Original Article

Upgrading Rate and Associated Factors of High-Risk Breast Lesions from Imaging Guided Breast Biopsy in King Chulalongkorn Memorial Hospital

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Objective: To determine the underestimate rate of high-risk lesions from imaging guided breast biopsy to be malignancy from subsequent surgical excision in King Chulalongkorn Memorial Hospital and to determine the factor associated to imaging characteristics and geographic data.

Materials and Methods: A retrospective review of 79 high-risk breast lesions of 78 patients who underwent imaging guided breast biopsy studies between January 1, 2010, and August 31, 2020, on women, aged 30 years or older in King Chulalongkorn Memorial Hospital. The upgrading rate of the high-risk lesions were calculated. Radiologic findings were analyzed by SPSS version 26.

Results: Seventy-nine lesions were divided into three groups with 24 lesions of atypical ductal hyperplasia (ADH), 50 lesions of the papillary lesion, and five lesions of the complex sclerosing lesion. The authors found that the upgrade rate was about 58% in the ADH group, 28% in the papillary lesion group, and 20% in the complex sclerosing lesion group. Moreover, the authors found an increased upgrade rate among patient 50 years or older (43%) as compared with fourteen patients age under 50 years (32%). However, there was no statistically significant difference in radiologic findings or factors associated with upgrading rate to malignancy under subsequent surgical excision.

Conclusion: Upgrading rate of high-risk lesions including ADH, papillary lesions, and complex sclerosing lesion were high in each lesion and the upgrade rate increased slightly in patient 50 years or older. However, there was no demonstrable radiologic manifestation or factor associated with upgrading to malignancy at subsequent surgical excision. Hence, radiologic-pathologic correlation or multidisciplinary discussion will be important roles in management of high-risk lesions.

Keywords: Breast; High risk lesion; Atypical ductal hyperplasia (ADH); Papillary lesions; Radial scar; Complex sclerosing lesion

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According to the World Health Organization (WHO), breast cancer is the most common cancer of female worldwide and in Thailand. It will contribute to the national cancer burden in the future. Diagnosis is usually made following image guided breast biopsy, which the findings are categorized to one of five categories according to the Breast Imaging Reporting and Data System (BIRADS)[(1)].

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A mammogram and ultrasonography are effective tools for early diagnosis of abundant breast lesions, with various degrees from benign to malignancy. Pathological diagnosis is usually achieved by using image guided breast biopsy when the imaging findings are classified as categories 4 or 5 according to the BIRADS. Then the pathology-radiological correlation will be done afterward to make decision on treatment or follow up.

High-risk lesions are defined as features of atypia but are not shown as malignancy and include atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), lobular carcinoma in situ (LCIS), papillary lesions, flat epithelial atypia (FEA), and radial scar. High-risk lesions are the subject of a great deal of interest, precisely because of their uncertain malignant potential and the lack of a definitive consensus on how they should be managed once diagnosed. They represent groups of diverse histopathological entities with variable degrees of associated malignancy. In isolation, these pathological

changes are not necessarily malignant, however, malignant change can coexist with these high-risk lesions. Furthermore, the presence of these lesions confers and increases the risk of subsequent breast malignancy over time, such as ductal carcinoma in situ (DCIS) and invasive ductal carcinoma (IDC)[2-4].

Most high-risk lesions will undergo surgery after needle biopsy to achieve a definitive diagnosis and rule out coexisting cancer. Therefore, some are upgraded to malignancy at the final whole tissue pathology. There are studies and reviews with a wide range of upgrade rates to cancer and hence different recommendations. Accordingly, the physician knew about the upgrade rate of each type of high-risk lesion and factor precisely determine malignancy among the high-risk lesions, these would help in operative planning and management.

Imaging guided breast biopsy is the less invasive procedure to obtain the tissue from a suspicious breast lesion for histopathologic assessment. In King Chulalongkorn Memorial Hospital, the biopsy techniques included ultrasound-guided 14-G core needle biopsy, stereotactic-guided 14-G core needle biopsy, and stereotactic-guided 9 or 10-G vacuum-assisted biopsy. The procedure performed will depend on the imaging characteristics.

The purpose of the present study is to evaluate upgrading rate and associated factors of high-risk lesions to malignancy using proven surgery.

