RESEARCH ARTICLE

Clinical Outcome of Breast Cancer BI-RADS 4 Lesions During 2003-2008 in the National Cancer Institute Thailand

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Abstract

To determine the clinical outcome of breast cancer BI-RADS 4 lesions and seek a more effective management guideline, we conducted a retrospective study of all BI-RADS4 patients diagnosed between 2003-2008 with follow up time not less than 2 years. A total of 392 cases of BI-RADS 4 were identified and 320 could be sub-categorised as 4a, 4b and 4c. Overall malignant positive results were 7.65, 38.7 and 58.percent, respectively. In all cases assigned to the close follow up group, no malignancy was detectable (P<0.02). The results of the study suggested that BI-RADS sub-categories have benefit for cancer diagnosis and treatment decisions of clinicians and it might be possible to set up a safe follow-up guideline in selected groups of patients to minimize un-necessary tissue biopsy for breast cancer detection.

Keywords: Breast cancer - mammography - BIRADS - breast screening

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Introduction

Since the classic work by Phillip Strax was published in 1960's, screening mammography has rapidly become the standard tool for breast cancer detection (Richard, 1990). Unfortunately, the result of the screening program did not have only positive impact to overall decline in breast cancer mortality but they also caused negative side effects, including the detection and biopsy of many non-palpable lesions that eventually proved to be benign, resulting in psychological distress to many women and a substantial contribution to burden of costs on health care systems (Mary et al., 2004). As a consequence, adequate diagnostic procedures with optimum balance between a minimum rate of false-positive results and an acceptable rate of false-negative results are mandatory. So the management of mammographic lesions has been continuously redeveloped and standardized. There were attempts to avoid un-necessary biopsies, by categorizing the low cancer risk lesions by using BI-RADS classification developed by The American College of Radiology. BI-RADS 4 lesions constitute a subset of mammographic detected lesions that have a certain risk of being malignant. However, due to the wide range of the malignant positive rate between 5-70% (Wendie et al., 2000) and the final assessment recommendation to do biopsy, these mammographic lesions would probably be the most difficult decision-making findings for clinicians.

The purpose of this study was to determine the malignant outcome of these lesions in our institute and to seek a more efficient guideline possibility.

Materials and Methods

Patients and Classification

The institutional review board at National Cancer Institute of Thailand approved this study and waived the requirement for informed consent. The study reviewed the data of the mammogram and breast ultrasound, the cancer of the breast from January 2003 to December 2008. Mammographic findings were defined and classified according to BI-RADS classification. BI-RADS 4 lesions were subdivided into three subtypes: BI-RADS 4a, 4b and 4c to compare with malignancy result by the pathologic report if the patients underwent any methods of tissue biopsy immediately or closed observed within 2-6 months. All patients had a follow up at least 2 years.

Through reviewing and analyzing the case records, mammogram, breast ultrasound, pathological reports and operative records, the study mainly analyzed the outcome of malignancy rate of these three types of BI-RADS4 lesions.

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Statistical Analysis

Data were shown as prevalence or mean (±standard deviation). Ordinal data was compared by the Chi-square test, P<0.05 was considered significant.

Results

During the study period, there were 432 cases (2.34%) diagnosed as BI-RADS 4 from 18,460 cases of mammographic study in our institute. 40 cases were excluded as un-available or in-complete data. Of the remaining 392 cases, total 320 cases could be sub-categorised to BI-RADS 4a, 4b and 4c.

The characteristics of women who underwent screening and diagnostic mammography and breast ultrasound are shown in Table 1. Data were included age, mean age, Standard deviation (S.D.) and modes of intervention in BI-RADS 4a, 4b, 4c and non-subcategorised group. Patient age was between 18-90 years. Mean age of BI-RADS4a group was lower compared to others (53 V.S. 57 and 56)

The patterns of mammographic and ultrasound findings in BI-RADS 4 lesions were as followings. Mass and microcalcification and asymmetrical density were the first, second and third most common findings in BI-RADS 4 (38.9, 33. 9% and 14.6%) as Table 2

The number of cases and percentage in Immediate tissue diagnosis group (IG) and Observe and follow up group (OG) were as Table 1 and the mean size and S.D. of mass with positive malignancy result was 12.76±7.07 mm.(IG) and the negative results were 18.39±16.11 (IG) and 20.39±20.22 (OG) respectively (Table 3).

