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Evaluation of lesions requesting biopsy according to imaging findings in breast cancer patients who have undergone breast-conserving surgery

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ABSTRACT

Aims: In patients undergoing breast-conserving surgery (BCS), the traditional follow-up imaging methods of the breast are mammography and ultrasonography. However, after BCS and radiotherapy, it becomes more difficult with imaging methods to detect the presence of recurrence or secondary focus due to the change of normal breast structure in patients. In this study, we aimed to investigate the sensitivity, specificity and malignancy prediction values of imaging methods in the follow-up of patients who underwent BCS.

Methods: 421 patients diagnosed with breast cancer who underwent BCS were retrospectively analyzed. 63 patients with histopathology results, which were categorized as BI-RADS 4 or 5 according to imaging findings in their follow-up after BCS, were included in the study. The age of diagnosis, time taken for biopsy and mammography, ultrasonography and magnetic resonance imaging findings were recorded. Patients were divided into 2 groups (benign and malignant) according to the results of biopsy. According to the pathology results, sensitivity, specificity, positive and negative predictive values and diagnostic accuracy levels of radiological imaging findings were calculated. The significance of the difference between pathology groups in terms of mean age of diagnosis and biopsy time was evaluated by Mann-Whitney U test. Categorical variables were assessed by Yates test or Fisher's exact test.

Results: Of the 63 patients, 49 (77.7%) were benign and 14 (23.3%) were malignant. There was a significant difference between the two groups in mass finding on mammography and posterior acoustic shadowing on US (p=0.011, p=0.049, respectively).

Conclusion: MRI is the most sensitive imaging method in post-BCS follow-up and mammography is the most specificity imaging method. The finding with the highest positive predictive value for malignancy detection is the presence of mass on mammography and posterior acoustic shadow on ultrasonography.

Keywords: Breast conserving surgery, biopsy, mammography, ultrasound, MRI

INTRODUCTION

Surgical treatment of breast cancer has evolved from radical mastectomy to breast conserving surgery (BCS). Currently, BCS with additional radiation therapy is the preferred treatment method for early breast cancer.[1-4]

Factors such as the fact that radical surgical treatments are not easily accepted by the patients, the good cosmetic results of BCS, advances in radiotherapy (RT) and systemic therapy, the increase in early diagnosis possibilities and the detection of breast cancer at an early stage play an important role in the widespread use of BCS.[1,5,6] While the rate of BCS application in our country was 25% before the 2000s, this rate reached 45% afterward.[7] However, with the more frequent use of BCS, multifocal and close/positive surgical margins requiring re-excision or mastectomy have become a current problem.[8]

The conventional follow-up imaging methods of the breast in patients undergoing BCS are mammography and ultrasonography.[9] However, after BCS and RT application, it becomes more difficult to detect with imaging methods the presence of recurrence or secondary focus due to the change of normal breast structure in patients.

Therefore, it is important for clinicians to determine the treatment approaches well, to know the sensitivity of imaging findings that may require re-excision after BCS and their values in predicting malignancy in order to reduce the cost and morbidity of such procedures.

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In this study, we aimed to investigate the sensitivity and malignancy prediction values of imaging methods (mammography, ultrasonography and magnetic resonance imaging) used in the follow-up of patients who underwent breast-conserving surgery.

METHODS

This thesis study was carried out before 2020 and since it is a retrospective clinical study, it was not necessary to take an ethics committee decision. However, the necessary permission was obtained from the hospital management to use the data. However, the necessary permission was obtained from the hospital management to use the data. A written informed consent form was approved by the each patients and necessary permissions were obtained for the use of their data. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

421 patients who were diagnosed with breast cancer and underwent BCS between December 1994 and May 2007 were retrospectively analyzed.

63 patients with a biopsied tissue diagnosis due to the presence of lesions categorized as BI-RADS 4 or 5 according to imaging findings were included in the study. The medical records of the patients included in the study (age, positive family history, time taken for the detection of lesion requiring biopsy in the follow-up after BCS) and radiological imaging findings were reviewed.