Material and Methods

Population

The authors collected data of patients that underwent imaging guided breast biopsy between January 1, 2010 and August 31, 2020 on women aged 30 years or older in King Chulalongkorn Memorial Hospital. All these patients had final pathological diagnoses from the whole tissue excision. Radiological imaging including mammogram and ultrasound, pathological data, geographic data, and a self-administered questionnaires that included questions about personal family of the breast cancer patients, family history of breast cancer in their first-degree relative, and history of hormonal usage were included.

Imaging guided breast biopsy

The imaging guided breast biopsies were performed when lesions were determined as BIRADS 4 or 5 according to ACR BIRADS Fifth Edition[1]. An ultrasound needle guided biopsy was typically performed when an imaging characteristic was shown as a mass using automated 14-gauge needle at least four to six times. In contrast, if the imaging showed a group of suspicious microcalcifications or architectural distortion, stereotactic guided biopsy was performed with 14-guage automated gun or 9 to 10-gauge vacuum-assisted biopsy applying in an upright position breast biopsy system, Hologic 3Dimensions™. Tissue sampling was done to obtain at least four pieces of tissue. Specimen radiographs were always taken in every case to confirm the retrieved microcalcifications. If the specimen radiograph failed to show microcalcifications or architectural distortion, more core samples were attempted.

Imaging and pathological data analysis

Radiologic data of the mammogram and ultrasound were retrospectively reviewed by two radiologists with up to 12-year experience in breast imaging. The radiographic assessment was performed according to the BIRADS to characterize and describe mass, microcalcifications, architectural distortion, or other abnormal findings. Observer were blinded to the patients' information, radiologic report, and histopathological information to avoid bias. Consensus was made in case of disagreement.

The authors reviewed pathological data of tissue samples from biopsies and final diagnoses from whole tissue excisions, separately.

Statistical analysis

Rates of the upgrade to cancer were calculated for each lesion type according to age, family and personal breast cancer history, mass characteristics, calcification characteristic, and size of lesion in papillary lesions. Significant associations were examined using chi-square test by IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized as mean with standard deviation, while categorical variables were done as counts and percentages. A p-value of less than 0.05 was considered statistically significant.

Ethical approval

The present study was approved by the Institutional Review Board (IRB) of Faculty of Medicine, Chulalongkorn University, COA No. 738/2019, IRB No. 351/62.

Result

Seventy-nine lesions were found in 78 patients and divided into three groups with 24 lesions of

Table 1. Demographic data

Characteristic	ADH	Papillary lesions	Complex sclerosing lesion
Total (79); n (%)	24 (30)	50 (63)	5 (6)
Age (years); mean±SD	49.3±9.37	52.3±16.3	43.4±13.2
History of hormonal use; n (%)			
No (54)	16 (30)	36 (67)	2 (3)
Yes (15)	3 (20)	9 (60)	3 (20)
Unknown (10)	5 (50)	5 (50)	-
Personal history of breast cancer; n (%)			
No (71)	21 (30)	45 (63)	5 (7)
Yes (8)	3 (40)	5 (60)	-
Family history of breast cancer; n (%)			
No (58)	13 (22)	40 (69)	5 (9)
Yes (9)	4 (44)	5 (56)	-
Unknown (12)	7 (58)	5 (42)	-
Indication for mammography; n (%)			
Routine screening (46)	19 (41)	24 (52)	3 (7)
Palpable mass (24)	5 (21)	17 (71)	2 (8)
Nipple discharge (9)	-	9	-
BIRADS assessment; n (%)			
4a (22)	4 (18)	18 (82)	-
4b (41)	16 (39)	22 (54)	3 (7)
4c (11)	4 (36)	5 (46)	2 (18)
5 (5)	-	5 (100)	-

SD=standard deviation; ADH=atypical ductal hyperplasia; BIRADS=Breast Imaging Reporting and Data System

ADH, 50 lesions of the papillary lesion, and five lesions of the complex sclerosing lesion. The mean age was about 49 years (SD 9.4) in ADH group, 52 years (SD 16.3) in papillary lesion group, and 43 years (SD 13.2) in complex sclerosing lesion group. Most patients showed no personal history of breast cancer (89.8%) and no family history of breast cancer (73.4%), without statistical significance (p=0.35 and 0.16, respectively). Indication for mammography included routine screening (58.2%), palpable mass (30.4%), and nipple discharge (11.4%). All nipple discharge patients were in the papillary lesion group. Most lesions were BIRADS 4b (51.9%) and BIRADS 4a (27.8%) (Table 1). The details of mammographic findings are shown in Table 2.

