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A New Imaging Workup of The Male Breast: Single-View Mammography and Ultrasonography

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ABSTRACT

Background: There is no generally accepted standard radiological approach to male breast diseases. Ultrasonography and mammography are the most preferred methods for imaging. The purpose of this study is to investigate the diagnostic performances of only single-view (mediolateral oblique) mammography and routine two-view mammography in the male breast diseases and also to evaluate the contribution of ultrasonography to the diagnosis and the management of the disease.

Methods: Three hundred-twenty male patients' breast imaging findings were evaluated retrospectively. Only mediolateral oblique and routine two-view mammograms were re-evaluated four months apart by two breast radiologists. The kappa value was calculated to measure consistency between two groups. The sensitivity, specificity, positive and negative predictive value, and detection accuracy of malignancy were calculated for both mammographic examinations and ultrasonography.

Results: The accuracy of detection of malignant breast masses according to mediolateral oblique and two-view mammograms, and ultrasonography were 96.3 %, 97.5 %, and 99.5 %, respectively. Consistency between single-view and two-view mammograms was excellent ($\kappa = 0.967$) and statistically significant ($p=0.000$). Two-view mammograms did not make any contribution to single-view mammograms.

Conclusion: Only mediolateral oblique mammogram is sufficient in terms of characterization, spread and localization of the lesion, as long as mastectomy is preferred and the findings are supported by ultrasonography. Since there is no diagnostic performance difference, only mediolateral oblique view would protect from the potential adverse effects of extra radiation exposure and this is an important advantage.

Introduction

The male breast is anatomically rudimentary and non-functional, but it may involve many benign and malignant pathologies. Most breast diseases in males are benign and the most common is gynecomastia.¹ Male breast cancer (MBC) is a rare disease that

accounts for less than 1% of all breast cancer cases and about 0.1% of breast cancer-related mortality and typically presents with associated symptoms.² With the increasing use of radiological methods, the diagnosis of breast cancer and benign conditions has increased in men.³ But there is no generally accepted standard radiological approach to breast diseases in the males.⁴ If no clinical suspicious finding is present in men, no imaging is usually recommended.

However, if the differentiation between benign or malignant pathologies cannot be made with the clinical findings, imaging is indicated. Ultrasonography (US)

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and mammography (MM) are the most preferred methods for the imaging of the male breast.⁵ Rarely, magnetic resonance imaging can be used to evaluate tumor extension such as pectoral muscle invasion.⁶

Although National Comprehensive Cancer Network has advised the use of MM as the initial imaging technique for men at and over the age of 25 who have indeterminate breast mass, some authorities state that US may be used as the first diagnostic tool of choice in palpable male breast abnormalities.⁷ The utility of MM in male patients with breast symptoms is not clear and MM adds little diagnostic contribution to the clinical evaluation.^{8,9} In a study published recently, diagnostic performance of unilateral and bilateral MM was compared.¹⁰ In this study it was reported that imaging only the symptomatic breast would be adequate and doing this would provide less radiation exposure.

We investigate the diagnostic performances of

only single-view MM and routine two-view MM in men and evaluate the contribution of US in the diagnosis of the disease and patient management. To the best of our knowledge to date, such a study for male breast patients has not been published yet.

Methods

The retrospective study was approved by the institutional ethics committee of our hospital (09.01.2020/532). Since the study was retrospective, informed consent by patients was not required. Between January 2013 and March 2018, 320 male patients presenting to our breast imaging center were reviewed. Symptomatic patients were included in the study. The patients excluded from the study are summarized in the Table 1. A total of 218 patients were included in this study (Figure 1).

