



Original Article

Ultrasonographic and Mammographic Findings in Malignant Tumors of the Breast in Young Women

Cholatip Wiratkapun MD.*, Arunee Lupreechased MD.*,
Panuwat Lertsittichai MD. MSc**

* Department of Radiology, ** Department of Surgery,

Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand

Abstract

Objective: To evaluate the ultrasonographic (US) and mammographic findings as well as their correlation in malignant tumors of the breast in women aged 35 years or younger.

Material and methods: The subjects included 79 patients (with 85 lesions) diagnosed with breast cancer at the age of 35 years or younger and with available US and mammographic images for retrospective review during 9 and a half-year period of the study at the Breast Diagnostic Center of the University Hospital.

Results: Most young patients presented with a palpable breast mass. US showed a higher detection rate of malignant tumors in young age (99% compared to 84% in mammogram). Many US features suggested the presence of malignant tumors such as noncircumscribed borders or thickened echogenic halo. However, mammogram was still needed because not all malignant lesions were visualized by US. Mammographic size was better correlated with pathological size than US-size, which tended to be underestimate the pathological size.

Conclusion: US was a useful diagnostic tool to detect malignant tumors in young women. Its value was not only to detect the lesion but also characterize it. Similar to the older age group, interpretation of US along with mammogram increased the accuracy of diagnosis.

Keywords: Ultrasonography, mammography, malignant, breast, young women

Introduction

Breast cancer is the most common female cancer worldwide¹. It is also the most common cancer in Thai women¹. Thai women develop breast cancer at a younger age than the American and European women. The mean age of breast cancer in Thai women is 55 years¹. Breast cancer is uncommon in women under 35 years, accounting for approximately 2% of all breast cancers². However, palpable breast masses in this young age group are not rare. The biopsy results of breast lesions in young women are largely benign, with fibroadenoma as the most common pathology^{2,3}.

Ultrasonography (US) is the initial imaging modality for evaluating breast problems in young patients because it is not compromised by dense fibroglandular tissue. Moreover, this tool has nearly 100% accuracy in differentiating between cysts and solid masses³⁻⁵. US is also able to distinguish between benign and malignant tumors^{6,7}.

Mammography is not routinely performed in young patients because it has low sensitivity in dense breasts⁸⁻¹⁰. Mammographic sensitivity decreases from almost 100% in the fatty breasts to 45% in the extremely dense breasts⁸. Nevertheless, the value of mammography in detecting breast cancer is well established. US performed concurrently with mammography increases sensitivity compared with the use of either modality alone^{8,9}.

The purpose of this study was to evaluate the US and mammographic findings as well as their correlation for the diagnosis malignant tumors of the breast in women aged 35 years or younger.

Material and Methods

The study was conducted with institutional review board approval and given a waiver of patient

informed consent, as it was a review of routine clinical data.

Subjects consisted of women aged 35 years and younger who were treated for breast cancer or in whom a diagnosis of breast cancer was made at the Breast Diagnostic Center, Ramathibodi Hospital, Mahidol University from January 1st, 2001 to July 31st, 2010. During the study period, eighty-five lesions in 79 patients with age 35 years old or younger had available images for review along with clinical data.

US was performed by experienced radiologists using the HDI 5000 Philips ultrasound (Bothell, WA, U.S.A.) and, beyond January 2008, using the iU22 Phillips ultrasound (Bothell, WA, U.S.A.). US was performed using a broadband linear probe (L12-5). Before November 2004, mammography was obtained with two analog mammographic units (Lorad M-IV, Danbury, CT, U.S.A., and Senographe DMR, GE, Milwaukee, WI, U.S.A.). After November 2004, mammography was obtained with digital mammography units as well (Lorad, Selenia, Hologic, Danbury, CT, U.S.A.). Routine craniocaudal (CC) and medio-lateral oblique (MLO) views were performed in all patients. All images were reviewed, and a diagnostic consensus reached, by all investigators.

The US features of each lesion were based on the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) lexicon¹⁰. These features included lesion shape, orientation, margin, lesion boundary, echo pattern, posterior acoustic features and associated findings which included abnormal duct, changes in Cooper's ligament, edema, architectural distortion, and skin thickening.