In the present study, the authors found that the upgrade rate was about 58% in the ADH group, 28% in the papillary lesion group, and 20% in the complex sclerosing lesion group. Moreover, increased upgrade rate among patients 50 years or older were discovered with six patients in the ADH group (75%), eight patients in the papillary lesion group (31%), and one patient in the complex sclerosing lesion group (100%). Fifteen patients aged 50 years or older in all groups tended to have upgrade to malignancy (43%) as compared with fourteen patients in patients younger

Table 2. Comparison of women with and without upgrade to cancer

Characteristic	ADH; n (%)			Papillary lesions; n (%)			Complex sclerosing lesion; n (%)		
	No upgrade	Upgrade	p-value	No upgrade	Upgrade	p-value	No upgrade	Upgrade	p-value
Total (79)	10 (42)	13+1* (58)		35+1° (72)	14 (28)		4 (80)	1 (20)	
Age at procedure			0.242			0.65			0.025
<50 years (44)	8 (50)	8 (50)		18 (75)	6 (25)		4 (100)	0 (0)	
≥50 years (35)	2 (25)	6 (75)		18 (69)	8 (31)		0 (0)	1 (100)	
Characteristic			0.963			0.853			0.392
Mass (35)	2 (40)	3 (60)		21 (72)	8 (28)		1 (50)	1 (50)	
Calcification (13)	6 (46)	7 (54)		-	-		-	-	
Mass with calcification (9)	1 (33)	2 (67)		5 (83)	1 (17)		-	-	
Architectural distortion (2)	-	-		-	-		2 (100)	0 (0)	
Duct change with internal echo (7)	1 (33)	2 (67)		3 (75)	1 (25)		-	-	
Complex solid-cystic lesion (11)	-	-		7 (64)	4 (36)		-	-	
Mass with distortion (1)	-	-		-	-		1 (100)	0 (0)	
Mass characteristic (57)			-			0.975			-
Circumscribed (14)	-	-		10 (71)	4 (29)		-	-	
Non-circumscribed (43)	3 (38)	5 (62)		23 (72)	9 (28)		2 (67)	1 (33)	
Calcification characteristic (23)			-			-			-
Amorphous (11)	5 (56)	4 (44)		2 (100)	0 (0)		-	-	
Coarse heterogeneous (3)	0 (0)	1 (100)		1 (50)	1 (50)		-	-	
Fine pleomorphic (7)	1 (17)	5 (83)		1 (100)	0 (0)		-	-	
Punctate (2)	1 (100)	0 (0)		1 (100)	0 (0)		-	-	

ADH=atypical ductal hyperplasia

* Combined ADH with flat epithelial atypia with main pathology shows ADH, ° Combined papillary lesion with ADH with main pathology shows papillary lesion

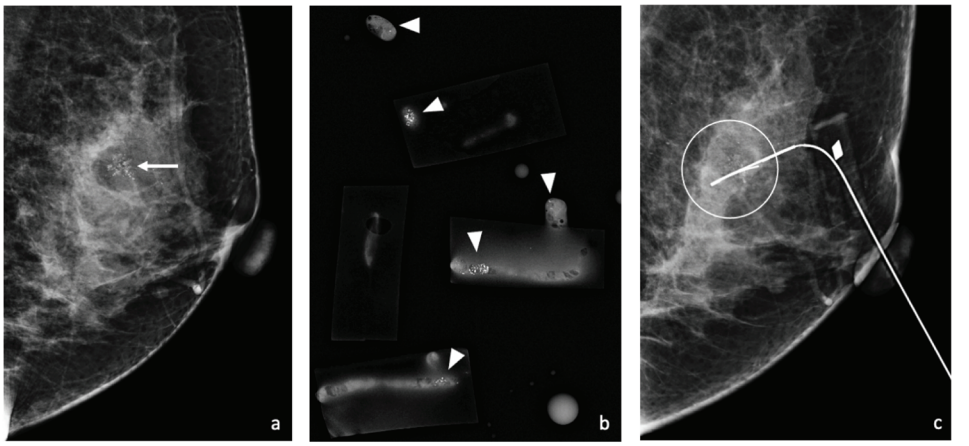

Figure 1. A 48-years old female with screening mammogram. (a) On mammogram MLO view shows group of amorphous and punctate microcalcification in left breast (arrow). (b) stereotactic 10-G vacuum-assisted biopsy was done with specimen radiograph shows multiple tissues containing microcalcification (arrowhead), ADH was diagnosed on biopsy. (c) wire localization (circle) was done, and final pathologic report show ductal carcinoma in situ (DCIS).