Sonographic assessment and US- guided

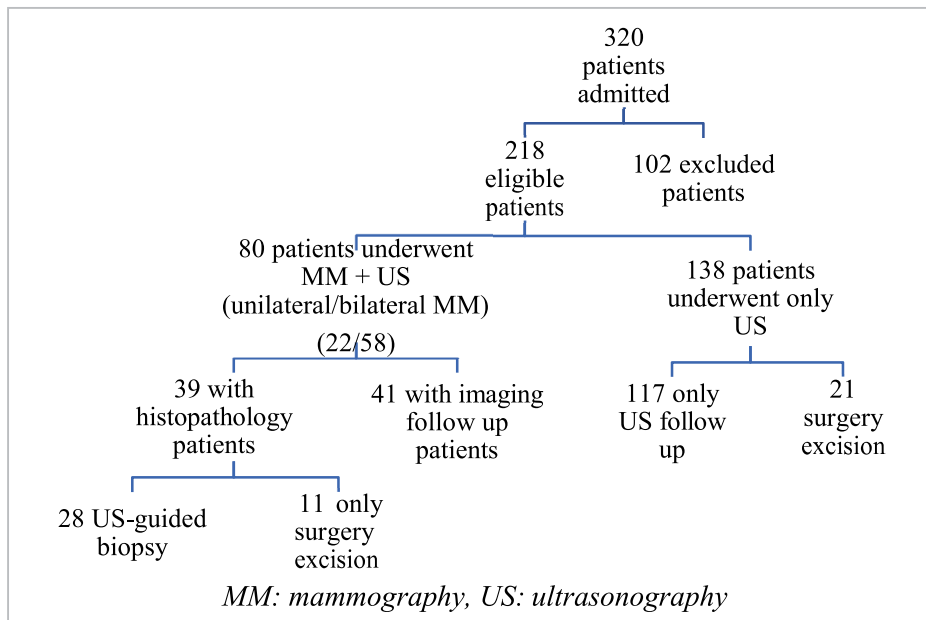


Figure 1. Flow chart of patient selection

Table 1. The patients excluded from the study.

Patients	N
Reactive axillary lymph nodes	4
Metastasis to axillary lymph nodes from extramammary malignancy	3
Desmoid tumor	2
Surveillance of the recurring patients	22
Who did not undergone a biopsy or a surgery operation	34
Absence of US- follow-up for at least 24 months	37
Total	102

biopsies

First, physical and US examination was done on male patients regardless of age in our department. Gray scale US examinations of all patients were performed by the radiologist with ten years of experience using a 13 MHz superficial probe (Hitachi Ezu-MT28-S1 model, Hitachi Inc. Japan). The reports were summarized according to the Breast

Imaging Reporting and Data System (BI-RADS) lesion as 1, 2, 3, 4, and 5. The operator was not blinded to the clinical information. The US-guided biopsies were performed by the same radiologist using the full- automatic 16-gauge biopsynedles (Bard Magnum, Covington, Georgia, USA).

Histopathological examination and immunohistochemical analyses were carried out by pathologists



experienced in breast diseases. Patients without biopsy or surgical operation were followed-up with US for a duration of 24-33 months.

Mammographic assessment

Mammography was used when the patients were defined as BI-RADS 4, 5 by US and using physical examination finding of the clinician. Mammograms were obtained by a direct digital device in the mediolateral oblique (MLO) and craniocaudal (CC) positions for each breast (IMS Giotto, Italy). All patients had histopathology or had follow-up of more than 24 months.

Two readings were made four months apart by two dedicated breast radiologists (with 8 and 10 years of experience in breast imaging) working in consensus. In the first reading, only bilateral or unilateral breast single view MMs (MLO) were reviewed. In the second reading, bilateral or unilateral two-view MMs (MLO and CC) were reviewed. The radiologists were aware that the patient was symptomatic, but they were blinded to the other imaging results, clinical findings, and pathologic results. The findings were scored between 1-5 according to BI-RADS.

Statistical Analyses

The specificity, positive predictive value (PPV), sensitivity and the negative predictive values (NPV), and accuracy were evaluated by binomial tests. We considered the BI-RADS categories 4 or 5 as malignant and 1, 2, 3 as benign for MM and US examinations. The pathological results of the biopsy and surgery specimen or undergoing at least 24 months of sonographic follow-up were accepted as the ‘gold standard’³

We calculated the kappa value to measure the consistency between single-view and two-view MM groups. A p value lower than 0.05 was accepted as statistically significant.