Mammographic findings were based on BI-RADS lexicon as well. Breast compositions were categorized as extremely dense (>75% glandular),

heterogeneously dense (51-75% glandular), scattered fibroglandular densities (25-50% glandular) and almost entirely fatty breasts (<25% glandular). The final assessments for each modality were also based on the BI-RADS¹⁰.

Continuous variables were summarized as mean (SD) or median (range) as appropriate. Categorical variables were summarized as counts and percentages. Correlations between the size of breast lesions as measured by US, mammography and pathological examination were estimated using Pearson's correlation coefficient. Agreement between BI-RADS grading using the US and that using the mammogram was measured using the unweighted kappa statistic. All statistical analyses were performed with the statistical software Stata version 9 (Stata-Corp, College Station, TX, U.S.A).

Results

The mean age of the patients at diagnosis was 31.1 years (standard deviation (SD), 3.7 years); ranging from 18 to 35 years. The majority of patients (61 patients, 77%) presented with a painless palpable mass. Other presenting symptoms in the order of frequency were painful palpable mass in 6 (8%), nipple discharge in 3 (4%), palpable mass with nipple discharge in 2 (2%), palpable axillary lymph node in 2 (2%), right arm and breast edema in 1 (1%). Four patients (5%) had no symptoms. Imaging study was performed because of a high-risk history. No data were available about the presenting symptoms in 6 patients.

Most patients (89%) were investigated by both mammography and US. US was the only imaging investigation for the remaining patients (11%). Almost all malignancies presented as a mass (99%).

Details of US features of 84 masses are shown in Table 1.

Mammographic evaluation was available for 73 lesions in 70 patients. There was good agreement between US and mammographic BI-RADS Classification (66 lesions, 89%) for the majority of lesions, despite dense breasts in almost all patients (extremely dense, 64%; and heterogeneously dense; 32%). Details of mammographic findings are displayed in Table 2.

In 7 patients whose lesions were retrospectively categorized as mammographic BI-RADS 0 (needing further imaging studies), malignancies presented as a focal asymmetric density and trabecular thickening, which required further investigation with US. Mammography was unable to detect any abnormality in 5 lesions (mammographic BI-RADS 1) due to extremely dense breasts.

The majority of malignant lesions were pure invasive ductal carcinoma (IDC) or included IDC (80%). Ten patients (12%) had pure ductal carcinoma in situ (DCIS). Fourteen percent of patients had stage 1 invasive cancers, 40% had stage 2 cancers, 21% had stage 3, and 6% had metastatic cancers. No staging data were available for the remaining 7% of the patients. See Table 3 for further details of pathological findings.

Mammography failed to detect 5 malignant lesions (7%) and was not assigned a category in 6 lesions (8%), which required further investigation. The histopathology of mammography-undetected lesions included 2 DCIS, 1 medullary carcinoma, 1 mucinous carcinoma and 1 IDC. All were detected by US.

The mean and median of tumor size seen on US, mammography and pathological examination

Table 1 Ultrasonographic features (n=85)

Characteristics	Summary: Number (%)	Characteristics	Summary: Number (%)
Mass lesion seen (yes)	84 (99)	Echo pattern	
Calcifications seen (yes)	41 (48)	Complex	5 (6)
Shape		Hypoechoic	79 (93)
Oval	3 (4)	No mass	1 (1)
Round	2 (2)	Posterior acoustic features	
Irregular	79 (93)	None	26 (31)
No mass	1 (1)	Enhancement	29 (34)
Orientation		Shadowing	16 (19)
Parallel to chest wall	65 (77)	Combined pattern	13 (15)
Right angle to chest wall or otherwise	19 (22)	No mass	1 (1)
No mass	1 (1)	Abnormal duct (yes)	7 (8)
Margin		Changes in Cooper's ligament (yes)	30 (35)
Circumscribed	5 (6)	Edema (yes)	9 (11)
Indistinct	56 (66)	Architectural distortion (yes)	29 (34)
Angular	5 (6)	Skin thickening (yes)	16 (19)
Microlobulated	17 (20)	US size (cm, n=81)	
Spiculated	1 (1)	Mean (SD)	2.75 (1.52)
No mass	1 (1)	Median (range)	2.4 (0.4 to 8.6)
Lesion boundary		BI-RADS for US	
Abrupt interface	10 (12)	3	2 (2)
Echogenic halo	74 (87)	4A	3 (4)
No mass	1 (1)	4B	10 (12)
		4C	16 (19)
		5	54 (64)

