Original Article

Radiographic features and molecular subtypes association of breast cancer in women younger than 40 years old

Phiraya Putto, M.D.
Jatuporn Chayakulkheeree, M.D.
From King Chulalongkorn Memorial Hospital, The Thai Red Cross Society.
Division of Diagnostic Radiology, Department of Radiology,
Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.
Address correspondence to J.C.(email: Jatuporn.C@chula.ac.th)

Received 25 November 2022; revised 6 December 2023; accepted 10 February 2024
doi:10.46475/asean-jr.v25i1.174

Abstract

Background: Breast cancer is the most commonly diagnosed cancer and the leading cause of cancer death among females, particularly in women under the age of 40 years. However, early detection of breast cancer in this population remains challenging and it tends to present at a later stage with poorer prognosis.

Objective: To review mammographic and ultrasonographic findings, pathological features and molecular subtypes of breast cancer in younger than 40-year-old patients diagnosed in King Chulalongkorn Memorial Hospital and to determine which radiological characteristics are associated with molecular subtypes.

Materials and Methods: The study included 278 patients aged under 40 years who were diagnosed with breast cancer and underwent mammographic and ultrasonographic studies between January 2009 and December 2019. A retrospective review of mammographic and ultrasonographic findings, histopathological reports as well as biological markers were made. The association of radiological characteristics and molecular subtypes was analyzed by SPSS.

THE ASEAN JOURNAL OF RADIOLOGY
ISSN 2672-9393

Results: In the 278 patients, the most common clinical presentation was palpable mass (268, 96.4%). The common mammographic findings were irregular shape mass (196, 77.8%) with hyperdensity (114, 45.2%) and an obscured margin (99, 39.3%). Presenting of microcalcification is not frequent (122, 48.4%). We found 27 patients with normal mammograms which were later detected in ultrasounds as 25 masses, 1 intraductal lesion and 1 focal duct change. The predominant ultrasonographic features were irregular shape mass (257, 91.5%), an angular margin (89, 31.7%), hypoechogenicity (198, 70.5%), no posterior feature (210, 74.7%) and internal vascularity (170, 60.5%). These radiological characteristics were classified as BI-RADS 5 in 194 lesions (69%). The most common histopathological type was mixed-type carcinoma (143, 50.9%), followed by invasive ductal carcinoma (114, 40.6%). Luminal B was the mostly found in this study (86, 30.6%). The patients frequently presented with stage IIA (91, 32.7%) while 15 patients were detected with an advanced stage at the first presentation. We found that triple negative, HER 2 overexpression and luminal B subtypes were associated with an obscured mass on mammography (p 0.048). Luminal B and HER 2 overexpression subtypes were also associated with the presence of fine pleomorphic microcalcification ($p < 0.001$).

Conclusion: In this study, we found an association of the mass margin and suspicious calcification morphology on mammography with molecular subtypes. It would be helpful for further clinical management in young patients. The knowledge can be used for planning appropriate treatments according to molecular subtypes which are associated with these characteristics. However, the precision of cancer treatment is still based on the tissue diagnosis.

Keywords: Breast cancer, Breast imaging, Histopathological type, Molecular subtype, Young women.

Introduction

Among females, breast cancer is the most commonly diagnosed cancer and the leading cause of cancer death [1-2]. Around 6.6% of all breast cancer cases are diagnosed in women less than 40 of age [3-5]. Although the diagnosis of breast cancer is much less common among young women, it can have a greater impact than in older counterparts, as it tends to present at a later stage, being more aggressive and having a poorer prognosis [3].

Screening recommendations for women younger than 40 years old are less clearly defined. In addition, younger women tend to have dense breasts and early detection of breast cancer in this population remains a challenge [6]. The radiological characteristics of breast cancer in young women can vary and there are different imaging findings according to the histopathological types. The prior studies also found a high frequency of young breast cancer with biologically more aggressive tumors, a negative hormone receptor, HER 2 overexpression, a late diagnosis and an unfavorable prognosis. However, the precise distribution of poor prognosis features in this population remains unclear.

Therefore, the purpose of this study is to review the radiological characteristics, pathological features and molecular subtypes of breast cancer in patients younger than 40 years old diagnosed in King Chulalongkorn Memorial Hospital and to evaluate the radiological characteristics associated with molecular subtypes.

Materials and methods

Population

This retrospective study was approved by the institutional review board. We collected data from 591 female patients younger than 40 years old who were newly diagnosed with breast cancer (ICD-10 code C50) at King Chulalongkorn Memorial Hospital between January 2009 and December 2019. After excluding patients that had previously undergone a breast surgery or post neoadjuvant chemotherapy, had had imaging as well as lacked radiological and pathological data, a total of 278 patients who were first diagnosed with breast cancer were available and fit the characterestics needed.

THE ASEAN JOURNAL OF RADIOLOGY
ISSN 2672-9393

Diagnostic Imaging

A whole breast ultrasonography was performed in all cases by on-site breast radiology specialists using a high-resolution linear-array transducer with a maximum frequency of at least 12-15MHz (GE Medical Systems, Philips, or Supersonic imagine). Mammograms were performed with routinely standard craniocaudal (CC) and mediolateral oblique (MLO) views (Hologic 3Dimension).

