Original article

Bilateral breast cancer: the role of mammography and ultrasonography in early detection

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Abstract

Purpose To determine the role of mammography and ultrasonography (US) in the early detection of bilateral breast cancer and ascertain its clinical, imaging, and pathologic features.

Materials and methods The pathologic and breast imaging records were searched from Maharaj Nakorn Chiang Mai Hospital between January 2009 and December 2011 to identify patients diagnosed with bilateral breast cancer. The clinical features, method of diagnosis, time interval between development of the first and second breast cancer, histologic type, staging of the tumor, mammography, and US findings of patients diagnosed bilateral breast cancer were analyzed.

Results Seven hundred and seventy one patients were pathologically diagnosed breast cancer. Of these, 20 (2.6%) had bilateral breast carcinoma. However, only 19 patients aged 35-76 years (mean, 56.6 years) had imaging studies that constituted the basis of this study. Among them, seven had synchronous and 12 metachronous bilateral breast cancer. The interval to detection of the second cancer ranged from 17 to 324 months (mean, 111.7 months). Of the seven patients with synchronous cancer, five contralateral cancers were presented with a palpable mass detected from physical examination, mammography and US, with one cancer detected by both mammography and US, and the other by US alone. Of the 12 patients with metachronous carcinoma, one had pathologically proved multicentric contralateral breast cancer. Thus, there were 13 contralateral cancers in this group. Of the 12 patients with metachronous cancer, six presented with a palpable mass and six came to the hospital for mammographic screening. Six of the 13 cases of contralateral cancers were detected by physical examination, mammography and US, six by both mammography and US, and one by US alone. Pathologic findings of the lesions were ductal carcinoma in situ in 4, invasive ductal carcinoma in 14, invasive papillary carcinoma in 1 and invasive lobular carcinoma in 1. Stages of tumors in asymptomatic patients were stage 0 in 3, stage I in 4 and stage III in 1, and in patients with a palpable mass; stage I in 4, stage II in 4 and stage III in 3.

Conclusion Contralateral breast cancers in bilateral breast cancer detected by mammography and US were less advanced than those found by physical examination. **Chiang Mai Medical Journal 2012;51(4):103-110.**

Keywords: bilateral breast cancer, diagnosis, mammography, ultrasonography

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Introduction

Patients with a history of breast carcinoma are at increased risk of developing cancer in the contralateral breast. The second cancer can be either synchronous, i.e., developing within one year of initial diagnosis, or metachronous, with the second cancer developing more than one year after the first [1-3]. The risk of developing a second contralateral cancer is 2-6 times higher than developing an initial breast cancer for women in the general population [3,4]. Several factors for the increased risk of developing contralateral breast cancer have been suggested such as young age at the diagnosis of initial cancer, long survival from the time of the first breast cancer, familial history of breast cancer, multifocality, multicentricity, lobular carcinoma in situ and invasive lobular carcinoma [3,5,6]. The prognosis for women with bilateral breast carcinoma depends on the stages at detection of both the first and second cancers. Screening mammography has been used to detect early breast carcinoma, which led to a 20-25% reduction in breast cancer mortality in women aged 50-74 years [7,8]. Careful evaluation of both breasts is crucial for early detection. Bilateral mammograms should be performed in patients found to have unilateral breast carcinoma in order to search for a nonpalpable contralateral carcinoma and establish a baseline for follow-up study of the other breast [2,9,10]. However, the sensitivity of mammography in detecting breast cancer is lower in dense breast and adjunctive studies such as ultrasonography (US) and magnetic resonance imaging (MRI) were introduced to improve sensitivity in breast cancer diagnosis [11-15]. The purpose of this study was to determine the role of mammography and US in the early detection of bilateral breast cancer and ascertain clinical, imaging, and pathologic features of bilateral breast cancer.