Abbreviation: BI-RADS= Breast Imaging Reporting and Data system

are shown in Tables 1, 2 and 3. The correlation between the size of tumors measured by mammography and pathology was high (correlation coefficient, 0.838), and moderately high for US and mammogram, as was for US and pathology (correlation coefficient, 0.727 and 0.565, respectively). US tended to underestimate the true pathological size.

The unweighted kappa measure of agreement in terms of BI-RADS categorization between mam-

mography and US was 0.466 (fair agreement). This finding suggested there were some differences between mammographic and US BI-RADS assessments for the same lesion. The BI-RADS category according to US findings were more likely to be higher than that according to the mammogram (see Table 4).

Examples of lesions are shown in Figures 1, 2 and 3.

Table 2 Mammographic features (n=73)

Characteristics	Summary: Number (%)	Characteristics	Summary: Number (%)
Correlation with US (yes)	66 (89)	Mammographic BI-RADS	
Mammographic density		0	7 (8)
Extremely dense	47 (64)	1	5 (7)
Heterogeneously dense	23 (32)	4A	1 (1)
Scattered	3 (4)	4B	10 (12)
Mammographic findings		4C	13 (18)
Ill-defined mass	14 (19)	5	37 (51)
Circumscribed mass	1 (1)	Mammographic size (cm, n=57)	
Mass with calcification	30 (41)	Mean (SD)	3.44 (1.94)
Linear branching calcification	1 (1)	Median (range)	2.9 (0.9 to 9.2)
Pleomorphic calcification	7 (10)		
Spiculated mass	3 (4)		
Lobular mass	4 (5)		
Asymmetrical density	5 (7)		
Trabecular thickening	2 (3)		
Negative	6 (8)		

Abbreviation: US= ultrasonography, BI-RADS= Breast Imaging Reporting and Data system

Table 3 Pathological features (n=85)

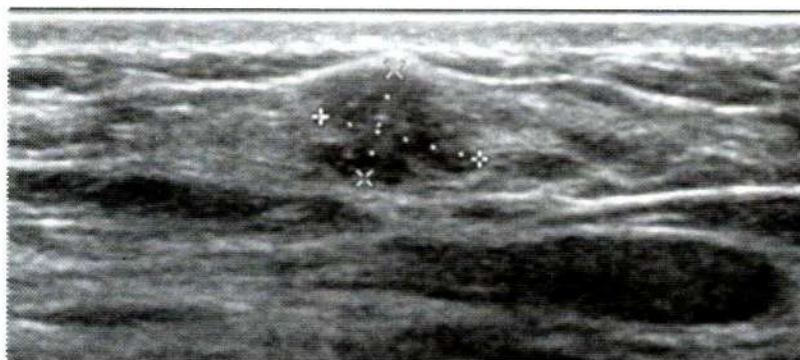
Characteristics	Summary: Number (%)	Characteristics	Summary: Number (%)
Pathological size (cm.)		Estrogen receptor status	
Mean (SD)	2.04 (1.64)	Positive	39 (46)
Median (range)	2.5 (0.8 to 9.5)	Negative	33 (39)
Type of cancer		Not done; loss to FU; phyllodes tumor	13 (15)
Pure DCIS	10 (12)	Progesterone receptor	
Pure IDC	53 (62)	Positive	38 (45)
IDC with DCIS	15 (18)	Negative	28 (33)
Mucinous cancer	3 (4)	Not done; loss to FU; phyllodes tumor	19 (22)
Medullary cancer	1 (1)	HER2/neu	
Papillary cancer	1 (1)	Positive	20 (24)
Malignant phyllodes tumor	2 (2)	Negative	46 (54)
		Not done; loss to FU; phyllodes tumor	19 (22)

Abbreviation: DCIS= Ductal carcinoma in situ, IDC= Invasive ductal carcinoma, FU= follow-up

Table 4 Agreement between ultrasonographic and mammographic BI-RADS (n=66)

