To cite this article: Memisoglu E, Sari R, Tosun Y, Tasdogan B, Rona G. Diagnostic efficacy of physical examination and radiological findings in palpable breast masses. Turk J Clin Lab 2022; 2: 269-274.

Original Article

Diagnostic efficacy of physical examination and radiological findings in palpable breast masses

Palpabl meme kitlelerinde fizik muayene ve radyolojik bulguların tanısal gücü

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ABSTRACT

Aim: Clinical breast examination (CBE) is important in the early diagnosis of breast cancer, especially in low- and middle-income countries. Tru-cut biopsy (TCB) is the most used method for pathological diagnosis in patients with breast mass. This study aimed to evaluate the advantages and diagnostic accuracy of TCB decision based on CBE in patients presenting with a breast mass.

Material and Methods: In this prospective cohort study, the data of patients who admitted to our outpatient breast clinic between September 2020 and March 2021 were evaluated. The presenting complaints, family history, hormone replacement treatment, mass size, contour, mobility, radiological findings, BI-RADS classification, and pathological diagnosis of TCB were recorded. Two hundred- two patients who underwent TCB in our outpatient breast clinic were included in the study.

Results: The presence of irregular and fixed mass was mainly observed in the malignant group compared to the benign group (67.1% vs 43.9%, P: 0.001; 75.9% vs 39%, P< 0.001, respectively). In regression analysis, age was significantly associated with breast malignancy (OR: 1.12, CI %95: 1.06-1.18). CBE showed 85.5% consistency for benign pathology, 88.5% for malignancy, and 90.2% for granulomatous breast mass.

Conclusion: The patients in advanced age and postmenopausal condition with irregularly, fixed breast mass in physical examination should be considered at high risk for breast cancer. TCB should be performed by experienced surgeons in low-middle-income countries and the diagnosis should be reached by reducing the long time and cost caused by radiology.

Keywords: Breast cancer; breast mass; clinical breast examination; tru-cut biopsy.

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Recevied: 12.04.2022 accepted: 18.05.2022
Doi: 10.18663/tjcl.1102235

Öz

Amaç: Klinik meme muayenesi (KMM), özellikle düşük ve orta gelirli ülkelerde meme kanserinin erken tanısında önemlidir. Tru-cut biyopsi (TCB), meme kitlesi olan hastalarda patolojik tanı için en sık kullanılan yöntemdir. Bu çalışmada meme kitlesi ile başvuran hastalarda KMM'ye dayalı TCB kararının avantajlarını ve tanısal doğruluğunu değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Bu prospektif kohort çalışmada, meme polikliniğimize Eylül 2020 ile Mart 2021 tarihleri arasında başvuran hastaların verileri değerlendirildi. Başvuru şikayetleri, aile öyküsü, hormon replasman tedavisi, kitle boyutu, kontur, mobilite, radyolojik bulgular, BI-RADS sınıflaması ve TCB'nin patolojik tanısı kaydedildi. Çalışmaya meme polikliniğimizde TCB uygulanan toplam 200 hasta dahil edildi.

Bulgular: Malign grupta düzensiz ve fikse kitle varlığı Benign gruba kıyasla daha fazla gözlendi (sırasıyla %67.1'e %43.9, P: 0.001; %75.9'a %39, P< 0.001). Regresyon analizinde yaş, meme malignitesi ile anlamlı olarak ilişkiliydi (OR: 1.12, CI %95: 1.06-1.18). KMM, benign patoloji için %85,5, malignite için %88,5 ve granülomatöz meme kitlesi için %90,2 tutarlılık gösterdi.

Sonuç: Fizik muayenede düzensiz sınırlı, fikse meme kitlesi saptanan ileri yaş ve postmenopozal hastalar meme kanseri görülmesi açısından yüksek riskli kabul edilmelidir. TCB, düşük-orta gelirli ülkelerde deneyimli cerrahlar tarafından uygulanmalı ve radyolojinin neden olduğu zaman kaybı ve maliyet azaltılarak kısa sürede tanıya ulaşılmalıdır.

