Original Article

Rate of Malignancy of Probably Benign Mass and Masses (BI-RADS3) Detected by Screening Mammography with Adjunctive Breast Ultrasound at Phramongkutklao Hospital

Kamolwan Jungmeechoke MD[1], Tanitti Limpratya MD[1], Supakajee Saengruang-Orn PhD[1]

[1] Department of Radiology, Phramongkutklao Hospital, Bangkok, Thailand

Objective: To determine the rate of malignancy of probably benign mass and masses (BI-RADS3) detected by screening mammography with adjunctive breast ultrasound at Phramongkutklao Hospital.

Materials and Methods: Probably benign breast mass and masses detected by screening mammography with adjunctive breast ultrasound at Phramongkutklao Hospital between January 1 and August 31, 2012 and their follow-up were retrospectively reviewed with the hospital board approval. The study was conducted until either the stability of the mass was found at follow-up of at least two years or tissue diagnosis was needed. The rate of malignancy was then calculated.

Results: The study population was 241 women with 675 probably benign masses. After at least two years of follow-up, (usually at 6, 12 and 24 months), 667 masses showed no interval enlargement or any suspicious sign. Eight masses turned out to be suspicious lesions (BI-RADS4 or 5), all of which received core biopsies. One malignancy was found, at 17-month follow-up. It was early cancer, T1N1M0. The rate of malignancy was 0.41%.

Conclusion: The rate of malignancy of probably benign mass and masses (BI-RADS3) detected by screening mammography with adjunctive breast ultrasound at Phramongkutklao Hospital was low (0.41%). The malignancy was found at 17-month follow-up and was in early stage. Therefore, a recommendation of a 12-month follow-up may be more appropriate than a 6-month interval.

Keywords: Probably benign mass and masses (BI-RADS3), Screening mammography with adjunctive breast ultrasound, Rate of malignancy

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Mammography is the most effective screening tool used nowadays for breast cancer. Despite a lot of debates, it is the only imaging that has evidence supporting mortality rate reduction[1]. However, its sensitivity is reduced in women with dense breast tissue[2,3]. Even in the era of digital mammography, the sensitivity in dense breast has improved from 55% to only 70%[4]. Ultrasound has the potential to detect small breast cancer. Adjunctive screening breast ultrasound increases the cancer detection rate of about 3 to 4.6 cancers per 1,000 women screened[3,5-9]. However, it comes with substantial risk of false positive results, leading to multiple unnecessary biopsies and follow-ups. Short-interval follow-up recommendation increases from 2.2% of women screened based on mammography alone to 10.8% based on mammography plus ultrasound in the study of Berg et al[8]. At Ramathibodi Hospital, Thailand where screening mammography is done with adjunctive breast ultrasound in almost all cases, the cases that need short-term follow-up is about 15%[10].

At Phramongkutklao Hospital, screening mammography is done with adjunctive breast ultrasound in all cases because of high incidence of dense breast tissue in Thai women[10,11]. However, breast imaging reporting and data system [BI-RADS] is used as in the United States where adjunctive breast ultrasound is not usually done. BI-RADS, which was established by the American College of Radiology, is a scheme for putting the findings of mammography into seven well defined categories (BI-RADS 0-6) according to the likelihood of malignancy, accompanied by management recommendation. BI-RADS3 is probably benign. The finding placed in this category should have a very high probability of being benign with the risk to be cancer equal to or less than 2%. Management recommendation is follow-up at 6, 12, and 24 months to confirm stability of the finding. Findings that are categorized as BI-RADS3 according to BI-RADS, fourth edition,

Correspondence to:

Jungmeechoke K. Department of Radiology, Phramongkutklao Hospital, 315, Rajavithi Road, Bangkok 10400, Thailand.
Phone: +66-2-3547600 ext. 93814
Email: k_jungmeechoke@hotmail.com

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2003[12] are a cluster of round microcalcifications, focal asymmetry, and a non-palpable circumscribed mass. Adjunctive breast ultrasound shows more findings than those shown on mammogram. It shows more masses, complicated cysts, clustered microcysts, and spiculated lesions under surgical scar, etc. Furthermore, sometimes normal fat lobule and mass look so similar that they cannot be differentiated from each other. These lead to increased number of BI-RADS3 cases. There are a lot of cases of probably benign mass and masses (BI-RADS3) in Phramongkutklao Hospital. They need multiple short-term follow-ups, consuming manpower and resources while increasing patient's anxiety. The authors want to lessen these problems while not risking an under diagnosis of breast cancer. The first step is to find out the malignancy rate of this subgroup of BI-RADS3. Therefore, the purpose of the present study was to determine the rate of malignancy of probably benign mass and masses (BI-RADS3) detected by screening mammography with adjunctive breast ultrasound.