US\Mam BI-RADS	1	3	4	5	Total
1	0	0	0	0	0
3	0	0	0	1	1
4	5	0	14	2	21
5	0	0	10	34	44
Total	5	0	24	37	66

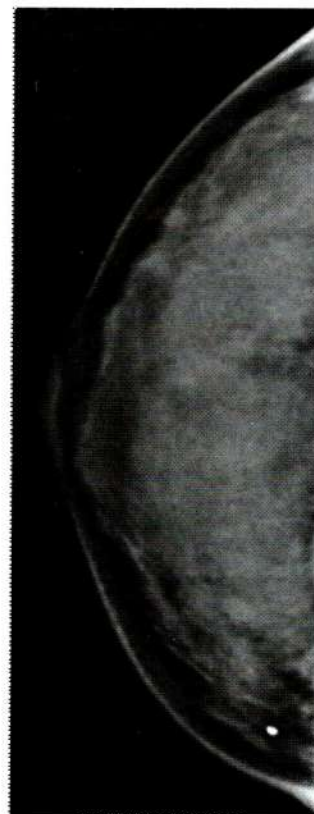
Unweighted kappa measure of agreement = 0.466 (fair agreement)


Fig.1A

A 19-year-old woman presented with painless palpable mass.

Fig 1A. US showed a 1.1-cm irregular indistinct mass with internal fine calcifications and echogenic halo.

Fig 1B. Mammography revealed extremely dense breast which totally obscured the mass. The pathology revealed ductal carcinoma in situ, grade 3 with foci of microinvasion.


Fig.1B

Figures 2

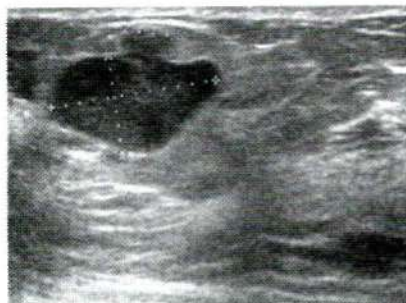


Fig.2A



Fig.2B

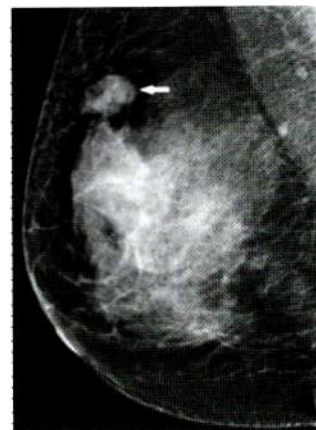


Fig.2C

A 32-year-old woman presented with a painless palpable mass. The US showed three lesions in the right breast. Fig 2A showed two contiguous solid masses with circumscribed borders, which were about 1.7 cm in total size. Heterogeneous echogenicity was noted in the larger mass. Fig 2B showed a 1.0-cm oval-shaped mass with circumscribed border. The mammography (Fig 2C) revealed heterogeneous dense breast with a lobular mass (arrow), which corresponds to the two contiguous masses seen on US. Faint internal calcifications were detected. The second mass failed to be demonstrated by mammogram. The histopathology of all lesions were mucinous carcinoma mixing with ductal carcinoma in situ.

Figures 3



Fig.3A



Fig 3B

A 27-year-old female presented with spontaneous left bloody nipple discharge for a few months. US revealed an ill-defined solid mass containing fine calcifications locating just beneath the left nipple (NIP) (Fig 3A). Mammography showed a cluster of linear branching and pleomorphic calcifications at the corresponding area (arrow in Fig 3B). Histopathology was intraductal papillary carcinoma and ductal carcinoma in situ, high grade. This case showed that microcalcifications were clearly visible despite extremely dense breast, unlike the cases shown in Figures 1 and 2, in which the mass was obscured by dense fibroglandular tissue.

