US. In order to detect this aggressive tumor, we need to evaluate this region of the breast carefully. Magnetic resonance imaging is superior to MG and US in evaluating the posterior part of the breast, particularly in dense and heterogeneous parenchyma. In our study, the amount of fibroglandular tissue was type C and D, with a total rate of 74% seen in patients with TNBC. One limitation of this study was that it was a retrospective design. We consider that in the future MRI will help in the characterization and treatment plan of the different subtypes of breast cancer and that more studies will be required.

CONCLUSION

Magnetic resonance imaging findings such as round/oval-shaped, rim or heterogeneous enhancement, high signal intensity on T2-W images, and posterior-prepectoral location may be important in diagnosing TNBC. These findings may allow us to estimate the diagnosis of TNBC before the histopathological diagnosis. Moreover, because of common localization and to be seen in more dense and heterogeneous breasts, TNBC can be diagnosed more easily with MRI.

Ethics Committee Approval: The study was approved by the ethics committee of Istanbul University (Date: July 29, 2022, Decision no: 2022/1296).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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