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Ultrasound-guided wire localization biopsy in non-palpable breast lesions: predictive factors for malignancy

S. YILMAZ[1], G.K. ÜNAL[2], H.S. ASLAN[3], S. DEĞIRMENCIOĞLU[4], M.R. AYKOTA[1]

[1]Department of General Surgery, Pamukkale University Faculty of Medicine, Denizli, Turkey
[2]Denizli State Hospital, General Surgery, Denizli, Turkey
[3]Department of Radiology, Pamukkale University Faculty of Medicine, Denizli, Turkey
[4]Department of Medical Oncology, Pamukkale University Faculty of Medicine, Denizli, Turkey

Abstract. – OBJECTIVE: The aim of the study was to evaluate the results of ultrasound-guided excisional biopsy in patients with nonpalpable breast lesions and examine factors associated with malignancy.

PATIENTS AND METHODS: A total of 380 patients who underwent ultrasound-guided excisional biopsy for suspected nonpalpable breast masses, between May 2012 and 2018, were retrospectively examined. Histopathological results of the patients were compared regarding age, ultrasound findings, ultrasonographic and mammographic Breast Imaging Reporting and Data System (BI-RADS) categories and factors predicting malignancy were determined.

RESULTS: The mean age of the patients was 48.35 ± 11.23 (17-86) years. There was a history of breast cancer in the families of 22 (5.8%) patients, and 187 (49.2%) patients were in menopause. The complication rate was found to be 6.6%. Malignant lesions were detected in 76 (20%) patients and benign lesions were detected in 304 (79.99%) patients. Some benign lesions were high-risk lesions (16.8%). Most of the patients with malignant lesions had early-stage breast cancer (83.3%). In univariate analyzes, ultrasonographic BI-RADS, mammographic BI-RADS and age variables were found to be associated with malignancy (p = 0.0001). In the multiple logistic regression analysis, ultrasonographic and mammographic BI-RADS values were found to be risk factors for malignancy (p = 0.0001).

CONCLUSIONS: BI-RADS scoring was used to determine risk factors in predicting malignancy in the evaluation of suspected nonpalpable lesions. The ultrasound-guided wire localization biopsy is a useful method in nonpalpable breast lesions with suspected malignancy that cannot be diagnosed by core/vacuum biopsy or in cases where incompatibility between pathology and radiology results exists.

Key Words:
Breast cancer, Excisional biopsy, BI-RADS, Oncology, Radiology.

Introduction

Breast cancer is the most frequently seen cancer type among women all over the world[1]. The widespread use of breast cancer screening programs and the use of advanced mammography devices have increased the detection rate of nonpalpable breast lesions[2]. Thus, the chance of diagnosis and treatment of early-stage breast cancer increases and survival rates also significantly riseone[3,4].

Today, the first step in the approach to nonpalpable breast lesions is ultrasound (US)/mammography (MG)-guided core or vacuum biopsy[5,6]. However, in cases where core or vacuum biopsy cannot be performed or is found insufficient due to technical impossibilities, excision of the mass with wire marking still maintains its importance.

Various methods are used for the surgical excision of suspected nonpalpable breast lesions. The most widely used methods are US-guided wire localization or skin marking, MG wire localization, and radio-guided occult lesion localization (ROLL) techniques[7-9]. The US-guided wire localization technique is easier to apply because it does not require ionizing radiation, lying the patient in horizontal position and detailed equipment.

This study was aimed to evaluate the results of US-guided excision of nonpalpable suspicious breast lesions with wire marking, to examine the factors accompanying benign and malignant breast lesions, and contribute to the literature by investigating the factors predicting malignancy.

Corresponding Author: Muhammed Rasid Aykota, MD, e-mail: muhammedaykota@hotmail.com

Patients and Methods

Before starting the study, approval was obtained from the Ethics Committee of Pamukkale University Faculty of Medicine (protocol # 60116787-020/44429). The hospital records of 380 patients who underwent wire-guided excisional biopsy (WGEB) for nonpalpable breast mass lesions at the Denizli State Hospital (DSH) General Surgery Clinic, between May 2012 and 2018, were reviewed retrospectively. Wire markings of the patients were made by the same radiologist in the interventional radiology department of DSH, and mass excisions were performed by the same general surgery team in the General Surgery Department.

The patient files were examined and the sociodemographic characteristics of the patients, breast cancer risk factors, Breast Imaging Reporting and Data System (BI-RADS) scores, histopathological results of the patients and the stages of breast cancer according to the TNM classification in malignant cases were analyzed. The histopathological results of the patients were compared regarding age, ultrasonography findings, location of the lesion, and mammographic and ultrasonographic BI-RADS scores. The factors predicting malignancy were determined.

