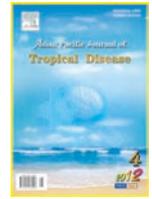




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Mammographic characterization of breast cancer associated with axillary lymph node metastasis

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ABSTRACT

Objective: To describe mammographic characterization of breast cancer associated with axillary lymph node metastasis at King Chulalongkorn Memorial Hospital. **Methods:** The data were collected retrospectively from female patients with breast cancers who underwent breast surgery and axillary node dissection at King Chulalongkorn Memorial Hospital during January 1, 2004 and July 31, 2011. One hundred and ninety histopathologically proven cases of invasive ductal carcinoma (IDC) were randomly recruited; consisted of ninety-five patients with axillary lymph node metastasis and the rest of patients without axillary lymph node metastasis. All patients were reviewed their mammograms with additional ultrasounds and correlation between each mammographic characteristic and ipsilateral node involvement was analyzed, using *P*-value (*P*), Odd ratio (*OR*) and 95% confidence interval (*CI*). **Results:** Mammographic characterization associated with the highest risk of axillary node metastasis was malignant pattern of ipsilateral axillary node ($P < 0.001$; $OR = 44.53$; 95% $CI = 13.10 - 151.37$) with following by intermediate pattern of ipsilateral axillary node ($P = 0.002$; $OR = 5.18$; 95% $CI = 1.79 - 15.04$). The other characteristics in descending orders for associated with axillary node involvement are upper outer quadrant tumors associated risk of ipsilateral axillary node involvement ($P = 0.02$; $OR = 3.36$; 95% $CI = 1.23 - 9.14$) and size of breast cancer by additional ultrasound ($P = 0.04$; $OR = 1.48$; 95% $CI = 1.02 - 2.17$). There was no association between risk of axillary node involvement and the rest of mammographic findings, including microcalcification of the tumor, vascularity of the tumor and size of axillary node. **Conclusions:** The highest predictive risk of axillary node metastasis in breast cancer was malignant axillary node pattern. The moderate risk was intermediate axillary node pattern and the lower risks were the tumor located in upper outer quadrant and increased tumor size. These results will be helpful for diagnostic mammogram to imply prognosis of breast cancer before patient undergo biopsy or surgical procedure.

1. Introduction

Breast cancer is the most common cancer in females worldwide^[1,2], with 1 151 298 new cases identified throughout the world each year. The age-standardized incidence rate is 37.4 per 1 000 000 women^[2]. In Thailand, breast cancer is the second most common cancer in Thai women^[2]. The incidence rate is 20.5 per 100 000 women^[2].

Axillary node metastasis is the most important predictor for breast cancer patients^[3-5]. Incidence of axillary node metastasis is 35%^[6]. Breast cancer patients with axillary node metastasis have 10-year overall survival rate of 25%^[3-5]. The

treatment is based on primary breast cancer excision and axillary node dissection. Axillary node dissection results in more complications such as wound infections, axillary seromas, paresthesias and lymphedema than sentinel node dissection alone^[7]. However, conventional axillary node dissection is the standard procedure in breast cancer patients with axillary node metastases because of the limited indication of the sentinel node dissection.

Several studies have reported risk factors included location of the breast cancer associated with axillary node metastasis^[8,9]. There is no available study that directly determines correlation between mammographic findings of breast cancers and axillary node metastasis

Mammographic findings of breast cancer which is associated with axillary lymph node metastasis may be further used for alternative non-invasive procedure to predict the prognosis of the breast cancer patients.

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2. Materials and methods

2.1 Samples collection

The cases were collected retrospectively from histological/pathological records, hospital data system and PACS[Picture Archiving and Communication System] of female patients with breast cancers who underwent breast surgery and axillary node dissection at King Chulalongkorn Memorial Hospital during January 1, 2004 and July 31, 2011. The study has received approval by the Ethics Committee of the Faculty of Medicine, Chulalongkorn University.

2.2 Methods

First, 1800 cases of histopathologically proven invasive ductal carcinoma[IDC] were collected for this study. Five hundred patients were randomly selected. Then the patients were excluded by exclusion criteria as following: unavailable images in PACS, unavailable histological or pathological reports, bilateral lesions, multicentric lesions [>2 lesions arising in separate quadrants of the breast], coexisting cancer, recurrent breast cancer or recurrent axillary node metastasis, previous surgery, previous chemotherapy and previous radiation.