Results

The mean age of the patients was 45±19 years (range, 6-90 years). The symptoms were bilateral or unilateral enlargement in the breast (142, 65.1%), palpable mass (37, 17%), mastalgia (36, 16.5%), and nipple discharge and/or retraction (3, 1.4 %) in the patients.

Cancer detection rate was 11 % (24/218) in our study population. The primary breast cancer (n = 22) and metastasis to the breast from extra mammary

malignancy (lung adenocarcinoma and rectum mucinous adenocarcinoma) (n = 2) were detected. The rate of gynecomastia was 80.7 % (176 /218). Different types of gynecomastia according to sonographic patterns are presented in table 2. Other patients showed lipoma (n = 2), mastitis (n = 2), and lipomastia (n = 16). Primary breast cancer patients underwent MM and US while two metastatic patients were detected by only US examination.

Mean age of the malignant patients was 60.9±11.4 (range 39-86). Tumor size ranged between 12-45 mm (mean 24.1 mm, SD ± 10.2 mm) in the malignant lesions. Primary breast tumors were defined as invasive ductal carcinoma (IDC) (n=18, 81.8 %), invasive lobular carcinoma (ILC) (n=1, 4.5%), invasive papillary carcinoma (IPC) (n=1, 4.5 %), and Paget’s disease and concomitant IDC (n=1, 4.5 %). There was no pure ductal carcinoma in situ. All malignant lesions were mass lesions; there was accompanying calcification in one, and no structural distortion was detected.

Twenty-eight patients (11.9 %) underwent US-guided biopsy (n = 23) and fine needle biopsy (n = 5). Surgery operations were performed on all of the malignant patients and 32 cases (13 cases underwent MM and 19 cases underwent only US) of gynecomastia (18.2 %, 32/176).

Modified radical mastectomy and axillary dissection were performed on nine malignant diagnosed patients (9/22, 40.9%), and simple mastectomy and sentinel lymph node biopsy were performed for 13 patients (13/22, 59.1%), two of whom received this after neoadjuvant chemotherapy. Six patients (6/22, 27.3 %) received radiotherapy after simple mastectomy. Local excision was applied in a case of rectum mucinous adenocarcinoma metastasis. In another metastatic patient, the lesion was not excised; systemic lung adenocarcinoma treatment was continued.

The sensitivity, specificity, PPV, NPV and accuracy of detection of malignant breast masses according to US are 100, 99.5, 95.8, 100, 99.5, respectively and the values according to MLO and two-view MMs are given in Table 3. The consistency between MLO-view and two-view MM is excellent ($\kappa = 0.967$) and statistically significant ($p=0.000$). The core biopsy result of one false positive patient in US was gynecomastia. False positive and false negative patients on MMs are shown in Table 4. False negative results were reported in the both groups.

Table 2. The distribution of the sonographic patterns of gynecomastia and the laterality of involvement (n=176).

	Nodular N=38	Dendritic N=61	Diffuse N=77
Unilateral N=81	10.1 %	14.2 %	22.7 %
Bilateral N=95	11.5 %	20.4 %	21.1 %

**Table 3.** Diagnostic performance of single-view and two-views mammography for male patients

	Single-view (MLO)	Two- views (MLO + CC)	Kappa value	P value
Sensitivity	90.9	90.9	0.967	0.000
Specificity	98.2	100		
Positive predictive value	95.2	100		
Negative predictive value	96.6	96.6		
Accuracy	96.3	97.5		

MLO: Mediolateral oblique, CC: craniocaudal

Table 4. Discordant assessments in single-view and two-view mammography

Single-view MM	Two-views MM	Diagnosis
BI-RADS 4	BI-RADS 3	Gynecomastia
BI-RADS 3	BI-RADS 3	Invasive cancer
BI-RADS 2	BI-RADS 2	Invasive cancer