The malignant result (%) in IG was 7.5, 38.71, 57.95 and 41.67 and OG was 0 with p value <0.01 (Table 4) and the most common malignant histology was invasive ductal carcinoma (80.1%) and most common benign histology was fibroadenoma (37.9%) Table 5.

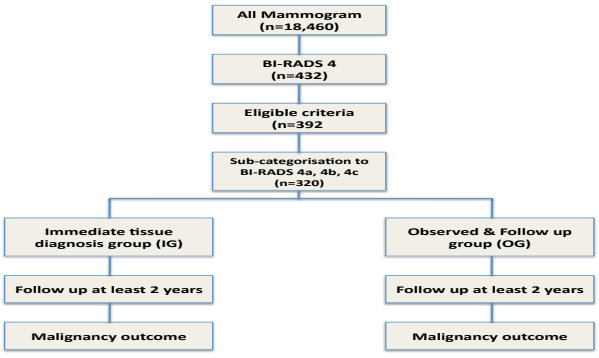

Figure 1. Protocl Design for the Mammary Cancer BI-RADS 4 Patients

Table 1. Patients Characteristics (n = 392)

BI-RADS	No.	Age range	Mean age±SD	Intervention mode	
				Immediate tissue diagnosis	Observed &Follow up
	(case)	(year)	(year)	case (%)	case (%)
4a	170	31-83	53±9	103 (60.59)	67 (39.41)
4b	62	41-90	57±10	51 (82.26)	11 (17.74)
4c	88	18-86	56±11	76 (86.36)	12 (13.64)
4(non-subcategorised)	72	31-83	56±11	60 (83.33)	12 (16.67)

Table 2. Mammogram and Ultrasound Findings in BI-RADS 4 (n=443)

Finding	No. of imaging	(%)
Mass lesion	171	38.6
Microcalcification	150	33.9
Mass and calcification	22	4.9
Architectural distortion	4	0.9
Asymmetrical density	66	14.9
Skin thickening, skin or nipple retraction	4	0.9
Hypo echoic lobulated mass	4	0.9
Other (Cyst, complicated cyst, etc)	22	5.0

Table 3. Tissue diagnosis

	Tissue diagnosis group		Observed group	
	Negative	Positive	Negative	Positive
Mean±SD	18.4±16.11	12.8±7.07	20.4±20.22	-

Table 4. Malignancy Positive Result Group (%) (n = 320)

BIRADS	Immediate tissue diagnosis	Observe & Follow up	P value
4a	7.65	0	<0.01
4b	38.71	0	<0.01
4c	57.95	0	<0.001
4(non-subcategorised)	41.67	0	<0.0016

Table 5. Pathologic Characteristic for Malignant Positive Results

Malignant result		Benign	
Histology	(%)	Histology	(%)
Invasive ductal carcinoma (IDC)	80.1	Fibroadenoma	37.9
Ductal carcinoma in situ (DCIS)	14.9	Fibrocystic change	30.3
Invasive lobular carcinoma (ILC)	3.4	Fibrosis	9.1
Invasive ductal carcinoma with DCIS	1.7	Others (papilloma, phylloides, etc)	22.7

Discussion

The American College of Radiology BI-RADS (2003) was developed to provide a standardized reporting system for mammography (Wendie, 2000; Lazarus, 2006). The BI-RADS final assessment category 4 (Suspicious abnormality, biopsy should be considered) is meant to be used for findings with imaging characteristics that suggest about the malignancy rate 20-78% (Susan, 1999; Wendie, 2000; Zonderland, 2004; Lazarus, 2006; Resende, 2008; Hamy, 2011). There were efforts to score and sub-categorise these findings into 4a, 4b, 4c according to the degree of radiologic suspicion of malignancy with the malignant results from less than 5% in BIRADS 4a to 70% in BI-RADS 4c, (Cholatip, 2010; Sanders, 2010; Wanaporn, 2011). These patterns were similar to our result, (7.65%, 38.71%, 57.95%) and the degree of radiologic abnormalities was also correlated well with the decision-making for tissue diagnosis proved of clinicians (60.59, 80.26, 86.36%) in Table 1.