Materials and methods

This study was approved by the Institutional Review Board and informed consent was waived. The pathological and breast imaging records from Maharaj Nakorn Chiang Mai Hospital between January 2009 and December 2011 were reviewed retrospectively. Clinical records included age at diagnosis of the first and second primary breast carcinomas, clinical presentation, time interval between development of the first and second carcinomas, histologic type, method of diagnosis and staging of the tumor. Bilateral breast cancer was classified as synchronous if the second tumor was detected within one year of the initial cancer, and metachronous if found more than one year after the first carcinoma. The criteria for diagnosing the second primary tumor included: 1) no evidence of local recurrence or distant metastasis from the first primary breast cancer, and 2) different histologic type, grade of differentiation, or in situ change in the second tumor. In synchronous cancer, the first suspected tumor found either clinically or mammographically was designated as the initial cancer. The tumor found subsequently in the opposite breast was designated the contralateral cancer. Methods of detecting the contralateral cancer were recorded as physical examination alone, mammography alone, US alone, or a combination. Staging of contralateral breast cancers found in symptomatic patients were compared with that of cancers detected from screening mammography.

Mammography was performed using the Computed Radiography System (Siemens Mammomat 3000 Nova, Germany and Fuji Corporation, Tokyo, Japan) until May 2010, and the Senographe Essential Full-Field Digital Mammography System (GE Healthcare) from June 2010 until the present. Two standard views (mediolateral oblique and craniocaudal) were obtained, with additional ones acquired as needed. US was performed using a 12 MHz linear array transducer (Toshiba Aplio XG, Japan). Mammographic images were reviewed by one senior breast radiologist, who had knowledge of the pathologic report to determine the presence of mass, microcalcifications, architectural distortion, asymmetrical density, axillary adenopathy, and skin and nipple change. US images were assessed for the presence of mass, shape, margin, echo pattern and calcifications. The mammographic and US findings were determined according to the American College of Radiology Breast Imaging Reporting and Data System (BI-RADS) lexicon [16].

Results

Seven hundred and seventy one patients were pathologically diagnosed breast carcinoma during a 3-year period, and 20 of those had bilateral breast carcinoma, which accounted for 2.6% of all breast carcinomas. Of the 20 bilateral breast cancer patients, 19 had complete clinical and imaging studies that constituted the basis of this study. They were all women, aged 35-76

years (mean, 56.6 years). Seven of them (7/19 = 36.8%, 7/771 = 0.9%) had synchronous bilateral breast cancer (mean age, 55.9 years) and 12 (12/19 = 63.2%, 12/771 = 1.6%) metachronous bilateral breast cancer (mean age at the first and second cancer, 46.5 and 57 years, respectively). The interval to detection of the second cancer ranged from 17 to 324 months (mean, 111.7 months). Of the seven patients with synchronous cancer, five contralateral cancers were presented with a palpable mass detected from physical examination, mammography and US, with one cancer detected by both mammography and US (Figure1), and the other by US alone (Figure 2). Of the 12 patients with metachronous carcinoma, one had pathologically proved multicentric contralateral breast cancer. Thus, there were 13 contralateral cancers in this group. Of the 12 patients with metachronous cancer, six presented with a palpable mass and six came to the hospital for mammographic screening. Six of the 13 contralateral cancers were detected by physical examination, mammography and US, six were detected by both mammography and US, and one was detected by US alone (Figure 3). Overall, results of US were truly positive in all 20 cancers (100%), mammography in 18 of 20 cancers (90%), and false negatives occurred in two of 20 cancers (10%). Mammographic findings of the two patients with a negative mammogram revealed heterogeneous dense breast. The histologic subtypes of the 20 contralateral cancers (7=synchronous, 13= metachronous) were ductal carcinoma in situ (DCIS) in four, invasive ductal carcinoma in 14, invasive papillary carcinoma in one and invasive lobular carcinoma in one. The method for detecting the contralateral cancers was compared with the pathologic stages in Table 1. The mammographic and US findings of all 20 contralateral cancers are summarized in Table 2 and 3.