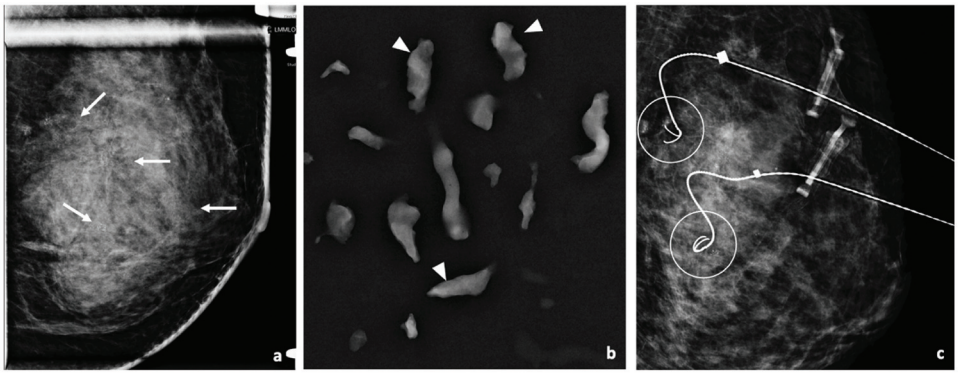

Figure 2. A 40-year-old female with screening mammogram. (a) On mammogram spot compression of the left MLO view shows multiple group of amorphous microcalcification in left lower part (arrow). (b) stereotactic 10-G vacuum assisted biopsy was done with specimen radiographs show faint amorphous microcalcification (arrowhead), ADH was diagnosed on biopsy. (c) No upgrading to malignancy after wiring localized excision (circle).

than 50 years (32%). However, there was no statistical significant difference among these groups.

According to ADH group, the characteristics associated with upgrade included mass with calcification with two lesions (67%) and focal duct change with internal echo with two lesions (67%). The most common type of calcification that associated with upgrade to malignancy was fine pleomorphic microcalcification (83%) (Figure 1). Though, there was no statistical significance of any radiologic findings associated with upgrading to malignancy after surgical excision (Figure 2).

In papillary lesion group, the imaging characteristic most associated with upgrade were complex solid cystic lesion (36%) and non-circumscribed mass (28%). There was one calcified lesion that was upgraded to malignancy after surgical excision, which showed coarse heterogeneous calcification. No statistical significance of radiologic manifestation associated with upgrading after surgical excision (Figure 3, 4).

In complex sclerosing lesion group, one lesion associated with upgrading was non-circumscribed mass (50%).

Discussion

High-risk lesions, also known as controversial lesion depending on the presence of atypia and pathological features, increases suspicion for the presence of malignancy. Hence, there is controversy regarding the need for follow-up surgery. Studies and reviews have been published on the surgical

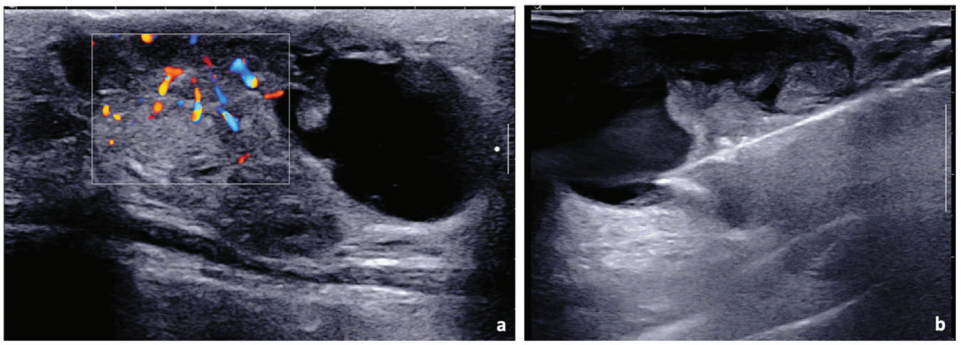

Figure 3. A 50 years-old female with palpable breast mass, (a) ultrasound shows complex solid-cystic mass with internal vascularity at solid component. (b) Papillary lesion was diagnosed on biopsy. Surgical excision reveals intraductal papilloma with ADH.