Radiographic and histopathological data analysis

A retrospective review of the patients' data including patient characteristics, clinical presentations, risk factors according to the American Cancer Society in 2019 [7], histopathology and staging according to the American Joint Committee on Cancer (AJCC) cancer staging manual 8th edition in 2017 [8] and the World Health Organization (WHO) classification of breast cancer 2012 [9], an estrogen receptor (ER), a progesterone receptor (PR), the HER2 status from histopathological reports, and molecular subtypes, were collected and categorized.

The mammogram and ultrasound were retrospectively reviewed together by an in-training diagnostic radiology resident and a radiologist with 12 years of experience in breast imaging with blind histopathology. The radiographic features including breast density, characteristics of masses, microcalcifications and associated findings (e.g., asymmetries, axillary lymphadenopathy, architectural distortion, skin thickening, nipple or skin retraction) were recorded according to American College Radiology (ACR) BI-RADS Atlas, 5th edition in 2013 [10]. A consensus was made in case of disagreement.

Statistical analysis

The radiographic data, histopathological and molecular subtype data were categorized and calculated in terms of the association between the radiographic group and the molecular subtype group. The significant association was examined using Fisher's exact test by SPSS version 28 (Statistical Package for the Social Sciences, IBM Corporation, United States). A value of $p<0.05$ is accepted as statistically significant. Continuous variables were summarized as mean with standard deviation, while categorical variables were performed as counts and percentages.

Results

Patient data

There were 278 patients ranging who were 18 to 39 years old with the mean age of about 34.9 years old (SD 3.64). The clinical presentations were palpable breast masses in 268 (96.4%) patients, nipple discharge in 7 patients (2.5%) and 3 patients remained asymptomatic (1.1%). In the 278 patients, 3 (1.1%) patients presented with bilateral breast masses which later were proven as cancer, bilaterally. Furthermore, six patients had risk factors of breast cancer including three patients who had genetic predisposition (BRCA1 gene and Li-Fraumeni syndrome), one patient with a history of contralateral breast cancer, one patient with a history of hormonal use and one patient with a history of chest wall radiation. We also found 4 patients, who had undergone breast augmentation.

In our study, a mammogram and an ultrasound were performed with 250 (89.9%) patients, while 28 (10.1%) patients only had an ultrasound. Lastly, there were a total of 281 proven cancerous lesions in the 278 patients. We found 252 lesions on the mammogram results in 250 patients who underwent mammograms with ultrasounds. Also, there were 27 (10.7%) in 252 lesions that had a negative mammogram, but the abnormalities were detected by an ultrasound. Most of the lesions were BI-RADS 5 (194, 69%). The most common stage of breast cancer at first presentation was IIA at about 91 (32.7%) patients. Moreover, 15 patients had the advanced stage at presentation with 2 liver, 1 lung, 1 nodal, 3 bone and 8 multi-organ metastases. Regarding histopathology, mixed-type carcinoma (e.g., IDC with DCIS, IDC with papillary carcinoma or IDC with mucinous carcinoma) in 143 (50.9%) lesions and luminal B subtype in 86 (30.6%) lesions were mostly found. The details of demographic data are shown in Table 1 and details of histopathology, molecular subtypes and the stage of cancer are shown in Table 2.

THE ASEAN JOURNAL OF RADIOLOGY
ISSN 2672-9393

Table 1. *Demographic data.*

Characteristics (Total = 278 patients)	Number (%)
Mean age (years ± SD)	34.9 ± 3.64
Clinical presentation	
- Palpable mass	268 (96.4%)
- Nipple discharge	7 (2.5%)
- Asymptomatic/Screening	3 (1.1%)
Risk factors	
- Family history of breast cancer/genetic predisposition	3
- History of contralateral breast cancer	1
- History of hormonal used	1
- History of chest wall radiation	1
Breast side	
- Right	143 (51.4%)
- Left	132 (47.5%)
- Bilateral	3 (1.1%)
Imaging modality	
- Ultrasound only	28 (10.1%)
- Mammogram with ultrasound	250 (89.9%)
BI-RADS assessment (Total = 281 lesions)	
- category 4A	11 (3.9%)
- category 4B	30 (10.7%)
- category 4C	46 (16.4%)
- category 5	194 (69%)

Table 2. *Histopathology, molecular subtypes, and stages of breast cancer.*

Characteristics	Number (%)
Histopathological types (Total = 281 lesions)	
- DCIS	11 (3.9%)
- invasive ductal carcinoma (IDC)	114 (40.6%)
- invasive lobular carcinoma (ILC)	2 (0.7%)
- Mixed-type carcinoma	143 (50.9%)
- Mucinous type	7 (2.5%)
- Papillary type	3 (1.1%)
- Other	1 (0.4%)
Molecular subtypes (Total = 281 lesions)	
- Luminal A	62 (22.1%)
- Luminal B	86 (30.6%)
- Luminal B/HER 2 positive	29 (10.3%)
- HER 2 overexpression	58 (20.6%)
- Triple negative	46 (16.4%)
Stage of breast cancer at presentation (Total = 278 patients)	
- stage 0	11 (4.0%)
- stage IA	68 (24.5%)
- stage IB	1 (0.4%)
- stage IIA	91 (32.7%)
- stage IIB	43 (15.5%)
- stage IIIA	28 (10.1%)
- stage IIIB	8 (2.9%)
- stage IIIC	13 (4.7%)
- stage IV	15 (5.4%)