Statistical Analysis

The data were analyzed using IBM SPSS Statistics for Windows 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation, and categorical variables as numbers and percentages. Univariate and multiple logistic regression analysis were used to determine the risk factors affecting the malignancy status, which was the dependent variable. Chi-square analysis was used to examine the differences between categorical variables. $p < 0.05$ was considered statistically significant.

Results

A total of 380 female patients who underwent WGEB for nonpalpable breast lesions were included in the study. The sociodemographic characteristics of the patients are given in Table I. The mean age of the patients was 48.35 ± 11.23

Table I. Sociodemographic characteristics of the patients.

		N	%
Age (mean ± SD; med (min-max)		48.36 ± 11.24	48 (17-86)
Ultrasonographic findings	A heterogenous hypoechoic mass containing microcalcification(s)	42	11.1
	Irregular contour	101	26.6
	Mass + lobulated contour	193	50.8
	Hypoechoic area + posterior enhancement	44	11.6
Family history	Yes	22	5.8
	No	358	94.2
Menopause	Yes	187	49.2
	No	193	50.8
Malignancy	Yes	76	20
	No	304	79.99
FNAB	Malignant	5	7.5
	Benign	6	9
	Nondiagnostic	10	14.9
	Malignancy suspected	46	68.7
Location	UOQ	256	67.5
	UMQ	64	16.9
	LOQ	41	10.8
	LMQ	18	4.7
Laterality	Right	192	50.7
	Left	187	49.3
Complication	Yes	25	6.6
	No	354	93.4
History of surgical intervention to the contralateral breast	Yes	23	7.2
	No	298	92.8

UOQ: upper outer quadrant, UMQ: upper medial quadrant, LOQ: lower outer quadrant, LMQ: lower medial quadrant; A.O: Arithmetic means ; SD: Standard deviation; FNAB, fine-needle aspiration biopsy.

Table II. Histopathologic results of the patients.

		N	%
Benign lesions (n=240)	Fibroadenoma	131	34.47
	Fibrocystic changes	28	7.37
	Ductal Hyperplasia	48	12.63
	Others	33	8.68
High-risk lesions (n=64)	Papillary Lesion (intraductal papilloma)	19	5
	Atypical Ductal Hyperplasia	6	1.58
	Radial Scar	1	0.26
	Sclerosing Adenosis	38	10
Malignant lesions (n=76)	Invasive Ductal Ca	50	13.16
	Invasive Lobular Ca	4	1.05
	Invasive Micropapillary Ca	10	2.63
	Ductal Carcinoma In situ	5	1.32
	Other types	7	1.84

(17-86) years, and 22 (5.8%) patients had a family history of breast cancer. While 187 (49.2%) patients were in menopause, 23 (6.1%) patients had previously undergone an intervention from the contralateral breast. Complications developed in 25 patients (6.6%), including vasovagal symptoms in 15 patients, wire migration in 9 patients, and bleeding in 1 patient.

After histopathological examination, malignant lesions were detected in 76 (20%) patients and benign lesions were detected in 304 (79.99%) patients. Sixty-four benign lesions (16.8%) were high-risk lesions (11). High-risk lesions constituted 21.05% of the benign lesions. The definitive diagnoses of the patients based on histopathological examination are given in Table II. BI-RADS scores of high-risk lesions are given in Table III.

The clinical features of the benign and malignant lesions are summarized in Table IV. When the tumor node metastasis stages (TNM) of the patients with malignant lesions were examined, it was observed that 52 patients (83.3%) had early stage (carcinoma *in situ*, stages 1 and 2) breast cancer.

The BI-RADS scores and sizes of the lesions for which fine needle aspiration biopsy was performed are given in Table V.

The relationship between the patients' BI-RADS scores and pathology results is seen in Table VI. Accordingly, both BI-RADS ultrasonography and mammography values were significantly higher in the malignant patients when compared to those who were benign.

As shown in detail in Table VII, variables that had a statistically significant effect on malignancy in the univariate analyses were the ultrasonographic and mammographic BI-RADS scores, and age (p = 0.0001). Regarding the results of

Table III. BI-RADS scores of high-risk lesions.

