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Targeted Ultrasound of an Indeterminate Breast Lesion on Mammography: When Does It Influence Management?

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ABSTRACT

Objective: To determine the change over mammographic diagnosis, BI-RADS category and management following targeted ultrasound of an indeterminate lesion seen on mammography and associated factors, if any.

Study Design: Descriptive, analytical study.

Place and Duration of Study: Radiology Department, The Aga Khan University Hospital and Clifton Medical Services, Karachi, from April 2010 to May 2011.

Methodology: Patients referred for targeted breast ultrasound following X-ray mammography were selected regardless of age. Targeted Ultrasound (TUS) was defined as a limited ultrasound of a specific lesion or breast part as indicated by the referring source. Comparison was made between the post mammography and post TUS lesion characterization, diagnosis and BI-RADS category (0-5) which was taken as a measure of management change. Those were evaluated to determine significance of age, marital status, parity, breast parenchymal pattern (dense, fatty, heterogeneous), referring source for the TUS (radiology resident, radiologist or surgeon), lesion characteristics (density, echogenicity, shape, location, margins, size, depth-to-width ratio, enhancement or shadowing), presenting symptoms or signs and reason for TUS. A p-value of 0.05 or less was taken as significant.

Results: There were a total of 342 patients with mean age of 49.7 ± 13.5 years. It assigned a definite category in 232 patients with an indefinite category (0) on mammography requiring further investigation. It decreased the suspicion for malignancy in 180 (77.58%) by assigning a low BI-RADS category and increased the suspicion in 52 (22.41%). The factors significantly associated with this changes included clinical indication being diagnostic ($p < 0.001$), lesion characteristics on imaging ($p < 0.001$), heterogenous breast parenchymal pattern ($p < 0.001$) and presence of known risk factors ($p=0.049$).

Conclusion: TUS served as a problem solving tool in the evaluation and management of an indeterminate breast lesion in a high number of patients, particularly when there was a lump as indication for imaging in the presence of risk factors in a patient with otherwise heterogeneously dense breast parenchyma.

Key Words: Targeted ultrasound. BI-Rads. Indeterminate lesion. Mammography.

INTRODUCTION

Approximately 232,340 new cases of breast cancer are expected in the USA with stable rates among the Asian Americans.¹ The rate of breast cancer is high among Pakistani women as such, X-ray mammography is considered a useful modality both for screening and diagnosis of breast cancer² acting as gold standard for new techniques. However, its use is limited by breast density,³ small size of lesions⁴ and indeterminate characteristics of a lesion on mammography including the probably benign solid lesion detected for the first time. Either ultrasound or MRI is advised as the next investigation. Breast MRI, despite good sensitivity falls short of expectations due to less than desirable specificity and positive predictive value,⁵ cost constrains and availability. These have important implications in a

self-financed healthcare system such as the one existing in Pakistan, so that diagnostic workup practices and algorithms vary considerably among tertiary care, public sector and privately financed diagnostic centers, to the extent of becoming "intuitive".^{5,6}

The usual approach adopted for dense breasts with or without indeterminate solid masses or vice versa is ultrasound of breast due to lower cost and wider availability. Again, referral practices differ among clinicians for asking whole breast or targeted ultrasound. The latter is more focused and less costly than the former but it is usually recommended as per interpreting radiologist's discretion.

At the study centre, the practice is to refer for either targeted or whole breast ultrasound, any clinically and/or mammographically indeterminate lesion that cannot be placed in either definite benign or malignant rather than the probably benign (BI-RADS-3) short term follow-up category. While it may seem to contrast with ACR recommendations,⁶ it helps allay patients anxiety while waiting during the follow-up period and reduces the negative biopsy rate with comparative cost implications.

As of yet, there is no published data as to how this practice affects the management and which factors are

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Received: October 09, 2014; Accepted: July 08, 2015.

associated with a positive yield towards this approach. Since mammographic density is high in Asian women, their mammography yield and interpretation is likely to be different.⁸ This assumes importance in view of its implications among the increasing immigrant population from the region. More importantly, since there are no set guidelines for the use of targeted or diagnostic focused breast sonography in Asian women, this practice-based outcome is worth sharing.

The objective of this study was to determine the change over mammographic diagnosis, BI-RADS category and management following targeted ultrasound of mammographically indeterminate lesion and associated factors.

METHODOLOGY

Between April 2010 and May 2011, all female patients undergoing X-ray mammography at the Aga Khan University Hospital, Karachi, Pakistan for screening or diagnostic purpose, who were found to have a single focal pathology on X-ray mammography which was labeled as BI-RADS 0 or 3 (both constituting an indeterminate mass for the purpose of this study), with subsequent targeted ultrasound of the lesion were retrospectively inducted. Those with generalized or multifocal abnormality or a simple breast cyst were excluded. The study was a retrospective collection of data without any interventional measure, hence ethical permission from the institute was not acquired. As per departmental procedures, informed verbal consent for mammography was obtained for every patient.