Nineteen patients with unavailable data on PACs, seven patients with bilateral lesions, fifteen patients with multicentric lesions, thirty patients with history of previous biopsy and nine patients with previous chemotherapy were excluded from this study.

Then, included patients were categorized in two groups for patients with pathological approved axillary node metastasis and patients without axillary node metastasis.

Finally, one hundred and ninety patients were randomly recruited in this study; consisting of ninety-five patients with axillary lymph node metastasis and ninety-five patients without axillary lymph node metastasis as a control group.

Demographic data of all included patients were collected for age.

Mammography was used for evaluation of tumor characteristics according to ACR BI-RADS[American College of Radiology Breast Imaging Reporting and Data System] classification^[10], including location and intralesional microcalcification; and axillary lymph node characteristics including size and axillary node patterns (benign, intermediate and malignant patterns).

Size and vascularity of the breast cancers were assessed via an additional ultrasound.

Size of primary cancers and axillary nodes are defined by using the maximum diameter.

Tumor locations were recorded in quadrants which were defined as upper inner quadrant[UI], lower inner quadrant[LI], upper outer quadrant[UO] and lower outer quadrant[LO]. Central zone was used for lesion at subareolar region. If the tumor was located between two different quadrants, the quadrant was defined as the quadrant that the tumor mainly

involves.

For multifocal lesions [>2 lesions in one quadrant], characteristic assessment was performed in the largest tumor. Benign axillary node pattern was defined with presentation of preserved bean shape and preserved fatty hilum^[11].

Malignant axillary node pattern were defined as homogeneously dense, loss of bean shape, loss of fatty hilum, ill-defined or spiculated margin and intranodal microcalcification^[11].

The rest of axillary nodes which were not categorized in both benign and malignant group, were defined as intermediate pattern.

Mammographic and ultrasonographic characteristics were analyzed by a radiologist who specializes in breast imaging.

2.3 Statistical analysis

Data were analyzed with commercially available software [SPSS for windows version 17].

Axillary lymph node involvement was analyzed to find correlation with demographic data[age]; primary tumor characteristics, including location, size, vascularity and microcalcification; axillary node characteristic including size and axillary node patterns. Correlation between axillary lymph node involvement and each factors of mammographic characterization with additional ultrasonography was interpreted via binary logistic regression analysis, using *P*-value, Odds ratio [*OR*] and 95% confidence interval[*CI*].

Independent *T*-test analysis was performed for comparison of mean age and mean imaging-surgical duration between control group and axillary node metastasis group.

The level of statistical significance was set to *P*-value less than 0.05.

3. Results

The included one hundred and ninety IDC lesions from one hundred and ninety patients were diagnosed by mammograms and additional ultrasounds.

There were ninety-five lesions presented without axillary node metastasis and the rest of ninety-five lesions demonstrated with ipsilateral axillary node metastasis.

The mean ages of patients were (53.21±9.98) year olds in control group and (53.24±10.36) year olds in nodal metastasis group. There was no statistic significant between mean ages of control group and nodal metastasis group [*P* = 0.96].

The means of duration between diagnostic imaging performance and surgery were (41.20±30.61) d in control group and (37.64±3.86) d in nodal metastasis group.

There was a high association with statistically significant risk of ipsilateral axillary node metastasis in intermediate and malignant features of axillary nodes (Table 1).

The relation of axillary node metastasis with tumor locations is shown in Table 2. The rest of each quadrant as compared to the rest quadrants was not statistically significant associated

with ipsilateral axillary node metastasis (Table 2).

Table 1

Axillary node metastasis in relation to nodal patterns.

Nodal patterns	Lymph node negative cases	Lymph node metastasis cases	P-value	Odds ratio*	95% CI
Benign	82	26	<0.001	1.00	–
Intermediate	7	15	0.002	5.18	1.79–15.04
Malignant	4	52	<0.001	44.53	13.10–151.37
Missing cases ¹	2	2	–	–	–

1–Lymph node cannot be identified.

*–Adjusted for image–surgical interval, microcalcification of tumor, vascularity of tumor and size of axillary node.

Table 2

Axillary node metastasis in relation to tumor locations.

Locations: Quadrants	Lymph node negative cases	Lymph node metastasis cases	P-value	Odds ratio*	95% CI
UI	31 (16.3%)	19 (10.0%)	0.48	1.00	–
LI	15 (7.9%)	5 (2.6%)	0.33	0.44	0.81–2.34
UO	35 (18.4%)	54 (56.8%)	0.02	3.36	1.23–9.14
LO	8 (4.2%)	8 (4.2%)	0.50	1.71	0.37–7.99
C	6 (3.2%)	9 (4.7%)	0.31	2.23	0.47–11.12

*Adjust for imaging–surgery time interval, intralesional microcalcification, tumor vascularity and size of axillary lymph node.