Discussion

The overall incidence of bilateral breast cancer reportedly varies in the range from 1.4% to 12%, depending on the definition [3,12]. This study found that 2.6% of all breast carcinomas at Maharaj Nakorn Chiang Mai Hospital were bilateral breast cancer. The incidence of bilateral synchronous and bilateral metachronous breast

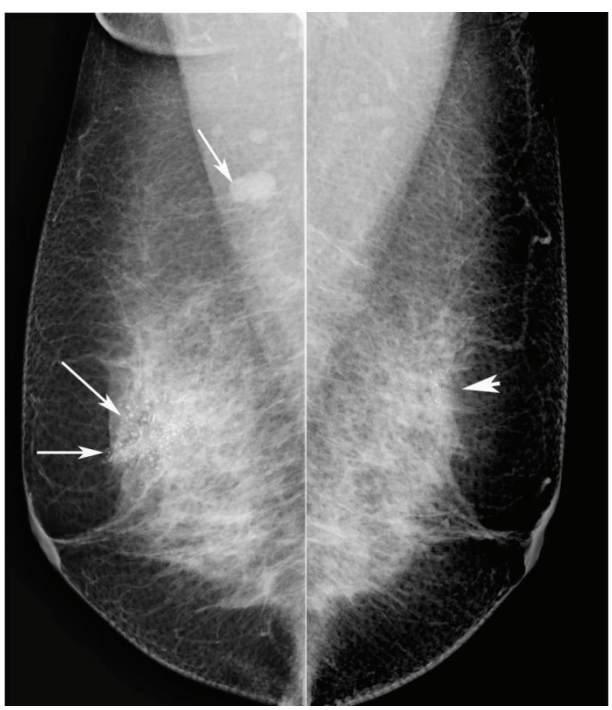

Figure 1. A 52-year-old woman presenting a right breast mass. Bilateral mediolateral oblique mammograms show a regional distribution of pleomorphic microcalcifications in the right upper breast (double white arrows), and an increased density of right axillary node with loss of fatty hilum (single white arrow). Another cluster of pleomorphic microcalcifications is shown in the left upper breast (arrowhead). US of the right and left upper breasts (not shown) revealed ill-defined hypoechoic masses with microcalcifications. A biopsy was performed under US guidance on both sides, with invasive ductal carcinoma showing on the right side and ductal carcinoma in situ on the left.