THE ASEAN JOURNAL OF RADIOLOGY
ISSN 2672-9393

Mammographic findings

225 proven cancerous lesions were detected from 252 lesions on mammograms. The detail of mammographic findings is summarized in Table 3. The breast composition in mammographic studies was mostly heterogeneously dense and extremely dense breasts in which about 183 (65.1%) and 68 (24.2%) patients were found with the conditions, respectively.

The most common abnormality, which was seen on mammography was masses in 200 (79.4%) lesions, followed by suspicious calcifications in 122 (48.4%) lesions. Most of the masses in mammographic findings were irregular shapes at about 196 (77.8%) lesions and the rest were an oval shape in 4 (1.6%) lesions, while 52 (20.6%) studies were non-visualized masses. The density of masses included 114 (45.2%) hyperdensity (as compared to the density of the fibroglandular tissue) and 86 (34.1%) isodensities. The margins of these masses were obscured margins in 99 (39.3%) masses, spiculated margins in 45 (17.9%), indistinct margins in 30 (11.9%), microlobulated margins in 25 (9.9%) and the least commonly found was circumscribed margins, found in 1 (0.4%) mass.

Table 3. *Mammographic findings.*

Characteristics (Total = 252 lesions)	Number (%)
Normal	27 (10.7%)
Breast composition	
- scattered areas of the fibroglandular tissue	1 (0.4%)
- extremely dense	68 (27%)
- heterogeneously dense	183 (72.6%)
Mass	200 (79.4%)
Mass shape	
- oval	4 (1.6%)
- irregular	196 (77.8%)

Characteristics (Total = 252 lesions)	Number (%)
Mass margin	
- circumscribed	1 (0.4%)
- obscured	99 (39.3%)
- microlobulated	25 (9.9%)
- indistinct	30 (11.9%)
- spiculated	45 (17.9%)
Mass density	
- high	114 (45.2%)
- equal	86 (34.1%)
Suspicious calcification morphology	
- amorphous	19 (7.5%)
- coarse heterogeneous	11 (4.4%)
- fine pleomorphic	87 (34.5%)
- fine linear or branching	5 (2%)
- no suspicious calcification	130 (51.6%)
Distribution of calcifications	
- diffuse	1 (0.4%)
- regional	5 (2.0%)
- grouped	80 (31.7%)
- linear	2 (0.8%)
- segmental	34 (13.5%)
Asymmetries	
- focal asymmetry	4 (1.6%)
- global asymmetry	1 (0.4%)
Skin thickening/retraction	30 (11.9%)
Architectural distortion	61 (24.2%)
Nipple retraction	16 (6.3%)
Axillary lymphadenopathy	79 (31.3%)

THE ASEAN JOURNAL OF RADIOLOGY
ISSN 2672-9393

Regarding the association between the mass margin on mammography and molecular subtypes, triple negative, HER 2 overexpression and luminal B subtypes were associated with the obscured mass on mammography with the p-value of 0.048 (22 lesions [52.4%], 23 lesions [46%] and 30 lesions [37.5%], respectively) as demonstrated in Table 4. We also found irregular masses were frequently in luminal B subtype (62 lesions, 77.5%). However, the mass shapes on mammograms did not show a statistically significant association with the molecular subtype (p-value 0.216).

Table 4. *Association between radiographic findings and molecular subtypes.*

Characteristics	Molecular subtypes				
	Luminal A	Luminal B	Luminal B / HER 2	HER 2 overexpression	Triple negative
Mass shape on mammography					
- oval	2 (3.6%)	2 (2.5%)	-	-	-
- irregular	37 (67.3%)	62 (77.5%)	21 (84%)	38 (76%)	38 (90.5%)
- no	16 (29.1%)	16 (20%)	4 (16%)	12 (24%)	4 (9.5%)
			P = 0.216		
Mass margin on mammography					
- circumscribed	1 (1.8%)	-	-	-	-
- obscured	19 (34.5%)	30 (37.5%)	5 (20%)	23 (46%)	22 (52.4%)
- microlobulated	3 (5.5%)	11 (13.8%)	3 (12%)	2 (4%)	6 (14.3%)
- indistinct	5 (9.1%)	6 (7.5%)	6 (24%)	6 (12%)	7 (16.7%)
- spiculated	11 (20%)	17 (21.3%)	7 (28%)	7 (14%)	3 (7.1%)
- no	16 (29.1%)	16 (20%)	4 (16%)	12 (24%)	4 (9.5%)
			P = 0.048		
Suspicious calcification morphology on mammography					
- amorphous	5 (9.1%)	6 (7.5%)	2 (8%)	5 (10%)	1 (2.4%)
- coarse heterogeneous	2 (3.6%)	4 (5%)	1 (4%)	3 (6%)	1 (2.4%)
- fine pleomorphic	12 (21.8%)	36 (45%)	14 (56%)	20 (40%)	5 (11.9%)
- fine linear or branching	1 (1.8%)	1 (1.3%)	1 (4%)	2 (4%)	-
- no suspicious calcification	35 (63.6%)	33 (41.3%)	7 (28%)	20 (40%)	35 (83.3%)
			P = <0.001		