Anahtar kelimeler: Meme kanseri; meme kitlesi; klinik meme muayenesi; tru-cut biyopsi

Introduction

Breast cancer is the most common type of women's cancer worldwide [1]. The incidence of breast cancer among women of all ages varies from 10.2% to 24.3% [2]. Breast cancer screening programs have been widely suggested in high-income countries (HICs) to reduce the burden of breast cancer [3]. To prevent cancer-related deaths, early diagnosis, self-examination, and annual screening are crucial.

The diagnosis could be made via the combination of clinical breast examination (CBE), mammography, ultrasound, fine needle aspiration cytology (FNAC), and tru-cut biopsy (TCB). FNAC was the most practiced method allowing biopsy for the pathological diagnosis in patients with breast masses. However, more and more surgeons are switching to TCB rather than FNAC since TCB provides a significant amount of tissue for pathological investigation [2,4].

The CBE and mammography are observer-dependent tests and could affect the patients' age, menopausal status, and breast density. Their accuracy has been evaluated in different countries, and the reliability of these tests has differed between countries. Moreover, mammography could not be affordable and inaccurate in the younger age group than >40 years old. Thus, it may restrict its diagnostic value in low- and middle-income countries (LMICs) [5,6]. CBE is among one of the important diagnostic methods preventing breast cancer especially in countries where health-care resources are restricted [6]. However, there are still conflicting recommendations and need robust data regarding the effectiveness of CBE in LMICs.

This study aimed to evaluate the accuracy and advantages of TCB decision based on CBE for diagnosis of breast masses in patients who admitted to a tertiary referral center.

Material and Methods

In this prospective observational study, the data of patients who admitted to our outpatient clinic with the presence of breast-related complaints between September 2020 and March 2021 were evaluated after obtaining ethical committee approval (no: 2020/514/184/6; dated August 26, 2020).

Inclusion criteria were as follows; age >18 years, the presence of a breast-related symptom, TCB performed in our outpatient breast clinic, and continuing to follow-up in our clinic. Exclusion criteria were no consent to participate in the study, known breast cancer diagnosis, and loss to follow-up.

Two hundred two patients who met the inclusion criteria were included in the study. Demographic data, presenting complaint, family history, use of hormone replacement treatment, physical examination findings (mass size, mass contour, and mass mobility), radiological findings (mass size, mass contour, and BI-RADS classification), preliminary clinical diagnosis, and the pathological diagnosis of TCB were recorded.

Clinic and radiologic examination

The breasts were first inspected while the patient was in a sitting position. The patients' hands were placed on their hips and also asked to raise them above their head. The breast tissue was evaluated using the examiner's finger pads using a palpation sequence from superficial to deeper layers. The radial "wagon wheel" or "spoke" technique was used [7]. The overall size, shape, symmetry, nipple size, texture, the color of the breasts, and overall breast consistency were evaluated. The characteristics of any abnormalities in size, shape, texture, mobility, and approximate depth were noted. The palpation of the breasts was performed in a supine position. If the patient had a complaint on one side, the examination began on the opposite side or "normal" side. Following a complete breast exam, the axilla and supraclavicular area were also palpated to detect any lymphadenopathy. All examination findings were noted.

Patients under the age of 40 were evaluated by ultrasonography, and patients over the age of 40 were evaluated by mammography. If necessary, additional radiological imaging was performed. Ultrasonography was performed by an experienced breast radiologist. All mammograms were obtained in standard craniocaudal (CC) and mediolateral oblique (MLO) projections. Average percent breast density was defined considering BI-RADS categories [8].

Tru-cut biopsy

A TCB was performed by an experienced surgeon who is blinded to the patients presenting with a palpable breast mass. Radiology reports were obtained for later comparison.

The patients were evaluated in outpatient clinic before TCB and their clinical preliminary diagnosis were noted. Allergy history and anticoagulant drug use were questioned before the procedure. After informed consent, the patient was placed in the supine position. The surgical site was cleaned with povidone iodine. After local anesthetic administration (1 ml prilocaine hydrochloride) a 5 mm skin incision was made over the lesion. At least four adequately sized tissue samples were taken from different localizations of the lesion using an automatic 14 Gauge-10 mm tru-cut biopsy needle. The biopsy samples were fixed in a 10% aqueous solution of formaldehyde.