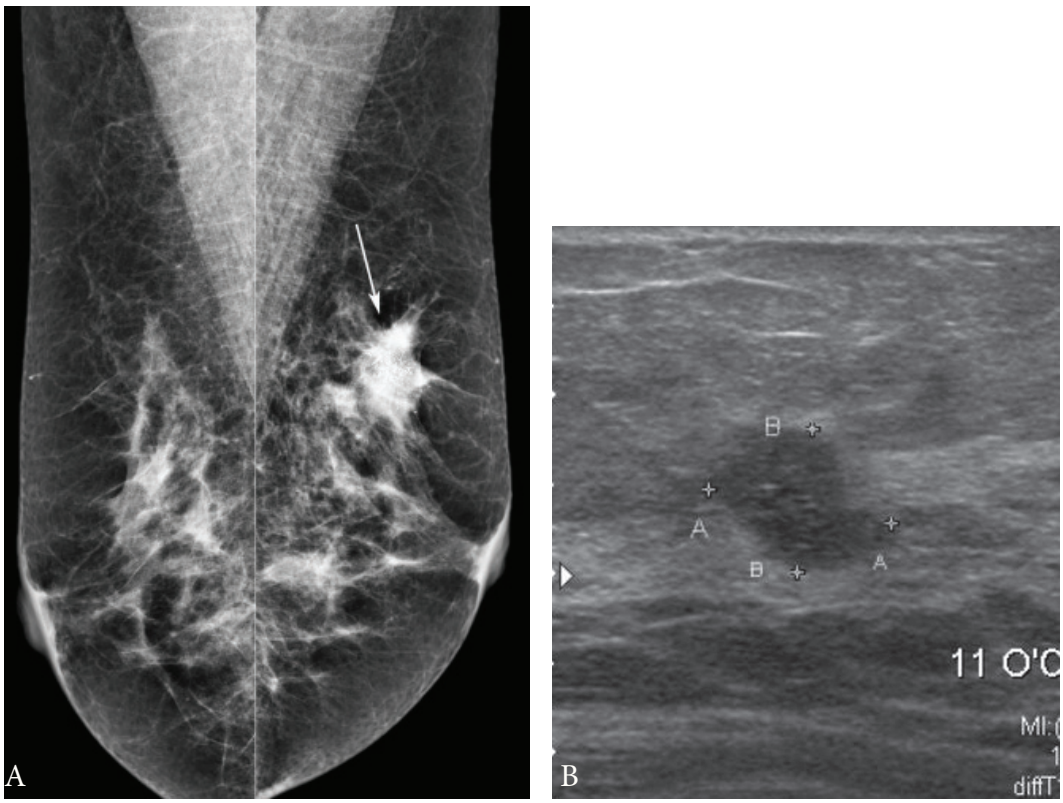

Figure. 2 A 54-year-old woman presenting a palpable mass in the left breast. (A) Bilateral mediolateral oblique mammograms showing heterogeneous dense breast and a hyperdense irregular mass with internal pleomorphic microcalcifications at the left upper outer quadrant (arrow). No abnormality is detected in the right breast, but (B) US of the right breast shows a 0.8x1.0 cm lobulated hypoechoic mass with faint microcalcifications at 11 O'clock. Pathology revealed invasive ductal carcinoma in both breasts.

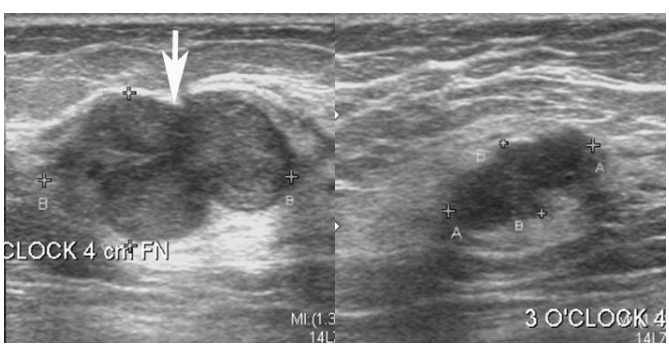

Figure 3. A 72-year-old woman with a history of right mastectomy for breast cancer 2 years previously, presenting a palpable left breast mass. Left craniocaudal mammogram showing a heterogeneous dense breast, with an ill-defined mass at its center (not shown). Composite US images show a lobulated hypoechoic mass at 12 o'clock (arrow), corresponding to the palpable mass and a mass seen on the mammogram. Another ill-defined hypoechoic mass (cursors) is also detected at 3 o'clock. This mass is mammographically and clinically occult. Pathology revealed invasive papillary carcinoma for the palpable mass and ductal carcinoma in situ for the clinical occult one.

Table 1. AJCC stages of 19 cancers in 19 patients

Stage	*Contralateral cancer [n=19]		
	US alone [n=1]	US&MG [n=7]	US&MG&PE [n=11]
Stage 0a	-	3	-
Stage I	1	3	4
Stage II	-	-	4
Stage III	-	1	3

Note: AJCC = American Joint Committee for Cancer, 0a Ductal carcinoma in situ, US = ultrasonography, MG = mammography, PE = physical examination
*All 20 contralateral cancers had 19 tumor stages. In the case of two tumors, T (tumor size) was defined as the size of the largest tumor [17].

cancer varies between 1% and 3%, and 5% and 7%, respectively [3,5,6,9]. In this study, 0.9% and 1.6% were synchronous and metachronous carcinoma, respectively. Of all bilateral breast cancers, the incidence of synchronous cancer is expected to increase, due to improvement in detection by multi-imaging modalities [2,9,11, 12,14,15]. Before the widespread use of mammography, 15% of bilateral breast cancer was found to be synchronous [18]. However, with more use of mammography, the percentage of patients found to have synchronous cancer increased to 43% [2]. This may be due to the improvement in mammographic techniques, which allow earlier detection of a contralateral tumor.

Table 2. Summarized mammographic findings and BI-RADS categorization in 20 contralateral cancers

Characteristics	n
BI-RADS assessment category	
BI-RADS 4	6
BI-RADS 5	14
Mammographic findings	
Mass	9
Microcalcifications alone	4
Mass with microcalcifications	2
Distortion	3
Other (skin thickening, coarse trabeculation, nipple retraction)	4
Dense axillary node	4
No abnormalities	2

This study found 36.8% and 63.2% of synchronous and metachronous bilateral carcinoma, respectively.