Characteristics	Molecular subtypes				
	Luminal A	Luminal B	Luminal B / HER 2	HER 2 overexpression	Triple negative
Mass shape on ultrasonography					
– oval	3 (4.8%)	1 (1.2%)	-	1 (1.7%)	3 (6.5%)
- irregular	56 (90.3%)	77 (89.5%)	26 (89.7%)	55 (94.8%)	43 (93.5%)
- intraductal lesion	2 (3.2%)	3 (3.5%)	3 (10.3%)	1 (1.7%)	-
- no	1 (1.6%)	5 (5.8%)	-	1 (1.7%)	-
			P = 0.217		
Mass margin on ultrasonography					
- circumscribed	2 (3.2%)	1 (1.2%)	-	-	2 (4.3%)
- indistinct	17 (27.4%)	21 (24.4%)	5 (17.2%)	13 (22.4%)	15 (32.6%)
- angular	18 (29%)	25 (29.1%)	10 (34.5%)	24 (41.4%)	12 (26.1%)
- microlobulated	9 (14.5%)	16 (18.6%)	4 (13.8%)	10 (17.2%)	15 (32.6%)
- spiculated	13 (21%)	15 (17.4%)	7 (24.1%)	9 (15.5%)	2 (4.3%)
- no	3 (4.8%)	8 (9.3%)	3 (10.3%)	2 (3.4%)	-
			P = 0.116		
Mass echogenicity on ultrasonography					
- complex cystic/solid	1 (1.6%)	-	-	-	1 (2.2%)
- hypoechoic	43 (69.4%)	61 (70.9%)	24 (82.8%)	39 (67.2%)	31 (67.4%)
- isoechoic	3 (4.8%)	-	1 (3.4%)	-	1 (2.2%)
- heterogeneous	14 (22.6%)	20 (23.3%)	4 (13.8%)	18 (31%)	13 (28.3%)
- no	1 (1.6%)	5 (5.8%)	-	1 (1.7%)	-
			P = 0.232		
Mass posterior features on ultrasonography					
- enhancement	4 (33.3%)	3 (25%)	-	1 (8.3%)	4 (33.3%)
- shadowing	8 (19%)	13 (31%)	1 (2.4%)	13 (31%)	7 (16.7%)
- combined	2 (11.8%)	7 (41.2%)	-	3 (17.6%)	5 (29.4%)
- no posterior feature	48 (22.9%)	63 (30%)	28 (13.3%)	41 (19.5%)	30 (14.3%)
			P = 0.144		

THE ASEAN JOURNAL OF RADIOLOGY
ISSN 2672-9393

Furthermore, suspicious calcifications were found in 122 (48.4%) lesions, including fine pleomorphic microcalcification in 87 (34.5%) lesions, amorphous microcalcification in 19 (7.5%) lesions, coarse heterogeneous microcalcification in 11 (4.4%) lesions and fine linear microcalcification in 5 (2.0%) lesions. The most major distribution of calcification was grouped, which was seen in 80 (31.7%) lesions. There was a statistically significant association between suspicious calcification morphology on mammography and molecular subtypes with a p-value of <0.001, as shown in Table 4. The presence of fine pleomorphic microcalcification was associated with luminal B and HER 2 overexpression subtypes (36 lesions [45%] and 20 lesions [40%], respectively). The majority of triple negative and luminal A lesions were associated with masses without calcification (35 lesions [83.3%] and 35 lesions [63.6%], respectively).

Asymmetries were not frequently discovered in this study. Only 4 (1.6%) lesions detected focal asymmetry and 1 (0.4%) global asymmetry were observed. The other associated findings included skin thickening or retraction in 30 (11.9%) lesions, architectural distortion in 61 (24.2%) lesions and nipple retraction in 16 (6.3%) lesions. Axillary node enlargement on mammograms was seen in 79 (31.3%) lesions. In some mammographic studies showed benign appearing axillary nodes, but ultrasonography could detect the abnormalities as enlarged nodes, loss of fatty hilum, a thickened cortex or a rounded shape.

In this study, there were 27 negative mammographic findings and abnormalities were later detected by ultrasonography, which included 25 masses, 1 intraductal mass and 1 focal duct change. All lesions were proven as cancer. Among these negative mammograms, extremely dense breast tissues were seen in 16 lesions (59.3%).