Statistical analysis

Data analyses were performed using Statistical Package for the Social Sciences Version 21 (SPSS Inc., Chicago, Illinois, United States). The Shapiro Wilk's test was used to evaluate the distribution of the continuous variables. Data are shown as the frequency, percentage, and mean ± SD where applicable. One way analysis of variance test was performed to compare multiple group comparisons, and Tukey's post-hoc test was used to determine two-group comparisons. Independent sample t-test or Mann Whitney U test was used for two-group comparisons. The Chi-square test was used to compare categorical variables. The logistic regression model was conducted with 'enter method' to find out individual effects of study variables on breast malignancy. Receiver operating characteristic (ROC) analysis determined the cut-off level physical or radiological mass size in predicting breast malignancy. Point biserial correlation analysis was performed to determine relationships between malignancy and BI-RADS. $P < 0.05$ indicated statistical significance for all comparisons.

Results

The mean age of the patients in the benign group was 33.91± 11.4 years, and it was significantly higher in the malignant group at 52.5± 13.1 years (P< 0.001). The majority of the patients (51.9%) were in the postmenopausal state in the malignant group. The most common presenting complaint was the presence of breast mass in both groups, but a higher rate was observed in the malignant group (74.8% versus 94.9%). The presence of pain and erythema were higher in the benign group. Regarding the shape and mobility of mass in physical examination, irregular and a fixed mass mainly were observed in the malignant group compared to the benign group (67.1% versus 43.9%, p:0.001; 75.9% versus 39%, P< 0.001, respectively). The irregularity rate was also higher as a radiological finding in the malignant group compared to the benign group (83.5% versus 45.5%, P< 0.001). The most common BI-RADS score was 3 for the benign group (66.7%) and 5 for the malignant group (62%). The majority (93.7%) of the patients in the malignant group underwent cancer surgery. No significant difference was observed between the study groups regarding time since complaint onset, family history, hormonal treatment, and mass size in physical and radiological examinations.

The patients were also divided into three groups considering clinical diagnosis as benign, granulomatous mastitis, and malignant. The patients in the malign group were older compared to both groups (P< 0.001, for all comparisons). There was a significant difference between benign and malignant groups regarding the time since compliant onset that a longer period was observed in the benign group (8.8± 13.7 versus 4.7± 7.3, P: 0.04). The benign group had the smallest mass size compared to the other groups in physical examination (P: 0.03 for all comparisons). In the radiological examination, the granulomatous group had a significantly larger mass size than the benign group (41.1± 17.2 versus 32.6± 16.2, P: 0.02) (Table 1).

Table 1. Comparison of the study variables regarding clinical diagnosis					
		Benign (n:71)	Granulomatous (n:51)	Malignant (n:80)	P-value
Age (years)		32.14± 12.3a	35.45± 7.4 a	52.5± 13.3 a	< 0.001
Menopausal status	Pre-	57(80.3%)	42(82.4%)	26(32.5%)	< 0.001
	Peri-	7(9.9%)	6(11.8%)	13(16.3%)	
	Post-	7(9.9%)	3(5.9%)	41(51.2%)	
The presenting complaint	Pain	5(7%)	10(19.6%)	4(5%)	< 0.001
	Mass	66(93%)	25(49%)	76(95%)	
	Erythema	0(0)	16(31.4%)	0(0)	
Complaint period (months)		8.8± 13.7 b	4.7± 8.4	4.7± 7.3	0.02
Family history	No	62(87.3%)	50(98%)	71(88.8%)	0.06
	Yes	9(12.7%)	1(2%)	9(11.3%)	
Hormonal treatment	No	61(85.9%)	44(86.3%)	64(80%)	0.94
	Yes	10(14.1%)	7(13.7%)	16(20%)	
Mass size in PE(mm)		30.4± 14.1	37.5± 13.3 c	36.6± 17.2 c	0.01
Shape of mass in PE	Regular	65(91.5%)	10(19.6%)	20(25%)	< 0.001
	Irregular	6(8.5%)	41(80.4%)	60(75%)	
Mobility of mass in PE	Mobile	70(98.6%)	10(19.6%)	14(17.5%)	< 0.001
	Fixed	1(1.4%)	41(80.4%)	66(82.5%)	
Mass size in RE (mm)		32.6± 16.2	41.1± 17.2 d	36.1± 18.1	0.02
Shape of mass in RE	Regular	62(87.3%)	8(15.7%)	10(12.5%)	< 0.001
	Irregular	9(12.7%)	43(84.3%)	70(87.5%)	
BI-RADS	0	0(0)	2(3.9%)	2(2.5%)	< 0.001
	1	0(0)	0(0)	0(0)	
	2	0(0)	2(3.9%)	0(0)	
	3	53(74.6%)	32(62.7%)	2(2.5%)	
	4	15(21.15)	15(29.4%)	27(33.8%)	
	5	3(4.2%)	0(0)	49(61.3%)	
Final pathology	Benign	59(83.1%)	3(5.9%)	6(7.5%)	< 0.001
	Malign	8(11.3%)	2(3.9%)	69(86.3%)	
	Granulomatous	2(2.8%)	46(90.2%)	3(3.8%)	
	Insufficient	2(2.8%)	0(0)	2(2.5%)	
Surgical treatment	No	58(81.7%)	49(96.1%)	14(17.5%)	< 0.001
	Yes	13(18.3%)	2(3.9%)	66(82.5%)	

