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Does Breast Magnetic Resonance Imaging Combined With Conventional Imaging Modalities Decrease the Rates of Surgical Margin Involvement and Reoperation?

A Case–Control Comparative Analysis

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Abstract: The objective of this study was to assess whether preoperative breast magnetic resonance imaging (MRI) combined with conventional breast imaging techniques decreases the rates of margin involvement and reexcision.

Data on patients who underwent surgery for primary operable breast cancer were obtained from the Changhua Christian Hospital (CCH) breast cancer database. The rate of surgical margin involvement and the rate of reoperation were compared between patients who underwent conventional breast imaging modalities (Group A: mammography and sonography) and those who received breast MRI in addition to conventional imaging (Group B: mammography, sonography, and MRI).

A total of 1468 patients were enrolled in this study. Among the 733 patients in Group A, 377 (51.4%) received breast-conserving surgery (BCS) and 356 (48.6%) received mastectomy. Among the 735 patients in Group B, 348 (47.3%) received BCS and 387 (52.7%) received mastectomy. There were no significant differences in operative method between patients who received conventional imaging alone and those that received MRI and conventional imaging ($P = 0.13$). The rate of detection of pathological multifocal/multicentric breast cancer was markedly higher in patients who received preoperative MRI than in those who underwent conventional imaging alone (14.3% vs 8.6%, $P < 0.01$). The overall rate of surgical margin involvement was significantly lower in patients who received MRI (5.0%) than in those who received conventional imaging alone (9.0%) ($P < 0.01$). However, a significant reduction in rate of surgical margin positivity was only observed in patients who received BCS (Group A, 14.6%; Group B, 6.6%, $P < 0.01$). The overall BCS reoperation rates were 11.7% in the conventional imaging group and 3.2% in the combined MRI group ($P < 0.01$). There were no significant differences in rate of residual cancer in specimens obtained during reoperation between the 2 preoperative imaging groups (Group A, 50%; Group B, 81.8%, $P = 0.09$). In multivariate analysis, multifocal/multicentric breast cancer (odds ratio = 2.38, $P = 0.02$) and without MRI use (odds ratio = 2.35, $P < 0.01$) were the major predisposing factors to margin involvement in patients received BCS.

Preoperative breast MRI combined with conventional breast imaging results in a lower rate of surgical margin involvement and reoperations in patients who receive BCS.

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Abbreviations: ADC = apparent diffusion coefficient, BCS = breast-conserving surgery, BI-RADS = Breast Image Reporting and Data System, CAD = computer aid diagnosis, CC = craniocaudal, CCH = Changhua Christian Hospital, ER = estrogen receptor, HER-2 = human epidermal growth factor receptor-2, IRB = Institutional Review Board, MLO = mediolateral oblique, MRI = magnetic resonance imaging, PR = progesterone receptor, SD = standard deviation, VIBE = volumetric interpolated breath-hold examination.

INTRODUCTION

Breast cancer treatment involves multidisciplinary and multimodality management, and surgery remains the mainstay of treatment for early stage breast cancer.[1,2] The goal of surgical resection is to remove the tumor with adequate safe margins.[3,4] A number of studies have shown that positive margins are associated with higher rates of local recurrence after BCS (lumpectomy with adjuvant radiotherapy),[5–7] thereby mandating reoperation.[8,9] A number of ways to optimize margin clearance have been proposed, including intraoperative surgical techniques, such as radioguided surgery and ultrasound-guided

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Synopsis: In our case–control study, we found that preoperative breast magnetic resonance imaging (MRI) combined with conventional breast imaging detected more multifocal/multicentric breast cancer, and resulted in a lower rate of surgical margin involvement in patients who underwent breast-conserving surgery (BCS). Breast MRI was also associated with a higher rate of breast reconstruction in patients who underwent mastectomy and a lower rate of reoperation in patients with margin involvement who underwent BCS. MR images obtained preoperatively, however, were not sufficient for predicting residual cancer after excision.
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resection, intraoperative pathology assessment techniques, and preoperative imaging.[10]

Accurate preoperative assessment of tumor location and extension is important for adequate surgical planning.[11] MRI is increasingly being used in the preoperative evaluation of breast cancer[12–15] and has been reported to have value in estimating tumor size,[11,16] high sensitivity for detecting ipsilateral and contralateral occult breast lesions,[13–15,17] and therefore could be complementary to conventional breast imaging modalities such as mammography and sonography.