BI-RADS: Breast Imaging Reporting and Data System, MM: Mammography

Discussion

A standard diagnostic algorithm is not available yet for MBC because of male breast anatomy and MBC cancer rarity. Mastectomy is the main treatment. In this study, we showed that the diagnostic value of single (MLO) and two-view MM is high in men with breast symptoms and the compatibility between them is excellent, with no additional significant data obtained by two-view MM compared to single-view MM. At the same time, US, which we applied in all male patients regardless of age, made important contributions to the diagnosis and management of the disease.

Unlike female patients, healthy male breast has a predominantly fatty tissue with few ducts and stroma.¹⁰ Therefore, mammographic sensitivity for cancer is excellent in men.³ In a study of male patients comparing unilateral and bilateral MM, it was found that there was no difference in diagnostic value and no pathology was detected in the asymptomatic breast, except benign conditions such as gynecomastia.¹⁰ It has been reported that radiation exposure would also be reduced as a result of evaluating only the symptomatic breast by MM.

As is known, there are potential side effects of ionizing radiation, and also radiation has stochastic (dose-independent) effects, so every dose taken matters.^{11,12} The right and left breasts are compared when interpreting MM, and asymmetries can be important for abnormality. In our study, bilateral MLO shots are recommended, which are obtained by reduced radiation allowing the visualization of both breasts. It is known that MM demonstrates the most breast tissue in the MLO position and one of the reasons for obtaining mammograms in two positions is to determine the localization of the lesion.^{10,13}

Calcification and structural distortion are mostly associated with breast cancer in women, and are very well demonstrated by MM.⁴ However, when the case

groups and articles including men were reviewed, we found a few cases of MBC demonstrating structural distortion.^{4, 14, 15} In addition, calcification has been reported to be uncommon in MBC.¹⁵⁻¹⁷ All of the cases were symptomatic in these studies. Calcification is rarely asymptomatic in MBC, usually accompanied by clinically and sonographically detectable lesions and the patients are high-risk.^{3,18, 19} Mammographic screening of 271 high-risk asymptomatic men revealed only three cancers (1.1%) in which the only finding was calcification.³ In our study, there was no structural distortion and there was one finding of calcification.

The sensitivity, specificity, PPV, and NPV values of MM were reported at 92-100%, 90-95%, 32-55%, and 99-100% in various studies.^{3,20,21} Our NPV values were also higher for single and two-view MM groups compared to these studies. Caruso has reported the NPV similar to our study, but by using the combination of US and MM.²¹

According to Chen, there is no statistically significant difference between the sensitivity and specificity of MM and US in the diagnosis of male breast diseases and US does not detect any malignancy in mammographically-negative cases.⁴ The opposite of this was observed in our study; we did not have a case that could not be detected by US but detected by MM. Our study did not aim to compare the diagnostic performance of US and MM.

Ultrasound is advantageous as it can demonstrate axillary lymphadenopathy and pectoralis muscle involvement, it guides biopsies, it is easy to apply, and no radiation exposure is present. Also, no masking takes place on US examination. However, in MM, when the malignant mass and gynecomastia coexist in the same breast, the mass may not be diagnosed efficiently.¹⁶ In single and two-view MM groups, in a case of false negative, dendritic gynecomastia masked the millimetric malignant lesion (Figure 1 a, b).