Sizes of breast cancer were associated with a statistically significant risk of ipsilateral axillary node metastasis [$P = 0.04$; $OR = 1.48$; $95\% \text{ CI} = 1.02 - 2.17$]. Size of breast cancer with axillary node metastasis are range from 0.7 cm to 6.7 cm (2.91 ± 1.26), while size of the control group are 0.5 cm to 5.7 cm (2.08 ± 1.05) (Table 3).

This study shows no association of other mammographic findings (including microcalcification of the tumor, vascularity of the tumor and size of axillary node) with risk for axillary node involvement (Table 4–6).

Table 3

Axillary node metastasis in relation to tumor size (cm).

Tumor size ¹ (cm)		P-value	Odds ratio*	95% CI		
Lymph node negative cases	Lymph node metastasis cases					
0.5 – 5.7	(2.08±1.05)	0.7 – 6.7	(2.91±1.26)	0.04	1.48	1.02–2.17

1– Longest diameter measured by additional ultrasonography.

*–Adjusted for image–surgical interval, microcalcification of tumor, vascularity of tumor and size of axillary node.

Table 4

Axillary node metastasis in relation to microcalcifications.

Microcalcifications	Lymph node negative cases	Lymph node metastasis cases	P-value
None	36	13	0.31
Punctate	5	6	0.70
Amorphous	21	28	0.90
Coarse heterogeneous	1	1	0.98
Linear	6	9	0.40
Pleomorphic	26	38	0.40

Table 5

Axillary node metastasis in relation to tumor vascularity.

Tumor vascularity ¹	Lymph node negative cases	Lymph node metastasis cases	P-value
None	36	13	0.31
Internal	26	38	0.40
Peripheral	21	28	0.90

¹ Evaluated by additional ultrasonography.

Table 6

Axillary node metastasis in relation to axillary node size (cm).

Axillary node size ¹ (cm)		P-value		
Lymph node negative cases	Lymph node metastasis cases			
0.5 – 3.9	(1.77±0.65)	0.6 – 5.3	(2.12±1.08)	0.30

¹ Longest diameter measured by mammogram.

24 Missing cases: Lymph node cannot be identified in 2 cases of negative lymph nodes and 2 cases of lymph node metastasis.

4. Discussion

In our study, the mammographic characteristic with the highest risk of ipsilateral axillary node metastasis was malignant pattern of ipsilateral axillary node [$P < 0.001$; $OR = 44.53$; $95\% \text{ CI} = 13.10 - 151.37$]. The moderate risk of was intermediate pattern of ipsilateral axillary node [$P = 0.002$; $OR = 5.18$; $95\% \text{ CI} = 1.79 - 15.04$].

The lower risks associated with axillary node metastasis were breast cancer in upper outer quadrant [$P = 0.02$, $OR = 3.36$, $95\% \text{ CI} = 1.23 - 9.14$] and increased size of breast cancer [$P = 0.04$, $OR = 1.48$, $95\% \text{ CI} = 1.02 - 2.17$].

Several previous studies show that outer quadrant tumors are associated with axillary node involvement [8,12,13–20]. There are reliable factors for increased risk of axillary node metastasis in upper outer quadrant tumors. Lymphatic drainage pathway plays a major role for axillary node metastasis. Estourgie SH, *et al.* found that majority (95.8%) of breast parenchyma in upper outer quadrant was drained to ipsilateral axillary region [21–26]. The shortest distance from upper outer quadrant to axilla than other quadrants seem to be another supportive reason for axillary node involvement.

However, there are some limitations of this study. Firstly, a small sample size was included in this study. Secondly, there was no comparison between other pathologic lymph nodes such as infection or inflammatory lymph nodes. Thirdly, there was no direct evidence to prove concordance between each axillary nodes seen in mammograms and pathologically proven axillary nodes.

The highest predictive risk of axillary node metastasis in breast cancer was malignant axillary node pattern. The moderate risk was intermediate axillary node pattern and the lower risks were the tumors located in upper outer quadrant and increased tumor size.

These results will be helpful for diagnostic mammogram to imply prognosis of breast cancer before patient undergo biopsy or surgical procedure. Further study with a larger sample size

will provide more accurate results.

Conflict of interest statement

We declare that we have no conflict of interest.

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