PE= physical examination; RE= radiological examination
aBenign versus granulomatous, aGranulomatous versus malignant, aBenign versus malignant P< 0.001
bBenign versus malignant P: 0.04
cBenign versus granulomatous, cBenign versus malignant P: 0.03
dBenign versus granulomatous P: 0.03

In the logistic regression analysis, age was significantly associated with the malignancy (odds ratio, OR: 1.12, confidence interval, CI % 95: 1.06-1.18). The mass shape in the physical and radiological examination, mobility of the mass, and the menopausal status were not significantly associated with the breast malignancy (Table 2).

We further evaluated the diagnostic accuracy of mass size in physical and radiological examinations and revealed unsatisfactory results for a cut of 32.5 mm for both variables. (area under the ROC curve, AUC: 54%, P: 0.29 and AUC: 51%, P: 0.86, respectively) (Table 3, Figure 1).

Table 2. Logistic regresyon analysis to determine factors affecting breast cancer					
	B	P-value	Exp (B)	CI (95%)	
					Upper
Age (years)	0.11	< 0.001	1.12	1.06	1.18
Shape of mass in PE	0.46	0.39	1.58	0.54	4.58
Mobility of mass in PE	-0.71	0.23	0.49	0.15	1.57
Shape of mass in RE	-1.12	0.06	0.32	0.11	1.05
Menopausal status	0.26	0.69	1.31	0.34	4.99

PE= physical examination; RE= radiological examination; CI= confidence interval

Table 3. The accuracy of physical and radiological mass size measurement in predicting breast malignancy								
	AUC	P-value	Specificity	Sensitivity	PPV	NPV	CI 95%	
							Lower	Upper
PE, mass size (32.5 mm)	54%	0.29	62%	41%	41%	62%	0.46	0.62
RE, mass size (32.5 mm)	51%	0.86	52%	48%	40%	61%	0.42	0.58

PE= physical examination; RE= radiological examination; CI= confidence interval; NPV= negative predictive value; PPV= positive predictive value; AUC= area under the ROC curve

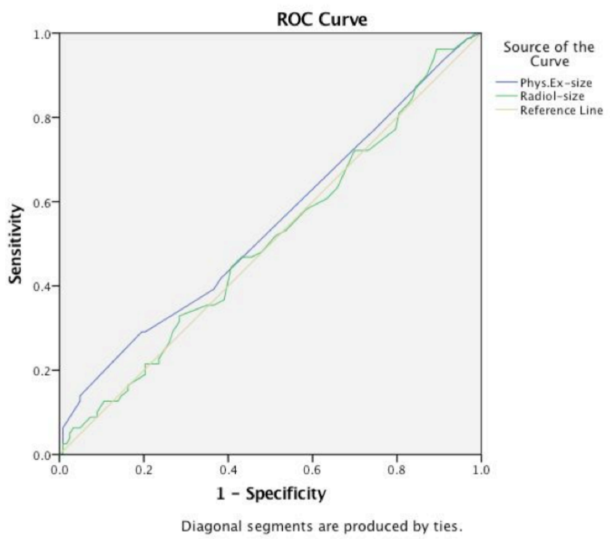

Figure 1. ROC analysis, physical and radiological mass size measurement in predicting breast malignancy