Postoperative Imaging Surveillance

After breast cancer surgery, all patients underwent follow-up examinations with imaging methods every 6 months for the first 2 years, and then annually.

Mammography examinations were performed with conventional mammography devices (Senograph 600T, General Electric Medical System; Flat SE, Metaltronica; Selenia, Hologic Inc.). All mammography examinations included images in two standard plans (mediolateral oblique and craniocaudal). Additional projections were used when necessary (lateral projection, roll graphy, spot compression, magnification).

Breast ultrasound examinations were performed with US machines (Schimatzu SDU-450, Hitachi EUB 6500, and GE Vivid 3 Pro) equipped with a matrix linear converter with a bandwidth of 5-18 MHz.

MRI examination was performed using a breast coil with a 1.5 Tesla MRI device (Signa excite HDx, General Electric, Milwaukee, WI, USA) using the following protocols: Fat suppressed TSE T1 and T2-weighted axial image, 3D FFE T1-weighted axial image, dynamic 3D FFE T1 and postcontrast 3D FFE T1-weighted axial image after 0.1 millimole/kg contrast injection. During the dynamic examination, 8 imaging (30 sec, 1 min, 1.40 min, 2.30 min, 3.30 min, 4.30 min, 5.30 min, 7 min) was performed for 7 minutes. MRI images were transferred digitally to the workstation (Advantage Windows, software version 4.4, GE Medical Systems) and the time signal intensity curves of the lesions were drawn.

Postoperative Imaging Interpretation

All imaging studies were interpreted according to the 4th edition of the Breast Imaging Reporting and Data System (BI-RADS) classification. BI-RADS category 4 or 5 was considered positive and tissue diagnosis was performed. For lesions classified as BI-RADS category 3, short-interval follow-up (6–12 months) was recommended. If the lesions were stable during the follow-up period, they were reduced to BI-RADS category 2. In case of any change, the lesions were upgraded to BI-RADS category 4 and biopsy was performed.

If a suspicious lesion was detected on MG or US, MG-guided or US-guided biopsy was performed. If a suspicious lesion was detected only on MRI, a second US was performed first. If there was a correlation on second-look US, US-guided biopsy was performed.

According to the tissue diagnosis, patients were divided into two groups as benign and malignant groups. For both groups, the presence of mass, microcalcification, focal asymmetric density and architectural distortion were evaluated on mammography. In BI-RADS mammography indication; skin and vascular calcifications, rough or popcorn type, round, rim, dystrophic, calcium milk, suture calcifications are typical benign calcifications; Amorphous, coarse heterogeneous, fine pleomorphic and fine pleomorphic branching microcalcification are stated as suspicious.[10] In our study microcalcifications were examined according to their morphology by dividing them into 3 groups (punctate, amorphous, pleomorphic). The distribution pattern of microcalcifications is also important in predicting malignancy; microcalcifications with linear and segmental distribution are the high-risk distribution pattern in terms of malignancy.[11] Therefore, microcalcifications were additionally examined by dividing them into 4 groups (regional, linear, segmental and cluster) according to their distribution regions. In US, the contour feature, shape, echo pattern, size, boundary feature and acoustic shadowing of the mass were noted. The type of contrast of the lesions was recorded on MRI.

Imaging findings were interpreted by two expert radiologists experienced in breast radiology.

Statistical Analysis

The analysis of the data was performed in SPSS for Windows 11.5 package program. Descriptive statistics and continuous variables were shown as mean ±

standard deviation, and categorical variables were shown as number of cases and (%).

Sensitivity, specificity, positive and negative predictive values and diagnostic accuracy levels were calculated to evaluate the diagnostic predictions of mammography, US and MRI indicators according to pathology.