High-risk lesions		Sclerosing adenosis	Intraductal papilloma	Atipical ductal hiperplasia	Radial scar
BI-RADS Ultrasonography	.00	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	2.00	0 (0%)	1 (5.26%)	0 (0%)	0 (0%)
	3.00	18 (47.37%)	10 (52.63%)	1 (16.67%)	0 (0%)
	4.00	20 (52.63%)	8 (42.11%)	5 (83.33%)	1 (100%)
	5.00	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total		38 (100 %)	19 (100%)	6 (100%)	1 (100%)
BI-RADS Mammography	.00	29 (90.63%)	16 (88.89%)	5 (83.33%)	1 (100%)
	1.00	0 (0%)	1 (5.56%)	0 (0%)	0 (0%)
	2.00	0 (0%)	0 (0%)	0 (0%)	0 (0%)
	3.00	2 (6.25%)	1 (5.56%)	0 (0%)	0 (0%)
	4.00	1 (3.13%)	0 (0%)	1 (16.67%)	0 (0%)
	5.00	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total		32 (100 %)	18 (100%)	6 (100%)	1 (100%)

BI-RADS: Breast Imaging Reporting and Data System.

Table IV. Clinical characteristics of malignant and benign lesions.

		Malignant			
		Yes	No	Total	*p*
Age	A.M ± S.S	53.47 ± 10.85	47.06 ± 10.98	48.36 ± 11.24	0.0001*
	med (min-max)	51 (30-82)	46 (17-86)		
Ultrasound	Heterogenous mass containing microcalcification(s) heterojen hipoekoik kitle	9 (11.7%)	33 (10.9 %)	42 (11.1%)	0.0001*
	Irregular contour	35 (45.45%)	66 (21.78%)	101 (26.58%)	
	Mass + lobulated contour	26 (33.88%)	167 (55.1%)	193 (50.8%)	
	Hypoechoic area + Posterior enhancement	7 (9.09%)	37 (12.2%)	44 (11.6%)	
Family History	Yes	6 (7.79%)	16 (5.28%)	22 (5.79%)	0.414
	No	71 (92.21%)	287 (94.72%)	358 (94.21%)	
Menopause	Yes	50 (64.94%)	137 (45.21%)	187 (49.21%)	0.002*
	No	27 (35.06%)	166 (54.79%)	193 (50.79%)	
Laterality	UOQ	44 (57.14%)	212 (70.2%)	256 (67.55%)	0.05*
	UMQ	15 (19.48%)	49 (16.23%)	64 (16.89%)	
	LOQ	10 (12.99%)	31 (10.26%)	41 (10.82%)	
	LMQ	8 (10.39%)	10 (3.31%)	18 (4.75%)	
Location	Right	41 (53.25%)	151 (50%)	192 (50.66%)	0.611
	Left	36 (46.75%)	151 (50%)	187 (49.34%)	
Complication	Yes	0 (0%)	25 (8.28%)	25 (6.6%)	0.009*
	No	77 (100%)	277 (91.72%)	354 (93.4%)	
Surgical intervention to the contralateral breast	Yes	7 (9.72%)	16 (6.43%)	23 (7.17%)	0.339
	No	65 (90.28%)	233 (93.57%)	298 (92.83%)	
Stages	Ductal carcinoma in situ	2 (3.23%)	-	2 (3.23%)	-
	Stage 1	**27 (43.55%)**	**-**	**27 (43.55%)**	
	Stage 2a	**20 (32.26%)**	**-**	**20 (32.26%)**	
	Stage 2b	**3 (4.84%)**	**-**	**3 (4.84%)**	
	Stage 3a	**9 (14.52%)**	**-**	**9 (14.52%)**	
	Stage 4	**1 (1.61%)**	**-**	**1 (1.61%)**	

*$p<0.05$: statistically significant difference,UOQ: upper outer quadrant, UMQ: upper medial quadrant, LOQ: lower outer quadrant, LMQ: lower medial quadrant; A.O: Arithmetic means; SD: Standard deviation; AM: arithmetic means.

the multiple logistic regression analysis adjusted for age, the ultrasonographic and mammographic BI-RADS scores were found to be risk factors for malignancy ($p = 0.0001$).

Discussion

Breast cancer is the most common cancer among women and is the most common cause of cancer-related deaths, at an incidence rate of approximately 15%[11]. Diagnosis of breast cancer at an early stage is very important in reducing morbidity and mortality rates[3,4]. Recently, the number of nonpalpable breast lesions has increased as a result of the importance given to screening programs in the health policies of countries, the widespread use of screening and the use of more advanced mammography devices[3].

Today, the first step in the approach to nonpalpable breast lesions is image-guided core or vacuum biopsy[5,6,12]. However, in cases where core or vacuum biopsy cannot be performed or is found to be insufficient due to technical impossibilities, excision of the mass with wire marking still maintains its importance.

In this study, the results of the patients who underwent US-guided wire localization excisional biopsy for a nonpalpable suspicious masses in the breast were examined and factors associated with malignancy were evaluated.