Ultrasonographic findings

There were 281 proven cancerous lesions in 278 patients who underwent an ultrasound. Ultrasonographic findings are depicted in Table 5. In 265 (94.3%) masses on the ultrasonography were 257 (91.5%) an irregular shape and 8 (2.8%) an oval shape. We also found 9 (3.2%) intraductal lesions. The most common

characteristics of masses were angular margins in 89 (31.7%) masses, followed by indistinct margins in 71 (25.3%) masses. Most of the masses were non-parallel orientations (253, 90%). The echogenicity of masses was hypoechogenicity in 198 (70.5%) masses, heterogeneous echogenicity in 69 (24.6%) masses, isoechogenicity in 5 (1.8%) masses and complex cystic/solid in 2 (0.7%) masses.

Table 5. *Ultrasonographic findings.*

Characteristics (Total = 281 lesions)	Number (%)
Mass	265 (94.3%)
Intraductal lesion	9 (3.2%)
No mass	7 (2.5%)
Mass shape	
- oval	8 (2.8%)
- irregular	257 (91.5%)
Mass orientation	
- parallel	12 (4.3%)
- not parallel	253 (90%)
Mass margin	
- circumscribed	5 (1.8%)
- indistinct	71 (25.3%)
- angular	89 (31.7%)
- microlobulated	54 (19.2%)
- spiculated	46 (16.4%)
Mass echogenicity	
- complex cystic/solid	2 (0.7%)
- hypoechoic	198 (70.5%)
- isoechoic	5 (1.8%)
- heterogeneous	69 (24.6%)

THE ASEAN JOURNAL OF RADIOLOGY
ISSN 2672-9393

Characteristics (Total = 281 lesions)	Number (%)
Mass posterior feature	
- no posterior feature	210 (74.7%)
- enhancement	12 (4.3%)
- shadowing	42 (14.9%)
- combined	17 (6%)
Vascularity	
- absent	76 (27%)
- internal vascularity	170 (60.5%)
- vessels in rim	35 (12.5%)
Calcification	
- in mass	108 (38.4%)
- outside of mass	8 (2.8%)
- intraductal calcifications	16 (5.7%)
Axillary lymphadenopathy	92 (32.7%)
Duct changes	74 (26.3%)
Architectural distortion	29 (10.3%)
Skin thickening/retraction	18 (6.4%)
Edema	3 (1.1%)

Almost all of the masses were no posterior features, which were found in 210 (74.7%) masses, followed by posterior shadowing (42, 14.9%). The mass with internal vascularity was the most frequently observed, at about 170 (60.5%) lesions, followed by masses with vessels in the rim (35, 12.5%) and absent vascularity (76, 27%). There were 108 (38.4%) masses with internal calcification, 16 (5.7%) intraductal calcification and the others were calcification outside of the masses (8, 2.8%). Ultrasound was a useful modality to detect lesions, especially in young patients with dense breasts, whose masses could be occulted on mammograms (Figure 1 and Figure 2).

In this study, there was no statistically significant association between ultrasonographic findings and molecular subtypes as demonstrated in Table 4.

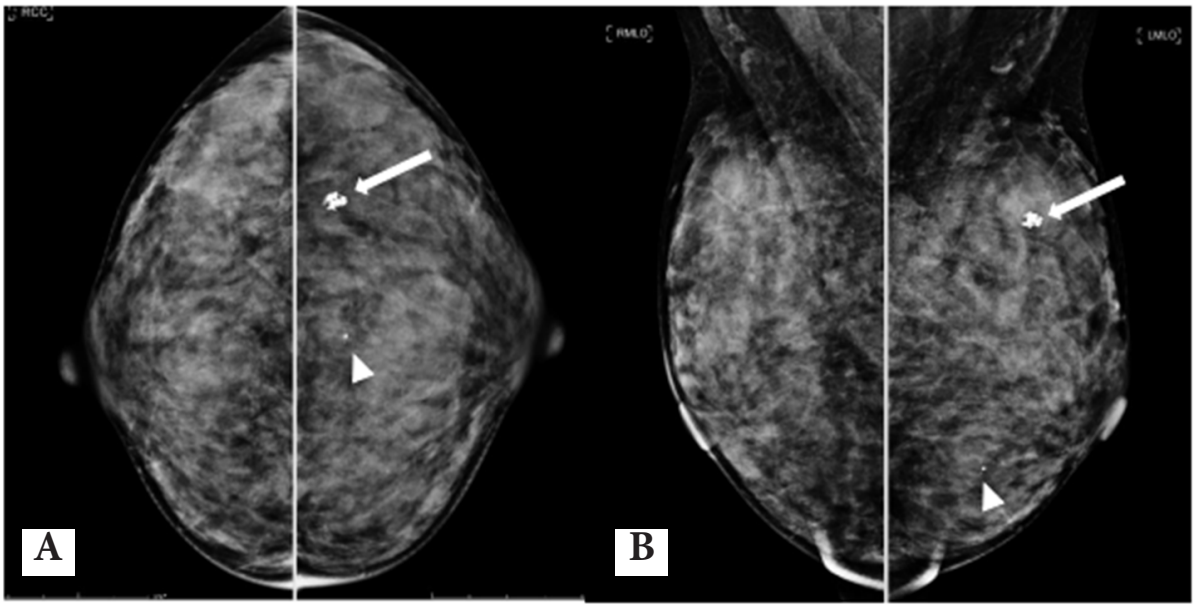

Figure 1. *Mammography of bilateral CC (A) and MLO (B) views of a 36-year-old female presented with palpable multiple bilateral breast masses revealed extreme density in both breasts, which may obscure small masses. There were a popcorn calcification at LUOQ (white arrow) and a group of coarse heterogeneous calcifications at the left lower mid part (arrowhead).*