All the mammograms were performed on Siemen Mammomat 3000 NOVA in standard CC and MLO projections. The images were viewed on console as well as workstation by a senior resident and two consultant radiologists with more than 5 years' experience in breast imaging. The targeted lesion was scanned on Toshiba Nemio or Xario ultrasound machine using linear 10 MHz probe employing grayscale as well as Color Doppler mode, by Fellow radiologists with 10 - 15 years' of post-Fellowship experience. After ultrasound BI-RADS category, 2 (benign) and 4 to 5 (malignant) was assigned according to ACR criteria.⁶ Change in the BI-RADS category implied a change in management. Targeted Ultrasound (TUS) was defined as a limited ultrasound of a specific lesion or breast quadrant as indicated by the referring source.

The outcome measure was the change in the finally assigned category that necessitated a change in management. Its correlates were labeled as the age of the patient, indication for mammography, marital status, parity, lesion characteristics (size, location, margins, density), positive family history of breast cancer in a first degree relative, breast parenchymal pattern and the source of referral for targeted ultrasound (resident, staff, radiologist, breast surgeon or others).

The data was entered and analyzed on SPSS version 19. Mean, standard deviation, and minimum to maximum values were determined for continuous variables; numbers and frequency percentages were determined for qualitative and categorical variables. The significance of these variables was set at $p < 0.05$ through chi-square test for comparison of proportions.

RESULTS

There were a total of 342 patients with mean age of 49.70 ± 13.50 years. Most were married, had a predominant fibroglandular breast parenchymal pattern and had originally undergone a diagnostic mammography to begin with (Table I). On targeted ultrasound, a definite solid mass was identified in only 160 cases with an average size of 1.5 ± 0.98 cm (ranging from 0.2-6.2 cm). While an originally assigned (0 or 3) category remained unchanged in 110 patients requiring either MRI (in 3 patients) or short term follow-up (in 107 patients), the remaining 232 patients or lesions were assigned a definite category changing the management which was in significant proportion ($p < 0.001$). A low (BI-RADS 2) category was assigned to 180 (77.17%) cases; and a higher (BI-RADS 4 or 5) category to 52 (22.43%) lesions. The factors significantly associated with this change in category included the clinical indication being a diagnostic rather than screening mammographic examination ($p < 0.01$), lesion characteristics (predominantly well defined margins on ultrasound, $p < 0.001$) and a heterogeneous breast parenchymal pattern ($p < 0.001$). Rest of the studied factors including the size of the lesion, did not show a significant association with change in the BI-RADS category (Table II). Absence of any risk factor had a borderline significant association with the queried lesion being benign ($p = 0.049$).

On subanalysis for correlates with the type of change in category, factors found to be significantly associated with change towards benign category were screening mammography ($p < 0.001$), well defined margins on ultrasound ($p < 0.001$) and fibroglandular breast pattern ($p < 0.001$). For malignant category change, diagnostic

Table I: Demographic characteristics of Pakistani women undergoing targeted ultrasound for a mammographically indeterminate focal lesion (n = 342).

Variable	Value/Result
Mean age in years \pm SD	49.70 \pm 13.50
History of previous breast Cancer in self	93 (27.19%)
Breast cancer in a first degree relative	12 (3.50%)
Predominant breast parenchymal pattern	Fibroglandular (n=162, 47.36%)
Category changed in	232 (67.83%)
Predominant category change	Benign (n=177, 51.75%)
Average size of the lesion in cm (available in 160 cases)	1.5 \pm 0.98

Table II: Association of the studied variable with change in BI-RADS category.

Variables	Change in category		p-value	Likelihood ratio
	Yes	No		
Referring sources				
Breast surgeon	190 (55.55%)	93 (27.19%)	0.46	0.34
Oncologist	15 (4.38%)	4 (1.16%)		
Radiologist	0 (0%)	3 (0.87%)		
Resident	22 (6.43%)	9 (2.63%)		
Gynecologist	1 (0.29%)	1 (0.29%)		
Not traceable	6 (1.75%)	2 (0.58%)		
Risk factor for breast malignancy				
Nil (n=226)	163 (47.66%)	63 (18.42%)	0.049	0.040
Positive (n=116)	69 (20.17%)	47 (13.74%)		
Predominant lesion characteristics on ultrasound				
Well defined	38 (11.11%)	10 (2.92%)	0.141	0.056
Ill defined margins	27 (7.89%)	16 (4.67%)		
Oval shape	15 (4.38%)	6 (1.75%)		
Lobulated outline	13 (3.80%)	2 (0.58%)		
Complex cyst	5 (1.46%)	0 (0%)		
Indication for mammography				
Screening	108 (31.57%)	74 (21.63%)	0.01	0.008
Diagnostic	115 (33.62%)	33 (9.6%)		
Indication for TVS				
Mammographic abnormality (124)	146 (42.69%)	58 (16.95%)	0.33	0.299
Clinical finding with dense breast (132)	83 (24.26%)	49 (14.32%)		
Not stated - (06)	3 (0.87%)	3 (0.87%)		
Breast parenchymal pattern				
Fatty	17 (4.97%)	14 (4.09%)	0.433	0.412
Fibroglandular	89 (26.09%)	73 (1.16%)		
Heterogeneous dense	53 (15.49%)	19 (5.55%)		
Dense	4 (1.16%)	2 (0.58%)		
Location of lesion				
UOQ	115 (33.62%)	41 (11.98%)	0.433	0.412
LOQ	16 (4.67%)	4 (1.16%)		
UIQ	9 (2.63%)	6 (1.75%)		
LIQ	17 (4.97%)	13 (3.80%)		
Retroareolar	27 (7.89%)	11 (2.04%)		
Periareolar	3 (0.87%)	1 (0.29%)		
Not mentioned	45 (13.15%)	34 (9.94%)		