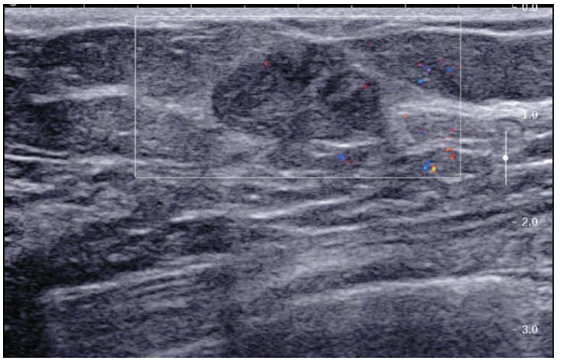

Figure 4. A 89 years-old female with palpable breast mass, ultrasound shows circumscribed hypoechoic nodule without vascularity. Papillary lesion was diagnosed on biopsy while surgical excision reveals mucinous carcinoma with solid papillary carcinoma.

results with a wide range of upgrade rates to cancer and hence different recommendations[4-9]. ADH and complex sclerosing lesion required further surgical excision, while papillary lesions, which have lower risk of upgrade rate to malignancy, tend to have short interval follow up[2,5,9].

From the present study, there was no significant radiologic finding associated with upgrading of high-risk lesions to malignancy after subsequent surgical excision. However, the authors found the highest upgrading rate in ADH. Furthermore, patients aged 50 years or older tended to have higher possibility of upgrade to malignancy in final surgical excision than the younger patient, though, with no statistical significance. Further data collection or more sample size may be helpful.

The upgrade rate of ADH group in the present study was 58%, which was higher than variable studies ranging from 18% to 28% according to Menes et al, and others[2-4]. However, there is no imaging characteristic or factor associated with upgrading to malignancy at surgery. Nonetheless, ADH diagnosed in combined mass with calcification may cause more upgrading than each pure mass or pure calcification. Calcifications, which associated to upgrading in the present study, are amorphous and fine pleomorphic microcalcifications, but there is no statistical significance between each calcification group.

The papillary lesions group is the largest group of sample size in the present study, showing an upgrade rate of about 28% which was in the range of 2% to 42% found in Armes et al, and other studies[2,6,9,10]. However, there is no significant radiologic findings associated with upgrade to malignancy after subsequent surgical excision, which was similar to a prior study[11]. Therefore, they were overlaps of radiologic features between benign and malignant papillary lesions that only slightly increased upgrade rate in the older age group. Accordingly, management of biopsy proven papillary lesions could not depend on only radiologic findings and pathology from biopsy samplings.

The upgrade rate of complex sclerosing lesion group in the present study was extremely high, at about 20%, which ranged from 4.8% to 26% in Ha et al, and other studies[3,8,12,13]. However, there was small number of radial scar/complex sclerosing lesion in the present study. Some surgeons preferred to perform surgical excision primarily for both diagnosis and treatment in one step, especially in case of parenchymal distortion.

Limitation of the present study is retrospective study and small sample size. Further data collection should be helpful.

Conclusion

Upgrading rate of high-risk lesions including ADH, papillary lesions, and complex sclerosing lesion

were high, at about 58%, 28%, and 20%, respectively. The authors found a slight increase in upgrade rate among patient aged 50 years or older (43%) in all type of high-risk lesions. There was no demonstrable radiologic manifestation or factor associated with upgrading to malignancy at subsequent surgical excision. Radiologic-pathologic correlation or multidisciplinary discussion will have a key role in management of the high-risk lesions.

What is already known on this topic?

Further management of high-risk lesions are controversial. There is no definite radiologic feature associated with upgrading to malignancy after surgery.

What this study adds?

The study shows a slight increase in upgrade among patient aged 50 years or older in all types of high-risk lesions.

Conflicts of interest

The authors declare that they have no conflict of interest.

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