Material and Method

The present study is a retrospective study with the approval of the hospital board review. Reported cases of probably benign mass and masses, BI-RADS3, done between January 1 and August 31, 2012 were collected. Then follow-up of each case was reviewed for at least two years to see whether the mass was stable in size, which was then categorized as BI-RADS2, benign, (essentially 0% likelihood of malignancy). If the mass showed any interval growth or developed any suspicious sign, it was categorized as BI-RADS4, suspicious, or BI-RADS5, highly suggestive of malignancy. Then core biopsy was obtained because of increased likelihood of malignancy. Finally, the malignancy rate was calculated. The identification and analysis of cases were based on final reports, not the images review. Only cases with a complete 2-year follow-up or receiving tissue diagnosis were included in the study

In Phramongkutklao Hospital, screening mammography was done with adjunctive breast ultrasound in every case. Not all radiologists doing mammography and breast ultrasound were breast imagers (the same as in most hospitals in Thailand). A radiologist was present at the time of the mammography and ultrasound study. The mammography was obtained by digital mammography system (Lorad Selinia, Hologic, Danbury, CT, USA) with additional views as needed. Hand held whole breast ultrasound (HDI 5000 Philips, Bothell, WA, USA) was then done by the radiologist. The findings were summarized and reported using BI-RADS, Fourth edition, 2003[12].

Only probably benign mass and masses were included in the present study. Other BI-RADS3 lesions such as complicated cyst or clustered microcysts were excluded. Probably benign masses included both unilateral and bilateral ones. There must be no suspicious sign in BI-RADS3 lesion. The palpable mass was not BI-RADS3, it was BI-RADS4A at least, according to BI-RADS, Fourth edition, 2003[12]. Follow-up for BI-RADS3 was recommended at 6, 12 and 24 months, although not all cases were followed up as recommended. BI-RADS4 and 5 masses obtained ultrasound guided core biopsy with 14-gauge needle. The rate of malignancy was calculated.

Results

Between January 1 and August 31, 2012, there were 241 cases with screening mammography reports of probably benign mass or masses with complete follow-up. All were Thai women, aged 34 to 79 years old. There were 676 masses in total, 83 of which were solitary mass.

At the end of the study, 199 cases (82.6%) were categorized as BI-RADS2 and two cases (0.8%) as BI-RADS1. There were 29 cases (12%) still categorized as BI-RADS3 because of new findings. Eleven cases were categorized as BI-RADS4 and 5, due to new findings in three cases and an increase in size and/or not circumscribed margin of the preexisting mass in eight cases (Table 1). All eight cases received biopsies and one cancer was found (Table 2). The positive biopsy rate was 12.5%.

Table 1. Change of BI-RADS at the end of the study

Change from BI-RADS3 to BI-RADS	Number of cases (%)
1. Negative	2 (0.8)
2. Benign	199 (82.6)
3. Probably benign	29* (12.0)
4. Suspicious	10 (4.2), 3*
5. Highly suggestive of malignancy	1 (0.4)

BI-RADS = breast imaging reporting and data system

* Number of cases categorized from new findings

Table 2. Pathological result of biopsies

Pathology	Number
Fibrosis or fibrocystic change	6
Fibroadenoma	1
Invasive ductal carcinoma	1
Total	8

Table 3. Malignancy rates among probably benign mass and masses

Probably benign mass and masses	Malignancy rate % (number)
Solitary probably benign mass	0.00 (0 in 83 cases)
Multiple probably benign masses	0.63 (1 in 158 cases)
Total	0.41 (1 in 241 cases)

The overall rate of malignancy was 0.41% (1 in 241 cases). However, when calculated separately, the rate of malignancy of a solitary probably benign mass was 0% (0 in 83 cases) while that of multiple probably benign masses was 0.63% (1 in 158 cases) (Table 3).

The cancer case was first categorized as BI-RADS3 because of multiple hypoechoic masses in both breasts. The lesions showed no significant change at first follow-up at eight months. At the second follow-up at about 17 months, one of the masses showed irregular margin and was taller than wide without significant interval enlargement, the change being seen only on ultrasound. The lesion was thus categorized as BI-RADS5. Ultrasound guided core biopsy was obtained with result of infiltrating ductal carcinoma grade III. The tumor was 9 mm in size and did not involve axillary node. It was T1, N0, M0 cancer.