Malignant lesions were detected in 20.3% patients and high-risk lesions were detected in 16.8% patients and the mammographic and ultrasonographic BI-RADS scores were determined as risk factors for malignancy.

The average age of the patients was 48.35 years. When the literature was scanned, it was

Table V. BI-RADS scores and sizes of the lesions undergoing Fine Needle aspiration biopsy.

		FNAB			
		Malignant	Benign	Nondiagnostic	Malignant Suspect
BI-RADS Ultrasonography	.00	0 (0%)	0 (%0)	0 (0%)	1 (2.17%)
	2.00	1 (20%)	1 (16.67%)	0 (0%)	1 (2.17%)
	3.00	0 (0%)	3 (50%)	4 (40%)	19 (41.3%)
	4.00	4 (80%)	2 (33.33%)	6 (60%)	25 (54.35%)
Total	5 (100%)	6 (100%)	10 (100%)	46 (100%)	
BI-RADS Mammography	.00	4 (80%)	3 (100%)	7 (100%)	31 (83.78%)
	1.00	0 (0%)	0 (0%)	0 (0%)	1 (2.7%)
	2.00	0 (0%)	0 (0%)	0 (0%)	1 (2.7%)
	3.00	0 (0%)	0 (0%)	0 (0%)	1 (2.7%)
	4.00	0 (0%)	0 (0%)	0 (0%)	3 (8.11%)
	5.00	1 (20%)	0 (0%)	0 (0%)	0 (0%)
Total	5 (100%)	3 (100%)	7 (100%)	37 (100%)	
Lesion size	n	5 (7.46%)	6 (8.96%)	10 (14.93%)	46 (68.66%)
	Mean ± S.D.	11.4 ± 11.06	15.17 ± 5.78	13.9 ± 9.11	11.63 ± 3.78
	Med (min-max)	6 (5-31)	15.5 (8-23)	10 (7-32)	11 (5-21)

BI-RADS: Breast Imaging Reporting and Data System. FNAB: Fine Needle Aspiration Biopsy.

Table VI. A crosstab analysis of the relationship between BI-RASDS scores, and pathology results.

		Malignancy		Total	*p*
		+	–		
BI-RADS Ultrasonography	.00	0 (0%)	2 (0.66%)	2 (0.53%)	0 .0001*
	2.00	1 (1.3%)	8 (2.64%)	9 (2.37%)	
	3.00	8 (10.39%)	146 (48.18%)	154 (40.53%)	
	4.00	62 (80.52%)	147 (48.51%)	209 (55%)	
	5.00	6 (7.79%)	0 (0%)	6 (1.58%)	
BI-RADS Mammography	.00	41 (56.16%)	210 (84%)	251 (77.71%)	0.0001*
	1.00	3 (4.11%)	8 (3.2%)	11 (3.41%)	
	2.00	2 (2.74%)	6 (2.4%)	8 (2.48%)	
	3.00	4 (5.48%)	18 (7.2%)	22 (6.81%)	
	4.00	14 (19.18%)	8 (3.2%)	22 (.81%)	
	5.00	9 (12.33%)	0 (0%)	9 (2.79%)	

*$p<0.05$ statistically significant difference BI-RADS: Breast Imaging Reporting and Data System.

Table VII. Multiple regression analysis of variables effective on malignancy relative to the age variable.

					CI 95%	
Model	Independent factors	B	*p*	O.R.	Min	Max
Univariate analysis	US size	-0.046	0.105	0.955	0.903	1.010
	US BI-RADS	2.022	0.0001*	7.554	3.844	14.847
	MG BI-RADS	0.504	0.0001*	1.655	1.398	1.959
	Age	0.052	0.0001*	1.054	1.029	1.079
Multivariate analysis	Age	0.051	0.0001*	1.052	1.028	1.078
	US size	-0.034	0.234	0.966	.913	1.022
Multivariate analysis	Age	0.053	0.0001*	1.055	1.027	1.083
	US BI-RADS	1.994	0.0001*	7.344	3.690	14.616
Multivariate analysis	Age	0.014	0.372	1.014	0.983	1.046
	MG BI-RADS	0.469	0.0001*	1.599	1.330	1.922

*$p<0.05$: Statistically significant difference; O.R: Odds Ratio; CI: Confidence interval; US: Ultrasound; MG: Mammography; BI-RADS: Breast Imaging Reporting and Data System.

seen that the average age of the patients with malignant breast masses was between 48 and 58 years, which was consistent with the results of this study[3,13,14]. Herein, the average age of patients with malignancy detected based on pathology reports was 53.25 years, with a statistically significant relationship between increased age and malignancy. This result can be explained by the fact that breast cancer is more common in women over 50 years of age[4,15]. Similar to this study, in the study by Bilgen et al[16], in which 550 patients were investigated, the rate of malignancy was higher in women over the age of 50.