There were some attempts to enhance the accuracy of the diagnostic procedures by accompanying of the breast ultrasound as an adjunct to mammography which could increase the sensitivity from 83-91% and the specificity from 97-98% especially in women younger than 50 years (Harmine, 1999). According to the more density

pattern of Asian, including Thai female's breasts than Western (Wong, 2005), combined of breast ultrasound and mammography imaging were routinely used for breast cancer screening and as diagnostic procedures in our institute.

With the variety rate of malignancy and the subjective categorisation, the management of these groups of radiologic findings seem to be the most challenge for clinicians. Based on the result of our study, BI-RADS 4a patients were the majority of the cases, and the malignant rate was only 7.65%, that meant 92.35% of patients would undergo unnecessary invasive tissue prove if we strictly followed radiologic suggestion guideline alone.

The ratio of patients in Observed group (OG) was less than an immediate tissue diagnosis group (IG), but the outcome of the malignant result was interesting (there was zero malignancy rate) with statistic significant (Table 3). These results suggested that it might be possible to create the safe follow-up guideline criteria in selected group of patients to avoid unnecessary invasive tissue proved. Although the serious complication of the invasive tissue obtained procedures was minimal, unfortunately the minor complications risk (bleeding, wound infection, pain, or vaso-vagal reactions) were ranged from 0.2-20.14% depended on the reports (Mark, 1991; Steve, 2000; Jacobs, 2001; Medina-Franco, 2005; Tonegutti M 2008; Al-Harethee, 2012).

The malignant type found in the tissue proved group shown that there was a high ratio of the invasive breast cancer (80.1%) compared to the DCIS (14.9%). This result indicated that there might be contamination of the mammographic indication for diagnostic purposes in symptomatic lesions to the screening purposes (Table 5).

In the Observed group (OG), we found that there were some similar decision-making patterns of the clinicians which composed of the exclusion criteria e.g., there was no familial history of cancer, no previous history of contra-lateral breast, not palpable lesion, the patients' follow-up compliance (within 3-6 months) and the inclusion criteria of i) within a year of post breast conserving surgery with radiation caused lymphatic obstruction in breast ultrasound and architecture distortion in mammogram (4c), ii) Infected cyst with totally disappear after aspiration (4c), iii) non-palpable lesions with disagreement of the radiologic findings among clinicians and radiologists (4a, 4b).

The quality of mammography varies greatly across the institutes, such that the predictive value of an abnormal screening mammogram may be three times higher in academic centres than in community-based practices (Retsky, 2001). The inter-observer, re-evaluation of mammogram and ultrasound with or without other complimentary investigation e.g., breast MRI have been used in our institute when there was any disagreement in clinical and radiologic findings. With this selected follow-up practice, we might be able to increase yield of the positive malignancy result from the invasive tissue obtained procedures 4.97, 8.35 and 9.15% and also increase the negative malignancy yield 34.44, 9.39, 4.49% for BI-RADS 4a, 4b and 4c respectively compared to the all tissue-biopsies-practice policy.

The suitable timing of follow up is another important issue to be considered to optimize the risk of tumour spreading especially in palpable mass (Tarhar, 1999). Based on the study of Oswald et al. (2004), Edward (1991), the initial follow-up time within 3-6 months for the non-palpable should be safe and would be able to see the changing pattern of these masses if they were unfortunately to be cancer without deterioration of the prognosis (Edward, 1991).

Our study has several limitations. First, on the basis of retrospective review of this study, the details of clinician decision-making might be in-sufficient to generalize the follow up concept. Second, our institute started to use the digital mammogram in 2005. So that some of film-based mammograms could not be reviewed and sub-categorised as they were destroyed due to the film-storage policy. However, the result of our study shown that there was no malignancy found in these film-destroyed Observed group (un-subcategorised BI-RADS4) as Table 4.

According to all evidences in the study suggested that it would be possible to set up a safe follow up guideline for the BI-RADS4 lesions to increase the positive malignancy result yield and to minimize the un-necessary invasive tissue obtainable methods. However the details of criteria in this selected group needed further investigation to validate and standardize.

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