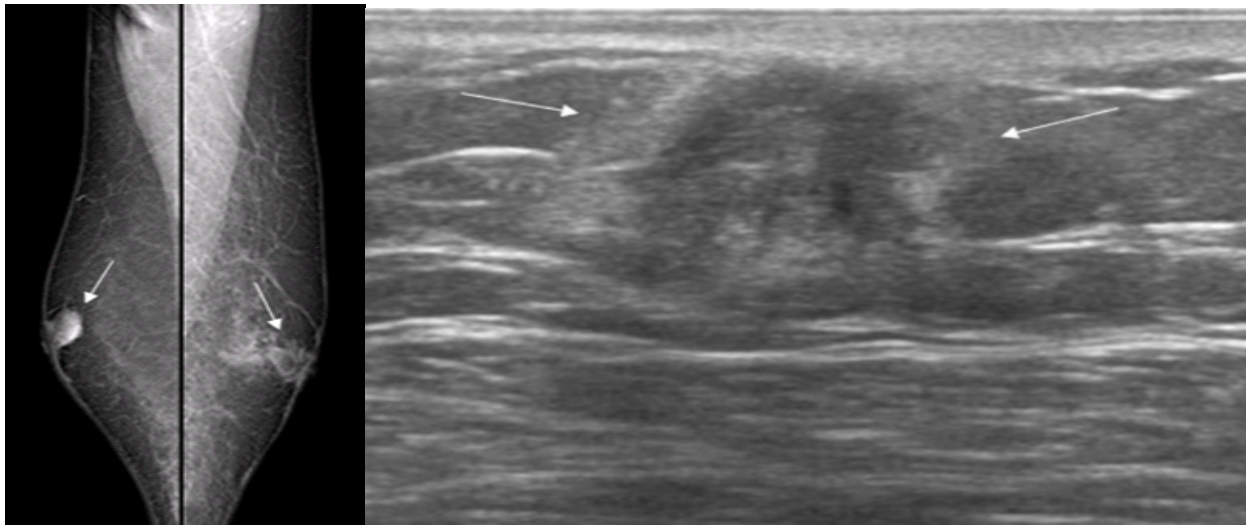


Figure 1 a, b: A 48-year-old male patient with invasive ductal carcinoma. Nodular retroareolar on the right side and flame shaped density on the left side (BI-RADS 2 –gynecomastia) on mediolateral oblique mammograms (arrows) (a). However, a hypoechoic lesion with irregular border (malignant) is observed in the ultrasound image in the left breast (arrows) (b).

Our cancer incidence (11 %) was significantly higher than that reported by some other studies.^{8, 22} However, we included patients who were symptomatic and had long-term US follow-up, and those with biopsy or surgical results. Lawson et al. reported a high incidence of 10.1% in their study including patients with metastasis to axillary from the other malignancy.² We think that this result was affected by the fact that our hospital is a tertiary academic medical center to which patients are referred for further examination and treatment from surrounding provinces.

Male breast cancer is usually diagnosed at an advanced stage. Anatomical reasons play a role in this, namely small breast tissue, its close location to the nipple and, therefore, having early lymphatic and dermal spread.²³ Some authors have suggested that cases are diagnosed at a late stage when they are symptomatic due to the lack of a widely accepted screening program for men. Most of our cases (59.1%) had stage 2-3 disease at the time of the diagnosis, which is in accordance with the literature³. In our study, the rate of axillary metastases (40.9%) was higher than the rate reported in a study by Lawson (31%), but lower than the rate reported in the study by Gao (58.3%).^{2,3}

As a result, mastectomy and axillary dissection are generally preferred for surgical approach in MBC, as in our study.²⁴ We did not have a primary breast cancer patient who underwent breast conserving surgery. A recent study found that male patients showed low compliance with radiotherapy after breast conserving surgery.²⁵ The limitation of our study is a retrospective evaluation of a relatively small group of patients in a single center.

In conclusion, there is no diagnostic value

difference between only MLO-view and routine two-view MM in men. Mediolateral oblique view is sufficient in terms of characterization, spread and localization of the lesion, as long as mastectomy is preferred and the findings are supported by US. Thus, it will prevent the potential adverse effects of extra radiation exposure and this is an important advantage. If there is no suspicious calcification and structural distortion on MLO view and if breast conserving surgery is not being planned, CC view may not be required. However, this diagnostic new approach must be supported by large series.

Conflict of Interest

The authors have no conflict of interests to declare.

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