THE ASEAN JOURNAL OF RADIOLOGY
ISSN 2672-9393

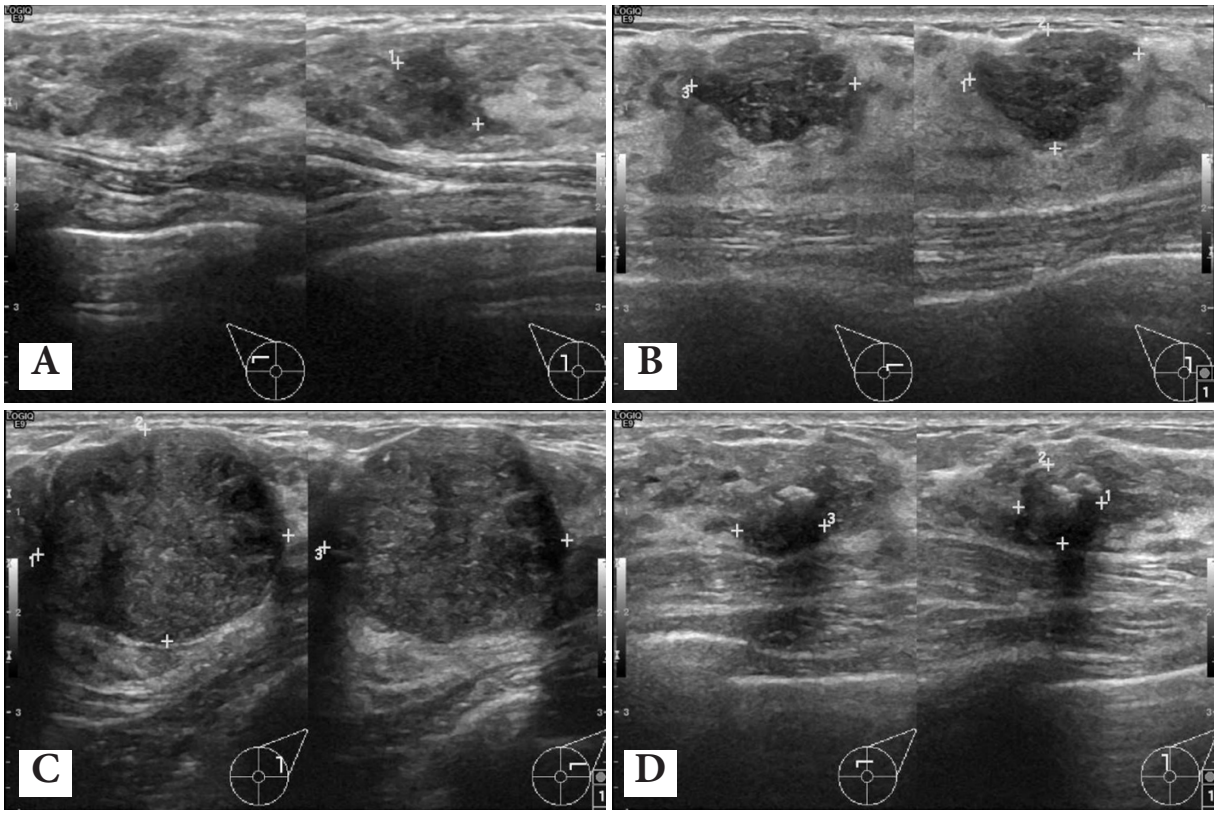

Figure 2. *Ultrasonography of both breasts of the same patient in Figure 1 showed multiple varying sized masses in both breasts. Two irregular hypoechoic masses with an angular margin at RUOQ and RUIQ, (A and B), respectively, high suspicion for malignancy (BI-RADS 4C). A well-circumscribed round-shape hypoechoic mass at LUOQ (C) and a well-circumscribed hypoechoic mass with internal macrocalcification at the left upper mid part (D), likely degenerating fibroadenoma. Histopathology at RUOQ and RUIQ masses revealed invasive ductal carcinoma with DCIS (luminal A) (A and B).*

Discussion

Breast cancer in younger women or younger than 40 years old is challenging in diagnosis and treatment. In this age group, there tends to be a late diagnosis, a more aggressive tumor and a poor prognosis [3, 11-15]. The high percentage of these patients presented with advanced stage breast cancer perhaps due to the absence of a screening protocol for patients under the age of 40 years old. Moreover, the diagnosis is challenging because of relatively denser breast parenchyma on mammograms which could obscure the lesions [16].