The significance of the difference between the pathology groups in terms of age at diagnosis and mean biopsy time was evaluated with Mann-Whitney U test. Categorical variables were evaluated with Yates test or Fisher's Exact Chi-Square test. For $p<0.05$, the results were considered statistically significant.

RESULTS

The mean age of patients included in the study was 48.5±8.7 (range:28-73) years. The primary diagnoses of the patients before lumpectomy were infiltrative/invasive ductal carcinoma in 48 (76.2%), ductal carcinoma in-situ in 10 (15.8%), infiltrative/invasive lobular carcinoma in 2 (3.2%) and 2 (3.2%) patients were lobular carcinoma in-situ and one (1.6%) was a mixed invasive ductal+infiltrative lobular carcinoma. Postoperative radiotherapy was applied to all patients who underwent BCS, chemotherapy to 51 patients, and hormone therapy to 55 (87.3%) patients with hormone receptor positive. In imaging, mammography was performed in all 63 patients, ultrasonography was performed in 53 patients, and MRI examinations were performed in 22 patients.

The biopsy results of 63 patients with lesions classified as BI-RADS 4 or 5 were as follows: 22.2% (14/63) of patients had malign lesions (11 patients with infiltrative/invasive ductal carcinoma, 3 patients with ductal carcinoma in-situ) and 77.7% (49/63) of patients had benign lesions (16 patients with fat necrosis, 8 patients with fibrocystic changes, 8 patients with granulation tissue, 7 patients with sclerosing adenosis, 7 patients with atypical ductal hyperplasia, and 3 patients with fibroadenoma) (Figures 1 and 2).

Although there was a higher rate of family history in patients with malignancy (n=4/14, 28.6%) than in benign group (n=10/49 20.4%), there was no significant statistical difference between the groups. Similarly, there was no significant difference between two groups in terms of biopsy application time after BCS and age of diagnosis (Table 1).

Table 1. The relationship between the groups in terms of biopsy application time and age at diagnosis

	Benign (n=49)	Malignant (n=14)	P
Age	49.2±8.8	45.2±8.1	0.161
Family history			0.725
Yes	10 (20.4%)	4 (28.6%)	
No	39 (79.6%)	10 (71.4%)	
Postoperative biopsy time (month)	46.3±31.6	55.2±45.0	0.823

Architectural distortion, microcalcification, and asymmetric density were the most common pathologies detected in referral to biopsy on mammography (Table 2). The diagnostic accuracy measures of mammography are summarized in Table 3. While pleomorphic microcalcification had the highest specificity value (93.9%), sensitivity and positive predictive value (PPV) were found to be quite low.