Advanced imaging technology has allowed early detection of both first and second cancers. Results in this study suggest that contralateral breast cancers diagnosed by mammography were less advanced than those detected from physical examination, which is similar to previous reports [2,9,10]. However, this study did not compare between the stage of the first and second tumors because some patients were diagnosed for the first breast cancer in other hospitals. Mammography remains the most sensitive imaging modality for early detection of breast cancer. Ductal carcinoma in situ (DCIS) accounts for 25-56% of all cancers found by screening mammography, as most DCIS is detected due to the presence of microcalcifications [19,20]. Since the sensitivity of mammography is lower in women with dense breast, US and MRI were introduced to improve detection of early cancer in patients

Table 3. Summarized ultrasonographic findings of 20 contralateral cancers

Findings	n=20 (%)
Mass	19 (95)
Round or oval shape	1 (5)
Lobular or irregular shape	18 (90)
Microlobulated margin	9 (45)
Indistinct margin	10 (60)
Parallel	13 (65)
Not parallel	6 (30)
Low internal echo	20 (100)
Presence of acoustic shadow	5 (25)
Absence of acoustic shadow	15 (75)
Calcifications	5 (25)
Axillary lymphadenopathy	4 (20)

with this condition. In 1995, Roubidoux et al. reported that 65% of contralateral cancers were detected from mammography alone [2]. In this study, nine out of 20 contralateral cancers were asymptomatic and detected from imaging studies. Of these nine, seven were detected from both mammography and US, and two from US alone. The two cancers not visualized from mammography were non-calcified masses in dense breasts. US is a useful adjunctive imaging modality to mammography in the detection of early breast cancer in women with dense breast, and is used as a guide for percutaneous biopsy [21,22]. Although US is less sensitive than mammography in detecting microcalcifications, given their known mammographic location, it still can depict lesions [23,24]. Two out of nine cancers in this study had microcalcifications detected by mammography alone. Additional US was performed with a known mammographic location as a guide for biopsy, because a US-guided biopsy is faster and less expensive than mammographic guidance [25]. Without mammography, microcalcification alone is difficult to visualize with US. Therefore, mammography undoubtedly plays an important role in the early detection of breast cancer.

During the last decade, MRI has shown the ability to detect clinically and mammographically occult contralateral carcinoma in 3-24% of women with a history of breast carcinoma [14,15,26,27]. MRI should be performed to evaluate patients with newly diagnosed breast cancer and detect occult contralateral carcinoma. However, this method has some practical limitations including high cost and difficulty to biopsy the lesions depicted only at MRI. This study did not perform many MRIs on breasts because of high costs and a long waiting list.

The interval between detection of the first and second cancer also affects the prognosis for patients. Patients who develop contralateral breast cancer more than five years after diagnosis of the first carcinoma have a longer survival rate than those who develop the second cancer in less than 5 years [3,5]. In this study, the time interval between detection of the first and second cancer ranged from 17 to 324 months. However, survival rate of the patients was not analyzed.

The histologic type of cancer in two breasts was similar in most studies [9,28]. This study analyzed only the histologic type of the contralateral tumor. As mentioned earlier, some patients had their first breast cancer diagnosed at other hospitals, so the histologic type between first and second tumors was not compared. The most common type of contralateral cancers in this study (14/20) was invasive ductal carcinoma, followed by DCIS, invasive papillary carcinoma, and invasive lobular carcinoma.

In conclusion, this study and other previous reports found that contralateral breast cancers in bilateral breast cancer, detected by mammography and US, were less advanced than those found by physical examination. This finding suggested the need for careful screening of patients with bilateral breast cancer in order to detect early contralateral breast carcinoma.