The most common presentation in women under 40 years old in this study was palpable masses (96.4%), which was similar to many previous studies. Mammographic findings frequently found in our study were irregular masses (77.8%), obscured margins (39.3%), followed by spiculated margins (17.9%), and fine pleomorphic microcalcification (34.5%), were consistent with the findings of previous studies [5, 14]. The most common ultrasonographic findings were irregular shape masses (91.5%), angular margins (31.7%), hypoechogenicity (70.5%), no posterior feature (74.7%) and internal vascularity (60.5%), which also resemble prior studies [5, 13, 17]. Radiographic data was assessed according to ACR BI-RADS 5th edition [10]. We found a majority of lesions (194, 69%) were categorized as highly suggestive for malignancy (BI-RADS 5) in line with the results of previous studies [11]. These radiographic findings of suggestive malignant lesions were similar findings in older women.

Additionally, we found these patients were more likely to be diagnosed with stage IIA (32.7%), similar to a prior study [6]. Nevertheless, 15 patients presented with advanced stage cancer and 8 of them had multi-organ metastases (e.g., liver, lung, bone, brain or lymph node). These patients represented a late diagnosis and a more aggressive tumor in young women; thus, early detection and increase awareness of breast cancer in this age group could be the principal management.

THE ASEAN JOURNAL OF RADIOLOGY
ISSN 2672-9393

According to association between mammographic findings and molecular subtypes, in previous studies reported that significantly more spiculated masses found in the luminal subtype and HER 2 overexpression subtype tumors significantly correlated with the presence of calcifications [17]. Our study also showed a statistically significant association between the presence of fine pleomorphic microcalcification with luminal B and HER 2 overexpression subtypes ($p < 0.01$) in the agreement with the prior study [17]. We also found triple negative and luminal A subtypes lesions were associated with masses without calcification, similar to the previous study [13].

Additionally, the present study showed that triple negative, HER 2 overexpression and luminal B subtypes were associated with obscured masses on mammography (p 0.048), which was inconsistent with the previous study [17]. Irregular masses were frequently in luminal B subtypes in this study, but did not show a statistically significant association with molecular subtypes.

According to the association between ultrasonographic features and molecular subtypes, Junwoo Kim et al. [13] revealed triple negative subtypes were significantly found with a posterior enhancement compared with the other molecular subtypes. Bullier B et al. [17] reported that triple negative cancers significantly more often had a round-oval shape compared to other phenotypes that were irregular and had circumscribed-microlobulated-indistinct margins compared to luminal phenotypes that were angular or spiculated. In our study, triple negative subtypes were predominant in masses with indistinct margins (32.6%) which were the same as ones with microlubulated margins (32.6%). This finding was similar to the prior study [17], but did not show a statistical significance in association. Furthermore, we found most of all molecular subtype lesions showed no posterior feature which disagrees with the previous study [13]. However, the molecular subtypes did not show a significant association with any ultrasonographic findings in our study.

Collins et al. [15] showed no significant differences in the molecular phenotype, the tumor stage or the grade among the different age groups of young women. Similarly, Erić et al. [8] found no difference in cancer laterality in both younger and older groups. In our study, the most common histological type was mixed-type carcinoma (50.9%) and no-special type invasive ductal carcinoma (40.6%), which resemble many prior studies [11, 14, 17-18]. Regarding the molecular subtype, luminal B was the most common (30.6%), followed by luminal A (22.1%) and HER 2 overexpression (20.6%), similar to Collins et al. reporting in their large cohort study that luminal B type is the most prevalent (35%) in young breast cancer patients compared to the general population. On the other hand, some previous studies showed more prevalence of triple negative subtypes [4, 11-12].

Mammography sensitivity is decreased in young women because of the higher breast tissue density, which can obscure breast masses [5, 19]. Therefore, ultrasonography is a useful initial modality for the diagnosis of breast cancer in young age group because with more sensitivity [15] and reduced accumulation of radiation in young women. In the current study, ultrasonography could detect abnormalities in all patients, while we found mammographically missed lesions in 27 patients (10.7%). Thus, we also agree with many studies before that recommended ultrasonography as the primary diagnostic tool for young patients.

There were some limitations of this study because it had a retrospective design and was a single center study. Further data collection should be taken into consideration for further research.

THE ASEAN JOURNAL OF RADIOLOGY
ISSN 2672-9393

Conclusion

In this study, we found that the mass margins and suspicious calcification morphology on mammography were significantly associated with molecular subtypes, so it would be helpful for further clinical management in young patients. For example, if mammographic findings of young patients with palpable breast masses, showing irregular masses with obscured margins and internal fine pleomorphic microcalcification, clinician could be planning the treatment for the luminal B or HER 2-overexpression tumor which was associated with these characteristics. However, the precision of cancer treatment was still based on tissue diagnosis.

Conflicts of Interest

The authors declare that there is no conflict of interest.

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394-424. doi: 10.3322/caac.21492.