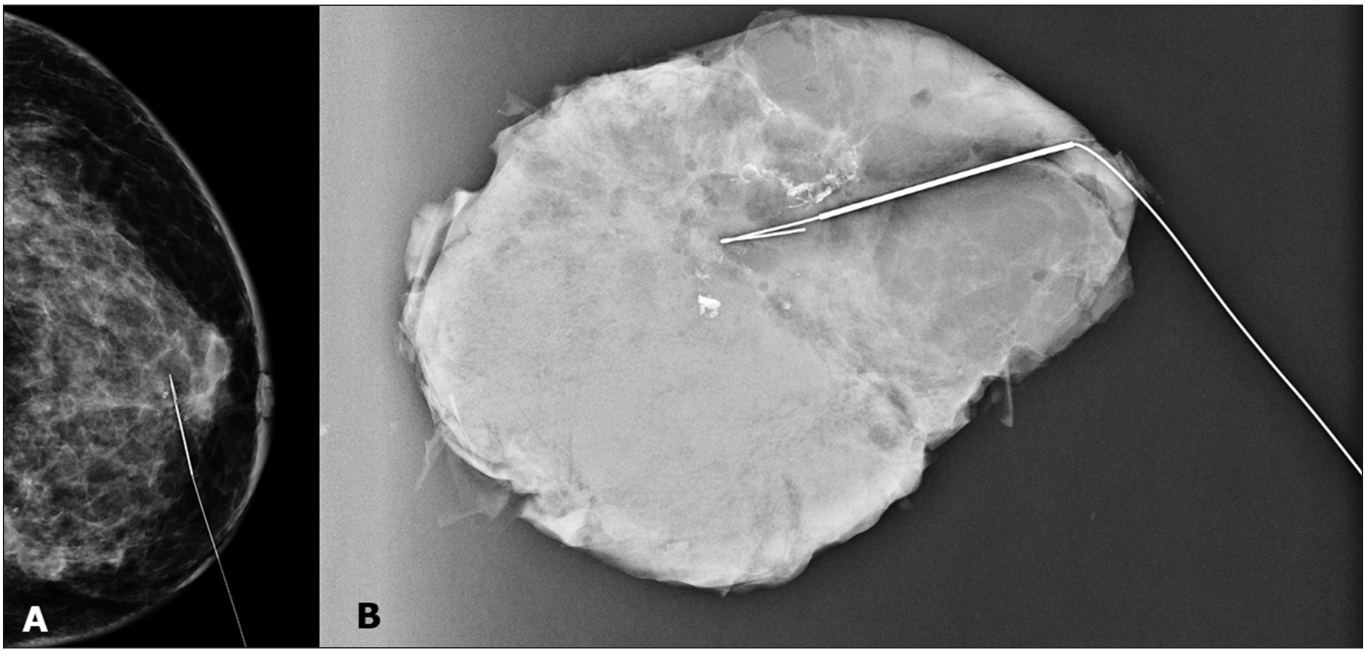

Figure 1. (A) Newly developed pleomorphic microcalcifications are observed in the lumpectomy area of a patient who underwent BCS for intraductal carcinoma. (B) The radiograph of the specimen. which was marked with wire localization. was consistent with intraductal carcinoma.