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บทบาทของแมมโมแกรม และอัลตราซาวด์ในการตรวจพบมะเร็งเต้านมระยะเริ่มต้นที่เป็นสองข้าง

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วัตถุประสงค์ เพื่อศึกษาบทบาทของแมมโมแกรมและอัลตราซาวด์ในการตรวจพบมะเร็งเต้านมระยะเริ่มต้นที่เป็นสองข้าง และศึกษาลักษณะทางคลินิก ภาพวินิจฉัยของเต้านมทางรังสีและพยาธิวิทยาของมะเร็งเต้านมที่เป็นสองข้าง

วิธีการวิจัย เป็นการศึกษาย้อนหลังโดยสืบค้นผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็นมะเร็งเต้านมสองข้างจากผลพยาธิวิทยาและภาพวินิจฉัยของเต้านมตั้งแต่มกราคม 2552 ถึงธันวาคม 2554 ข้อมูลที่วิเคราะห์ประกอบด้วยอาการทางคลินิก วิธีการวินิจฉัย ช่วงเวลาระหว่างที่เกิดมะเร็งเต้านมข้างที่ 1 และข้างที่ 2 ชนิดของพยาธิวิทยาของมะเร็ง ระยะของโรค ลักษณะภาพแมมโมแกรมและอัลตราซาวด์

ผลการศึกษา ผู้ป่วย 771 ราย ได้รับการวินิจฉัยว่าเป็นมะเร็งเต้านมและมี 20 ราย ที่เป็นมะเร็งเต้านมสองข้าง คิดเป็นร้อยละ 2.6 แต่ 1 ใน 20 ราย ไม่มีภาพวินิจฉัยเต้านม ดังนั้นการศึกษานี้จึงมีทั้งหมด 19 ราย ผู้ป่วยทั้ง 19 ราย เป็นผู้หญิงอายุเฉลี่ย 56.6 ปี จำนวน 7 ใน 19 ราย เป็นมะเร็งเต้านมสองข้างพร้อมกันภายใน 1 ปี และ 12 ราย เป็นมะเร็งเต้านมอีกข้างหนึ่งในเวลามากกว่า 1 ปี ระยะเวลาที่เกิดมะเร็งเต้านมข้างที่หนึ่งและสองอยู่ระหว่าง 17-324 เดือน (เฉลี่ย 111.7 เดือน) มะเร็งเต้านมด้านตรงข้ามของ 5 ใน 7 ราย ของผู้ป่วยที่เป็นมะเร็งเต้านมสองข้างพร้อมกัน มาด้วยคลำก้อนได้ที่เต้านมและตรวจพบจากการตรวจร่างกาย แมมโมแกรมและอัลตราซาวด์ อีก 1 มะเร็งตรวจพบได้จากแมมโมแกรมและอัลตราซาวด์ แต่อีก 1 มะเร็งตรวจพบจากอัลตราซาวด์อย่างเดียว สำหรับผู้ป่วยอีก 12 รายที่เป็นมะเร็งสองข้างไม่พร้อมกัน พบมะเร็งด้านตรงข้าม 13 ก้อน ซึ่ง 6 ก้อน ตรวจพบจากการตรวจร่างกายแมมโมแกรมและอัลตราซาวด์ 6 ก้อน พบจากแมมโมแกรมและอัลตราซาวด์อีก 1 ก้อน พบจากอัลตราซาวด์อย่างเดียว ผลทางพยาธิสภาพพบว่าเป็นมะเร็ง ductal carcinoma in situ 4 ก้อน invasive ducal carcinoma 14, invasive papillary carcinoma 1 และ invasive lobular carcinoma 1 ในผู้ป่วยกลุ่มที่ไม่มีอาการเป็นมะเร็งระยะ 0 จำนวน 3 ราย ระยะที่ 1 จำนวน 4 ราย ระยะที่ 3 จำนวน 1 ราย ในกลุ่มที่คลำได้ก้อนเป็นมะเร็งระยะที่ 1 จำนวน 4 ราย ระยะที่ 2 จำนวน 4 ราย และระยะที่ 3 จำนวน 3 ราย

ผลการศึกษา ในผู้ป่วยที่เป็นมะเร็งเต้านมสองข้าง ระยะของโรคของมะเร็งในข้างตรงข้ามซึ่งตรวจพบโดยแมมโมแกรมและอัลตราซาวด์ จะเป็นระยะที่ร้ายแรงน้อยกว่ามะเร็งที่ตรวจพบจากการตรวจร่างกาย **เชียงใหม่เวชสาร 2555;51(4):103-110.**

คำสำคัญ: bilateral breast cancer, diagnosis, mammography, ultrasonography