2. Paluch-Shimon S, Pagani O, Partridge AH, Bar-Meir E, Fallowfield L, Fenlon D, et al. Second international consensus guidelines for breast cancer in young women (BCY2). Breast 2016;26:87-99. doi: 10.1016/j.breast.2015.12.010.

3. Assi HA, Khoury KE, Dbouk H, Khalil LE, Mouhieddine TH, El Saghir NS. Epidemiology and prognosis of breast cancer in young women. J Thorac Dis 2013;5 Suppl 1:S2-8. doi: 10.3978/j.issn.2072-1439.2013.05.24.

4. Anders CK, Johnson R, Litton J, Phillips M, Bleyer A. Breast cancer before age 40 years. Semin Oncol 2009;36:237-49. doi: 10.1053/j.seminoncol.2009.03.001.

5. Durhan G, Azizova A, Önder Ö, Kösemehmetoğlu K, Karakaya J, Akpınar MG, et al. Imaging Findings and Clinicopathological Correlation of Breast Cancer in Women under 40 Years Old. Eur J Breast Health 2019;15:147-52. doi: 10.5152/ejbh.2019.4606.

6. Gillman J, Batel J, Chun J, Schwartz S, Moy L, Schnabel F. Imaging and clinicopathologic characteristics in a contemporary cohort of younger women with newly diagnosed breast cancer. Cancer Treat Res Commun 2016;9:35-40.

7. American Cancer Society. Cancer facts and figures 2019. Atlanta: American Cancer Society; 2019.

8. Hortobagyi GN, Connolly JL, D'Orsi CJ, Edge SB, Mittendorf EA, Hope S, et al. Breast. In: Amin MB, Edge S, Greene F, Byrd DR, Brookland RK, Washington MK, et al, editors. 8th ed. New York: Springer; 2017. p. 589-628.

9. Lakhani SR, Ellis IO, Schnitt SJ, Tan PH, van de Vijver MJ, editors. WHO classification of tumours of the breast: WHO Classification of Tumours, 4th ed. Volume 4. Lyon: IARC Press; 2012.

10. D'Orsi CJ, Sickles EA, Mendelson EB, Morris EA. ACR BI-RADS® Atlas, Breast Imaging Reporting and Data System. Reston(VA): American College of Radiology; 2013.

11. Davey MG, Brennan M, Ryan ÉJ, Corbett M, Abd Elwahab S, Walsh S, et al. Defining clinicopathological and radiological features of breast cancer in women under the age of 35: an epidemiological study. Ir J Med Sci 2020; 189:1195-202. doi: 10.1007/s11845-020-02229-z.

12. Shoemaker ML, White MC, Wu M, Weir HK, Romieu I. Differences in breast cancer incidence among young women aged 20-49 years by stage and tumor characteristics, age, race, and ethnicity, 2004-2013. Breast Cancer Res Treat 2018;169:595-606. doi: 10.1007/s10549-018-4699-9.

13. Kim, J, Jang M, Kim SM, Yun BL, Lee JY, Kim EK, et al. Clinicopathological and imaging features of breast cancer in Korean women under 40 years of age. J Korean Soc Radiol 2017;76:375-85.

14. Eugênio DSG, Souza JA, Chojniak R, Bitencourt AGV, Graziano L, Marques EF. Breast cancer diagnosed before the 40 years: imaging findings and correlation with histology and molecular subtype. Appl Cancer Res [Internet]. 2017 [cited 2024 Feb 19];37(16). Available from: https://appliedcr.biomedcentral.com/articles/10.1186/s41241-017-0019-7#article-info

15. Collins LC, Marotti JD, Gelber S, Cole K, Ruddy K, Kereakoglow S, et al. Pathologic features and molecular phenotype by patient age in a large cohort of young women with breast cancer. Breast Cancer Res Treat 2012;131:1061-6. doi: 10.1007/s10549-011-1872-9.

16. Tirada N, Aujero M, Khorjekar G, Richards S, Chopra J, Dromi S, et al. Breast cancer tissue markers, genomic profiling, and other prognostic factors: A primer for radiologists. RadioGraphics 2018;38:1902-20. doi: 10.1148/rg.2018180047.

17. Bullier B, MacGrogan G, Bonnefoi H, Hurtevent-Labrot G, Lhomme E, Brouste V, et al. Imaging features of sporadic breast cancer in women under 40 years old: 97 cases. Eur Radiol 2013;23:3237-45. doi: 10.1007/s00330-013-2966-z.

18. Erić I, Petek Erić A, Kristek J, Koprivčić I, Babić M. Breast cancer in young women: Pathologic and immunohistochemical features. Acta Clin Croat 2018; 57:497-502. doi: 10.20471/acc.2018.57.03.13.

19. Expert Panel on Breast Imaging; Mainiero MB, Moy L, Baron P, Didwania AD, diFlorio RM, , et al. ACR Appropriateness Criteria® Breast Cancer Screening. J Am Coll Radiol 2017;14(11 Suppl):S383-90. doi: 10.1016/j.jacr.2017.08.044.