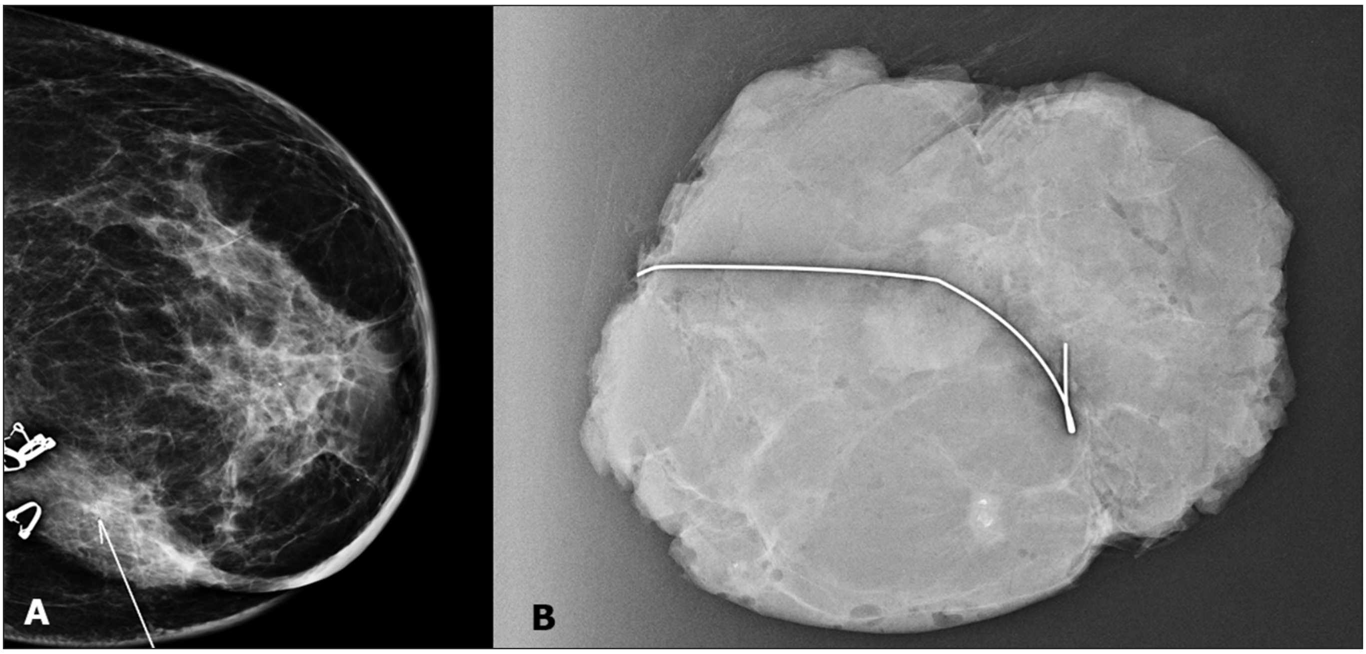

Figure 2. (A) Clustered punctate microcalcifications accompanied by asymmetrical density are observed in the lumpectomy area of a patient who underwent BCS for intraductal carcinoma. (B) The radiograph of the specimen removed by marking with wire localization was consistent with fat necrosis.

Table 2. Distribution of cases according to mammography findings

Variables	Benign (n=49)	Malignant (n=14)	p
Mass			0.011**
Yes	5 (10.2%)	6 (42.9%)	
No	44 (89.8%)	8 (57.1%)	
Microcalcification			0.110
Yes	21(42.9%)	2(14.3%)	
No	28 (57.1%)	12 (85.7%)	
Microcalcification morphology			0.122
Punctate	14 (28.6%)	1 (7.1%)	
Amorphous	4 (8.2%)	-	
Pleomorphic	3 (6.1%)	1 (7.1%)	
Microcalcification distribution			0.172
Local	3 (6.1%)	-	
Linear	2 (4.1%)	-	
Segmental	4 (8.2%)	-	
Cluster	12 (24.5%)	2 (14.3%)	
Focal asymmetric density			0.783
Yes	19 (38.8%)	6 (42.9%)	
No	30 (61.2%)	8 (57.1%)	
Structure distortion			0.298
Yes	17 (34.7%)	7 (50.0%)	
No	32 (65.3%)	7 (50.0%)	

In the comparison of the two groups according to the mammography findings, the mass finding was significantly higher in malignant cases (42.9%) than in benign cases (10.2%) (p=0.011). There was no statistically significant difference between the groups in terms of other mammography findings (Table 2).

The most common finding detected by ultrasound was the presence of a mass (n=53, 84.1%) In the comparison of both groups according to US findings, posterior acoustic shadowing was found to be significantly more common in malignant cases (46.2%) than in benign cases (15%) (p=0.049). No statistically significant difference was found between the two groups in terms of other US findings (Table 4). Diagnostic accuracy measures of US are summarized in Table 5. Posterior acoustic shadowing was found to have the highest specificity (85%), the highest PPV, and the highest accuracy.

MRI was performed as a further examination in 22 of 63 patients evaluated with mammography and US. When both groups were compared according to the contrast enhancement pattern of the lesion in MRI; Type 2-3 and type 3 contrast enhancement patterns were observed at

Table 3. Diagnostic performance levels of mammography findings according to pathology results

Findings	Sensitivity	Specificity	PPV	NPV	Accuracy
Mass	6/14 (42.9%)	44/49 (89.8%)	6/11 (54.5%)	44/52 (84.6%)	50/63 (79.4%)
Microcalcification1	2/14 (14.3%)	35/49 (71.4%)	2/16 (12.5%)	35/47 (74.5%)	37/63 (58.7%)
Microcalcification2	1/14 (7.1%)	46/49 (93.9%)	1/4 (25.0%)	46/59 (78.0%)	47/63 (74.6%)
Focal asymmetrical density	6/14 (42.9%)	30/49 (61.2%)	6/25 (24.0%)	30/38 (78.9%)	36/63 (57.1%)
Structural distortion	7/14 (50.0%)	32/49 (65.3%)	7/24 (29.2%)	32/39 (82.1%)	39/63 (61.9%)