Discussion

The rate of malignancy of probably benign mass and masses detected by screening mammography with adjunctive breast ultrasound was 0.41% in the present study, which was in the range of BI-RADS3.

The malignancy rate of a solitary probably benign mass in the present study was 0%, which should be categorized as BI-RADS2, contrary to the new BI-RADS, fifth edition, 2013[13], which was categorized as BI-RADS3. The ACRIN 6666 trial that used ultrasound for screening was done in high-risk patients. It showed three cancers in 836 women (0.4%) with probably benign solitary circumscribed mass[14]. The 0% malignancy rate in the present study was possibly due to the fact that the study population was small and the study was done in quite average risk patients.

The 0.63% malignancy rate of probably benign masses in the present study was in the range of BI-RADS3, contrary to the new BI-RADS, fifth edition, 2013, which was categorized as BI-RADS2. The ACRIN 6666 study[14] also supported BI-RADS2 with no cancer detected in cases of multiple bilateral similar appearing circumscribed masses (0 in 135 cases). In South Korea, the study of Hwang et al[9] found one cancer (invasive ductal carcinoma) during follow-up of multiple bilateral masses at 182 days because of change in size (from 0.8 to 1.2 cm) and shape. The difference in these results may be caused by the varying size of study population, expertise in doing breast ultrasound, types of breast parenchyma, and different natural history of breast cancer in different ethnic population.

The cancer case in the present study was early cancer. It was invasive ductal carcinoma, 9 mm in size with negative axillary node. The size of the cancer was comparable to early breast cancer diagnosed by screening mammography alone[15]. This result was the same as in other studies[9,14].

The cancer was found at 17-month follow-up without significant change at first follow-up at eight months. This was suggestive of unnecessary first follow-up at six months. This is contrary to the study of Kwang et al[9], which found the cancer at about 6-month follow-up. A possible explanation for this difference might be the different rates of tumor growth. In ACRIN 6666 study, one cancer had suspicious changes at 6-month follow-up, the other two at 12 and 24 months. Only the one found at 24-month follow-up had positive axillary node[16].

The reason cited for suggesting short-term follow-up in BI-RADS3 lesion was to detect existing breast cancer at early stage with prognostic factors equivalent to the cancer diagnosed at the time of initial screening[17]. However, the greater effectiveness of a short-term follow-up over regular one (at 12 months) has never been proven[10].

Since the malignancy rate of probably benign mass and masses in the present study was low, 0.41%, and the cancer was found at 17-months follow-up, it was suggested that a yearly follow-up may be more cost effective than short-term follow-up. This agreed with the conclusion from the study of Barr et al[16]. However, further study to validate this suggestion is needed. To prevent missing a fast-growing cancer, patients should be advised to observe the abnormal areas. A fast track channel should be provided for such patients to see the doctor if abnormality is suspected.

Limitations of the present study were retrospective study, small study population, no correlation between ultrasound and mammographic findings, and between imaging findings with clinical risk.

Conclusion

The rate of malignancy of probably benign mass and masses (BI-RADS3) detected by screening mammography with adjunctive breast ultrasound at Phramongkutklao Hospital was low, at 0.41%. A

malignancy was found at 17-month follow-up and was in an early stage. Therefore, a recommendation of a 12-month follow-up may be more appropriate than a 6-month interval.

What is already known on this topic?

BI-RADS, fifth edition 2013[13] states that a solitary circumscribed solid mass has a likelihood of malignancy equal to or less than 2% (BI-RADS3), short-interval follow-up (usually at 6, 12, and 24 months) is recommended, while multiple bilateral circumscribed masses may be assessed as benign (BI-RADS2, 0% likelihood of malignancy) with a recommendation of routine screening (usually at 12 months).

In the ACRIN 6666 trial, Barr et al[16] found that BI-RADS3 lesions had a low malignancy rate, and only 0.1% of the cancers had suspicious change at 6-month follow-up. A recommendation of 12-month follow-up may be appropriate for BI-RADS3 lesions.

What this study adds?

Although the present study does not confirm BI-RADS2 category for multiple circumscribed masses, the result supports the study of Barr et al[16] to do 12-month follow-up for these BI-RADS3 lesions (probably benign mass and masses).

Potential conflicts of interest

The authors declare no conflict of interest.

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