In line with the general literature information indicating that breast cancer is more common in the upper outer quadrants of the breast, the malignant lesions herein were more frequently seen in the upper outer quadrant of the breast[16]. The rate of detecting malignancy varies between 10% and 50% in studies using breast marking method for nonpalpable breast lesions[4,5,13,17-20]. The malignancy rate of 20.3% in this study was compatible with the literature.

It has been reported that most patients diagnosed with malignancy due to nonpalpable suspicious breast lesions have axilla-negative small tumors and disease-free survival was observed in 89% of these cases[4,21]. In the current study, early stage breast cancer was detected in 83.8% of the patients, including stage 1 disease in 43% of the patients and stage 2a disease in 32% of the patients. However, the results were consistent with the literature data.

When the literature was examined, it was seen that the rates of benign lesions after breast marking of the nonpalpable lesions were in a wide range, between 50% and 80%, and it was clearly stated that this high detection rate does not show the success of the method. Because the high rate may be related to the increase in the number of unnecessary biopsies, and the low rate may also suggest that the potentially malignant lesions have been overlooked[4,13,16,18,19]. In the current study, in accordance with the literature, benign lesions were detected at a rate of 79.7%, and 1/5 (21.12%) of these lesions were found to be pathologically high-risk lesions, such as intraductal papilloma, atypical ductal hyperplasia, radial scar, and sclerosing adenosis.

The imaging findings of patients are among the most important factors in decision making process for biopsy. Previous studies have reported that there is a relationship between mammography findings and the rate of malignancy, and that mammographic imaging is the most important factor in the decision making process for biopsy[16,22]. On the other hand, it has also been reported in previous studies that typical mammographic findings may not be seen in many nonpalpable malignant lesions[16,22]. As seen in the literature review, the most common indication for biopsy is microcalcification[16,23,24]. In this study, ultrasonography was used as the localization method and the decision for biopsy was made accordingly. Moreover, irregularly circumscribed mass was the most common (45.4%) radiological finding in the malignant cases. This result can be explained by the fact that all of the markings were performed using ultrasonography and the detection of microcalcifications by ultrasonography is more difficult.

Considering the characteristics of the lesions and the degree of suspicion for malignancy, American College of Radiology (ACR) developed the BI-RADS scoring system[25,26]. Herein, the ultrasonographic and mammographic BI-RADS values were determined as risk factors for malignancy.

Complication rates are very low in image-guided marking procedures, and vasovagal reactions during the marking process are the most common complications seen at a rate of approximately 10%[16,24,27]. Bleeding, pneumothorax, infection, and displacement and cutting of the wire, or wires hooking on to the pectoral fascia during surgical excision are other complications that can be seen[16,24,27].

In addition, the inability to remove the marked lesion is another important complication reported that varies between 0% and 17% in different series[27,28]. In this study, complications related to the wire-localization system were observed at a rate of 6.6%, which was similar to the literature.

The retrospective design of the study, and the fact that only US-guided marking was performed due to the technical impossibilities of our hospital were limitations of the study. However, it is believed that the number of patients was sufficient and will contribute to the examination of nonpalpable lesions and the determination of malignancy-related factors regardless of the method used.

Conclusions

The BI-RADS scoring was found as a means of determining risk factors in predicting malignancy in the evaluation of suspected nonpalpable

lesions. US-guided wire localization biopsy is a useful method in nonpalpable breast lesions with suspected malignancy, which cannot be diagnosed by core/vacuum biopsy or in cases where there is an incompatibility between pathology/radiology.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the Ethical Standards of the University of Pamukkale Research Committee (Ethical Committee Application Number: 60116787-020/44429, date: 26.06.2018), and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Authors' Contribution

A – research concept and design: SY, HSA; B – collection and/or assembly of data: GKU, SY; C – data analysis and interpretation: MRA, SD; D – writing the article: SY, MRA,; E – critical revision of the article: SY, MRA; F – final approval of article: SY, MRA, SD, HSA, GKU.

ORCID ID

Sevda Yilmaz: 0000-0002-1309-0805. Gülnur Kaynar Ünal: 0000-0001-6132-9887. Halil Serdar Aslan: 0000-0002-5255-8618. Serkan Değirmencioğlu: 0000-0002-1213-2778. Muhammed Raşid Aykota: 0000-0003-1862-6186.

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