** PPV: Positive Predictive Value, NPV: Negative Predictive Value, Microcalcification1: Microcalcification cluster or segmental distribution, Microcalcification2: Pleomorphic microcalcification a higher rate in the malignant group than in the benign group (100%, 31.6%, respectively). However, no statistically significant difference was found between both groups (p=0.055) (Table 6). The contrast enhancement pattern in MRI was found to be the most sensitive finding in the detection of malignancy. However, the positive predictive value of malignant enhancement pattern in detecting malignancy was found to be low (Table 7).

Table 4. Distribution of cases in terms of ultrasonographic findings

	Benign (n=40)	Malignant (n=13)	P
Contour			0.667
Regular	6 (15%)	1 (7.7%)	
Irregular	34 (85.%)	12 (92.3%)	
Size			0.690
<1 cm	11 (27.5%)	4 (30.8%)	
≥1 cm	29 (72.5%)	9 (69.2%)	
Echo pattern			0.150
Homogeneous-hypoechoic	3(7.5%)	3 (23.1%)	
Heterogeneous-hypoechoic	37 (92.5%)	10 (76.9%)	
Posterior acoustic shadow			0.049**
Yes	6 (15%)	6 (46.2%)	
No	34 (85%)	7(53.8%)	
Shape			1.000
Regular	10 (25%)	3(23.1%)	
Irregular	30 (75%)	10 (76.9%)	

Table 5. Diagnostic performance levels of ultrasonography findings according to pathology results

Findings	Sensitivity	Specificity	PPV	NPV	Accuracy
Contour	12/13 (92.3%)	6/40 (15.0%)	12/46 (26.1%)	6/7 (85.7%)	18/53 (34.0%)
Size	9/13 (69.2%)	11/40 (27.5%)	9/38 (23.7%)	11/15 (73.3%)	20/53 (37.7%)
Echo pattern	10/13 (76.9%)	3/40 (7.5%)	10/47 (21.3%)	3/6 (50.0%)	13/53 (24.5%)
Posterior acoustic shadow	6/13 (46.2%)	34/40 (85.0%)	6/12 (50.0%)	34/41 (82.9%)	40/53 (75.5%)
Shape	10/13 (76.9%)	10/40 (25.0%)	10/40 (25.0%)	10/13 (76.9%)	20/53 (37.7%)

** PPV: Positive Predictive Value, NPV: Negative Predictive Value

Table 6. Distribution of cases in terms of MRI enhancement pattern

	Benign (n=19)	Malignant (n=3)	P
Enhancement pattern			0.055
Type 1-2/ type 2	13 (68.4%)	0 (0%)	
Type 2-3/ type 3	6 (31.6%)	3 (100%)	

In the classification of 63 lesions requiring biopsy according to the BI-RADS category, 6 lesions (9.5%) were BI-RADS 4A, 23 lesions (36.5%) BI-RADS 4B, 29 lesions (46.0%) BI-RADS 4C and 5 The lesion (7.9%) was evaluated as BI-RADS 5. Histopathological examination revealed that 11 (78.6%) of 14 lesions had malignant features and 23 (46.9%) of 49 benign lesions were in the BI-RADS 4C/5 category. When comparing between groups in terms of BI-RADS category, BIRADS 4A/4B lesions were higher in the benign group than in malignant patients (53.1% and 21.4%, respectively); BIRADS 4C/5 lesions were found to be higher in the malignant group than in benign patients (78.6% and 46.9%, respectively). However, no significant difference was found between the two groups in terms of BIRADS category (p=0.073) (Table 8).