mammography ($p < 0.001$) and fibroglandular breast pattern ($p < 0.001$).

DISCUSSION

The BI-RADS categories were developed in the 1980's by the American College of Radiology through a multidisciplinary collaboration to develop standardized mammography reporting with special emphasis on guiding the surgeons regarding management.⁹ However, there are certain gray areas that have evolved with practice and technology. In this study, it was attempted to evaluate if the use of targeted instead of

whole breast ultrasound can be of help before resorting to either the costlier and more elaborate use of MRI, or making the patient wait for another few weeks to months for a focal area of concern. It transpired that a targeted ultrasound can resolve the issue in a vast majority of patients, at a low cost and in a short time.

There are no set standardized guidelines for the use of targeted ultrasound. It has been used in the evaluation of focal breast pain,¹⁰ as a second-look procedure in young women with focal breast symptomatology,¹¹ and even for training surgical residents.¹² The standard ultrasound BI-RADS categories are not applicable on a targeted ultrasound and it is used as deemed appropriate by the interpreter with widely varying practices.⁷ This is despite the potential for better characterization of tumours and problem-solving capability.¹³ Current published practices have mainly pertained to and evidenced its utilization after breast MRI for a still deceitful or suspicious lesion.^{11,12,14-17} The authors offered targeted ultrasound after mammography, before MRI for cost saving via self financed healthcare system. The second reason was to address and allay the patient's anxiety who herself or through her clinician, could feel a lump but the mammography only gave a heterogeneously dense fibroglandular pattern limiting the evaluation.

Most of these targeted ultrasound procedures were asked by the breast surgeon and oncologist, who had marked or discussed their area of concern on hard copy images. Few were asked by the radiology residents and even fewer were asked by senior Radiologist. In some cases, the referral source was not traceable. While a majority of these suspicious lesions turned out to be benign, there was a sizeable proportion (22.4%) that was found to be malignant requiring either biopsy or staging workup.

Overall, only 3 out of a total 342 cases (less than 1%) required MRI to decide the odds of biopsy or waiting; and 107 that is about a third of all cases, were required to continue the watch- at- an- interval process without any need for immediate action or expense. This was a big advantage regarding the cost and anxiety spared to these patients which was the main implication.

The significant factors found to convert the mammographic area of concern towards a benign lesion were well defined margins of the lesion in a lady who had undergone a screening mammography to begin with. Malignant category conversion was found in those who had undergone a diagnostic rather than screening mammography when the referring clinician had mapped an area of concern on the mammography image, for further characterization. Heterogeneous glandular pattern of breast parenchyma was common to both scenarios, being the predominant overall pattern in the studied group of ladies who were aged about 50 years

on an average. The heterogeneous dense or predominantly dense breast was a reason for ultrasound by usually the Radiologist, the Radiology resident and the untraceable source. However, it was not found to be significantly affecting the outcome of TUS in the studied group. So did the other factors including other characteristics of the lesion and location of lesion etc. However, the size of the lesion which was 1.5 cm on an average, had a very wide range and multiple statistical modes in all categories. Also, it was available in only 160 cases, there being no mass on ultrasound under the palpable or apparent mammographic abnormality in the rest, so it was not considered in analysis.

Doppler ultrasound was routinely used in conjunction with gray scale ultrasound in TUS for problem solving purpose. It is known to increase the accuracy of BI-RADS category assessment of doubtful solid lesions.¹⁸

The main limitation in the generalization of this data is the retrospective method of data collection where some details like the lesion size (sometimes described as sub cm instead of an exact value), lactation and parity status could not be obtained and clarified in all cases. However, it has helped in defining the prevailing practices at a high turn-over tertiary care referral centre with local standard of care breast services in Pakistan.

It also showed that referral practices were towards a focused targeted abnormality. It is hoped that this data will generate sufficient evidence for planning further prospective trials to validate the practices or otherwise, with larger cohort and longer follow-up for better grounded evidence.

CONCLUSION

TUS resulted in a difference in BI-RADS category and, therefore, management decisions in a high number of patients. It served as a problem solving tool in the evaluation and management of an indeterminate breast lesion on mammography hence remained relevant when there was a lump as indication for imaging in the presence of risk factors in a patient with otherwise heterogeneously dense breast parenchyma.

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