Discussion

Diagnosing breast cancer in young women is not as straightforward as diagnosing breast cancers in the post-menopausal women. Firstly, since benign tumors such as fibroadenomas are much more common in young women, malignant breast lesions may be misinterpreted as benign lesions. Secondly, routine screening mammogram is not usually begun until the 40s in the average risk women¹¹⁻¹². Thus, DCIS, which traditionally manifests as microcalcifications, will be difficult to detect. Thirdly, the sensitivity of the mammogram declines in dense breasts, which is the typical breast pattern in young women⁸⁻¹⁰. US plays a major role in evaluating breast problems in young women because it is not compromised by dense breasts³⁻⁷. Moreover, the radiologist who performs US could correlate the US findings with the palpable mass at area of clinical concern, which is the most common presenting symptoms in young patients seeking medical attention⁷. Most patients in the present study (87%) had palpable masses. Thus, the present study emphasized the value of US in detecting and characterizing breast lesions in young women. All subjects in this study were evaluated by US and almost all malignant lesions (84 from 85 lesions, 99%) were detected as a mass by US.

Many suspicious US features are widely described in the literature⁴⁻⁶, including the that on the BI-RADS lexicon¹⁰. These descriptors are valuable for distinguishing malignant from benign lesions in the young patients in the present study as well. Most malignant lesions in the present study showed suspicious features. Seventy-nine mass lesions (93%) were irregular in shape. Most had indistinct, microlobulated, angular or spiculated margins (93%). Interestingly, echogenic halo was also an important

feature, as we found 87% of lesions manifesting this US feature. This sign suggested the infiltrative nature of the tumor.

As stated previously, mammography had limited sensitivity in young patients because of their dense breast composition. However, the findings in the present study showed that mammography was still valuable in evaluating breast lesions in young patients. Most of our patients had abnormal mammograms (67 in 73 patients, 92%). This finding agreed with Paredes, et al.'s study, which reported a 89% detection rate of mammography in young patients².

Medullary and mucinous carcinomas constituted two out of 5 malignant tumors in the present study which were undetected by mammography. These subtypes are well-circumscribed malignancies likely to develop by pushing the surrounding breast parenchyma outwards rather than infiltrating¹³. Unlike IDC, which typically produces spiculated border or causes architectural distortion, medullary and mucinous carcinomas may easily be overlooked by mammography, particularly in the patients with dense breasts. However, these two subtypes of cancers could be detected by US.

The present study found that US-measured tumor size tended to be underestimated when compared with pathological size (correlation coefficient, 0.565), similar to findings in the literature¹⁴⁻¹⁶. Tumor size measured by mammography showed a higher correlation with pathological size (correlation coefficient, 0.838). All these findings might be explained by the fact that US could only detect the tumor nidus, but not the spicules which could represent tumor infiltration more easily seen on mammogram.

In the present study, US was unable to detect cancer in one patient. The patient had

inflammatory breast cancer, which did not manifest as a mass lesion. On reviewing the US films, the only finding was edematous breast tissue. Mammography, however, showed diffuse skin and trabecular thickening, which raised the possibility of inflammatory carcinoma. This suggested that it was prudent to interpret the US along with a mammogram. On the other hand, US finding of edematous breast without appropriate explanation should raise the concern of inflammatory breast cancer.

Breast cancer in the young is reported to have an aggressive biological behavior and is associated with less immunoreactivity for estrogen receptor and progesterone receptor¹⁷⁻²⁰. In the present study, however, the majority of the patients (66%) presented with stage 2 cancer or lower, and almost half of all patients had positive immunohistochemistry for estrogen receptor (46%) and progesterone receptor (45%). Only one in fourth (24%) had positive HER2-neu.

There were some limitations in the present study. Because of the low incidence of breast cancer in young women, a long period of data collection was required and digital archiving of the images were not available in most of that time, thus only a quarter of all young patients with breast cancer had available images for retrospective review by the researchers. This could imply significant selection bias. Secondly, limited US images recorded on films may be not represent the true US features of the lesions. Thirdly, this study could not measure intra- and inter-observer variability. Future studies with prospective study design along with standardized mammographic and US interpretation should improve the validity of the research.

Conclusion

US showed a high detection rate for breast cancer in young patients. Many US features suggested the likelihood of the lesions being malignant. Mammography had a lower detection rate compared with US because lesions were hidden in the dense fibroglandular tissue. However, mammography was essential for diagnosis in some malignant lesions with nonspecific US findings, such as inflammatory breast cancer. Although US provided a high detection rate, it tended to underestimate the tumor size.

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Potential conflicts of interest

None.

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