Table 8. Distribution of cases in terms of BI-RADS categories

	Benign (n=49)	Malignant (n=14)	P
BI-RADS			0.073
4A/4B	26 (53.1%)	3 (21.4%)	
4C/5	23 (46.9%)	11 (78.6%)	

DISCUSSION

Most women diagnosed with early-stage breast cancer can be successfully treated with BCS. For this reason, the prevalence of use of BCS is gradually increasing. Our study is very important in terms of revealing the sensitivity of the findings of imaging methods used in the follow-up of patients with BCS and their predictive value for malignancy.

Recurrences that develop in or around the BCS bed after BCS are usually caused by failure to eradicate the primary tumor and occur within the first few years following treatment. Recurrences that develop long after surgery (10 years on average) are more likely to occur outside the BCS bed and probably indicate new metachronous cancer.[12] Ultrasonography and mammography are the basic imaging methods in BCS follow-up. Recurrences may or may not have mammographic features similar to the original lesion. Gunhan-Bilgen et al.[13] reported that 66% of recurrences had mammographic findings similar to those of primary tumors. Liberman et al.[14] in their series of 162 patients, they were reported that local recurrence was found in 13 of 20 patients (65%) with malignant mass on mammography performed after BCS. Similar results have been reported by different authors.[15,16] The findings of our study also reveal

Table 7. Diagnostic performance levels of MRI findings and BI-RADS categorization according to pathology results

	Number of cases	Sensitivity	Specificity	PPV	NPV	Accuracy
MRI						
Enhancement pattern	n (22)	3/3 (100%)	13/19 (68.4%)	3/9 (33.3%)	13/13 (100%)	16/22 (72.7%)
BI-RADS						
BI-RADS 4/5	n (63)	11/14 (78.6%)	26/49 (53.1%)	11/34 (32.4%)	26/29 (89.7%)	37/63 (58.7%)
Mass	n (63)	6/14 (42.9%)	44/49 (89.8%)	6/11 (54.5%)	44/52 (84.6%)	50/63 (79.4%)

** PPV: Positive Predictive Value, NPV: Negative Predictive Value that the finding of a mass on mammography is the most significant parameter to predict the malignant pathology (PPV: 54.5%).

The presence of microcalcification has been reported as one of the most common morphologic criteria for biopsy in mammograms.[15,16] It is common to see new calcifications in the area where the tumor was removed after BCS. In previous studies, the predictive value of the presence of microcalcifications has been reported to be 25-35%.[17,18] Dershaw et al.[18] investigated the relationship between morphology of microcalcification and recurrence risk, reported that 68% of recurrent microcalcifications was linear, 77% of them was pleomorphic, 73% of them was cluster-forming, and 18% of them was segmental distribution. In our study, microcalcification was detected in 23 (36.5%) patients. Of these patients, 2 had malignant pathology and 21 had benign pathology. There was no significant difference between the groups in the presence and morphology of microcalcifications. According to the morphology and distribution characteristics of microcalcifications in predicting malignant pathology, PPVs were found to be 25.0% and 12.5%, respectively.

In patients who underwent BCS, mammography findings may resemble local recurrence and may hide the recurrence. For this reason, ultrasonography has been accepted as an additional imaging to mammography. Park et al.[19] in their study investigating the effectiveness of US and MG in detecting ipsilateral metachronous tumors in patients who underwent BCS, they found a similar effectiveness of US and mammography in detecting recurrence (84.2% vs. 85.7%; P=0.898, respectively). They also reported that the effectiveness of US and mammography in detecting recurrence when used together was higher than mammography. In ultrasonography, heterogeneous-hypoechoic echo pattern, indistinct contour, irregular shape and presence of posterior acoustic shadow have been reported as malignant criteria for breast mass.[20] In the ultrasonography study in which Hong et al.[21] examined 141 malignant breast masses, the PPV of the presence of posterior acoustic shadow was found to be 52.8%. Our findings reveal that the presence of posterior acoustic shadow has the highest PPV value in ultrasonography.