After excluding 4 cases with inconclusive results, we evaluated the accuracy of CBE considering pathological diagnosis, and the kappa analysis revealed 85.5% accuracy for benign pathology, 88.5% for malignancy, and 90.2% for the diagnosis of granulomatous breast mass. The mean kappa score of CBE was reported as 81% for all pathological diagnoses. Besides, CBE has 91% specificity and 87% sensitivity in predicting breast malignancy.

In point biserial correlation analysis, there was a significant positive correlation between BI-RADS and breast malignancy (r: 0.6, P< 0.001).

Discussion

Breast cancer is associated with various risk factors such as aging, family history, early menarche, late menopause, late age at first pregnancy, and nulliparity. Moreover, excessive alcohol consumption increases dietary fat intake, and a sedentary lifestyle can increase the risk of breast cancer [9]. Aging is one of the most relevant risk factors for the occurrence of breast cancer. Approximately 71.2% of all breast cancer-related deaths were reported in women over the age of 60 [10]. In our study, the mean age of the patients was significantly higher, and the majority of the patients were in the postmenopausal state in the malignant group.

The presences of irregular and fixed mass were primarily observed in the malignant group. In the radiological examination, the granulomatous group had a significantly larger mass size than the benign group. Age was an independent risk factor for breast malignancy.

Available data reports significantly longer intervals of symptom discovery to treatment in LMICs compared to high-income countries [11]. This longer waiting interval could be related to limited access to primary care, health system barriers, and the lack of screening programs. To shorten the periods between the symptom occurrence and the diagnosis, affordable diagnostic techniques such as CBE, mammography, or a combination of both methods should be used efficiently.

Regarding the effectiveness of CBE, there are controversial data in the literature [12]. CBE has similar specificity as 93%–97% but lower sensitivity as 40%–69% compared to mammography. On the other hand, CBE has a lower false-positive rate than mammography 1%–5% versus 7%–12%, respectively [13]. In another study, the sensitivity of CBE was reported as 39.1% (95% CI 37.9–40.3), and the specificity was 83.4% (95% CI 82.6–84.3) [14]. Furthermore, CBE was associated with the risk of downstage breast cancer that the median tumor size at final diagnosis was greater [15]. In our study, CBE has 91% specificity and 87% sensitivity in predicting breast malignancy. Since the sensitivity of CBE can vary depending on the experience of the practicing physician, the higher sensitivity result of our study could be attributed to the examiner's experience since our research was conducted in a tertiary referral hospital.

The accuracy of another screening method, mammography, is also evaluated in previous studies. In a study by Alba et al., the sensitivity and specificity of mammography were 78.3% (95% CI 77.3–99.3) and 99.4% (95% CI 99.2–99.6), respectively. The authors concluded that several factors could influence the accuracy of mammography, including age, breast density, menopausal status [16]. Besides, significant variation could be due to the interpretation of the mammography by different readers. In our study, was a significant positive correlation between BI-RADS score and breast malignancy. Aside from the confounding factor that may affect the accuracy of mammography, it still accounts for the first-line screening tool with high specificity and sensitivity rates. Nowadays, the increasing use of imaging methods and the lack of experience of physicians leads to unnecessary biopsies [17]. Considering the increasing cost and patient stress, the decision for biopsy should be given by evaluating CBE performed by experienced breast surgeons and radiological findings together.

The limitation of our study could be the low number of patients admitted to a tertiary referral breast clinic. However, the results of our research are valuable since it depicts the overview of a high-volume hospital in our country. Future studies, including the data of patients attending screening programs, could confirm our results.

Conclusion

CBE could significantly reduce the requirement of radiological examination before TCB in women presenting with breast mass in low-middle income countries. The women in advanced age, postmenopausal condition, presenting with an irregular, fixed breast mass could be candidates for a direct TCB in low resource settings.

Declaration of conflict of interest

The authors have no conflicts of interest to declare. The authors received no funding for this work.

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