Due to the high sensitivity of MRI, the tendency to use it for diagnostic purposes before BCS has gradually increased. MRI is now used as the imaging of choice for surveillance evaluation of mammographically occult tumors, familial tumors, and tumor size and detection, especially in young women with dense breast tissue.[22] Additionally, in a recent randomized controlled multicenter study, the re-operation rate was compared between patients who underwent MRI in the preoperative period and patients who did not undergo MRI. The results of the study found that preoperative MRI significantly reduced the re-operation rate in women who underwent BCS.[23] Compared to traditional imaging methods such as MG and US after BCS, MRI is considered the most sensitive imaging method in distinguishing between postoperative scar and tumor recurrence.[24,25] Current data support MRI as a postoperative surveillance method with high diagnostic yield, sensitivity, and specificity for detecting recurrent cancer.[24,26-29] Gorechlad et al.[30] in their MRI study, they reported that the malignant enhancement pattern (types 2-3 and type 3) is an important finding in detecting recurrence after BCS, but the malignancy predictive value of the malignant enhancement pattern is low. In our study, when the biopsy results of 22 patients who underwent MRI were examined: In all 3 lesions with malignant histopathology, type 2-3 or type 3 contrast enhancement pattern (sensitivity:100%) was detected on MRI. Malignant histopathology (PPV:33.3%) was present in 3 of 9 lesions with a malignant enhancement pattern on MRI. A type 2-3/type 3 contrast enhancement pattern of MRI was observed in all 3 (100%) patients with malignant biopsy results and in 31.6% (6/19) of patients with benign biopsy results. However, no statistical difference was detected between the two groups in terms of malignant contrast enhancement. Our results are compatible with to the study of Gorechlad et al.[30] and show that the detection of malignant enhancement pattern on MRI in patients undergoing BCS is highly sensitive for recurrence, but the positive predictive value is low.

The purpose of surveillance in breast cancer survivors is to detect second breast cancers in the asymptomatic phase; this allows for interventions that increase chances of survival and can lead to improved quality of life. Careful clinical and imaging surveillance is required in patients undergoing BCS, as early detection of tumor recurrence will allow rapid treatment decisions that may affect the patient's prognosis.31 It is extremely important to know the sensitivity and positive predictive values of the findings in the imaging methods, since the imaging findings after treatment (BCS+RT) will differ from those of normal breast tissue.

Our study had several limitations. Its main limitation was the small sample size. Significant results can be obtained in different parameters in higher sampling groups. The second is the histopathological subtypes could not be evaluated due to the limited number of patients with malignant pathology results in our study. Thirdly, in cases that are considered benign, the absence of tissue diagnosis can be considered as a limitation. However, no progression was noted in the follow-up of these lesions. The last restriction is that the lesions were not examined by removing all of them by operation. A comprehensive examination by evaluating the excisional biopsy results, dimensions, and histopathological subtypes of the lesions would provide more information.

CONCLUSIONS

Our study, in which we examined 63 patients who underwent biopsy and required tissue diagnosis, categorized as BI-RADS 4 or 5 according to imaging findings after BCS reveals that MRI is the imaging method with the highest sensitivity and mammography is the imaging method with the highest specificity in the follow-up after BCS. The presence of a mass on mammography and a posterior acoustic shadow on ultrasonography are the findings which have the highest positive predictive value for the detection of malignancy. Further studies are needed to better understand the diagnostic accuracy of imaging methods for screening breast lesions.

ETHICAL DECLARATIONS

Ethics Committee Approval

This thesis study was carried out before 2020 and since it is a retrospective clinical study, it was not necessary to take an ethics committee decision. However, the necessary permission was obtained from the hospital management to use the data.

Informed Consent

A written informed consent form was approved by the each patients and necessary permissions were obtained for the use of their data.

Referee Evaluation Process

Externally peer reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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