Some studies have demonstrated that the high sensitivity of MRI for detecting cancer aids in the selection of patients for BCS[18–20] and increases the likelihood of obtaining negative margins during the first lumpectomy attempt,[21,22] reduce reexcision rates,[22–24] decreasing the rate of ipsilateral tumor recurrence,[25] and the development of new breast cancer on the contralateral side.[25] However, other studies have shown that breast MRI is not associated with improved margin status[12,24,26–28] or a reduction in reoperation,[26–30] but instead is associated with treatment delay[12] and an increased rate of mastectomy.[12,25,27–30]

In this case–control comparative analysis, we evaluated whether combining breast MRI with conventional imaging techniques results in lower rates of margin involvement and reexcision. We compared the surgical methods and margin status between patients who underwent conventional preoperative imaging and those who received conventional imaging combined with MRI group. We also evaluated whether preoperative breast MRI can predict residual cancer requiring further surgery.

MATERIALS AND METHODS

All patients enrolled at this study had primary operable breast cancer, underwent preoperative mammography and sonography with or without MRI examination during January 2009 to December 2013, and received breast cancer surgery at the Changhua Christian Hospital (CCH), a tertiary medical center in central Taiwan. Patients whose primary tumor was removed before definite cancer operation, those who received neoadjuvant chemotherapy, and patients with incomplete data were excluded. The clinical and pathologic data were collected through chart review of medical, surgical, and pathologic records by a well-trained study nurse (SLC), and the accuracy was confirmed by the principle investigator (HWL). This study was approved by the Institutional Review Board (IRB) of the CCH (IRB number #140404).

In this case-controlled analysis, we retrospectively collected 2 groups of patients for evaluating the effect and value of adding preoperative breast MRI to conventional breast images (mammography and sonography). The proportion of patients at CCH received breast MRI increased dramatically since January of 2011 when our hospital started to cover the expense of breast MRI. To prevent the selection bias of patients who did not receive breast MRI, we decided to choose the control group of patients diagnosed and treated during 2009 to 2010. Because during January 2009 to December 2010, breast MRI was rarely performed, and this could prevent the possible selection bias. As after January 2011, when the breast MRI expanse covered program was started, patients selected for conventional breast images only or combined with MRI images might be biased according to physicians or patients' preference.

A total of 1468 patients fulfilled the inclusion criteria and were enrolled in this study. Patients were stratified into 2 preoperative imaging groups. Group A ($n = 733$) comprised patients who underwent conventional preoperative imaging (mammography and sonography) and Group B ($n = 735$) comprised patients who received MRI combined with conventional imaging. Figure 1 shows the flow chart of patients in the present study.

The type of operation (BCS, mastectomy or mastectomy with breast reconstruction), and the rate of surgical margin involvement were compared between the 2 groups of patients. To further evaluate the effect of preoperative breast MRI on the rate of margin positivity, index surgeons, defined as surgeons who had performed more than 100 breast cancer operations, were selected and analyzed. We also analyzed and compared the rate of reoperation among patients with positive margins and the rate of residual cancer detection after reoperation between the 2 image study groups.

To prevent bias from confounding factors, a propensity-score matching[31] was also perform to select 2 groups of patients for further analysis of factors related to margin involvement in primary operable breast cancer patients.

Definition of Surgical Margins

Tumor margins were assessed microscopically by surgical pathologists. All margins were inked before sectioning. Each specimen was serially sectioned at 3- to 5-mm intervals and then stained with hematoxylin and eosin. Pathologic analysis included the assessment of proximity to or the involvement of each margin for invasive carcinoma or carcinoma in situ. When available, the pathology report was examined for the actual margin. Surgical margin involvement in the present study was defined as the presence of cancer cells at the surgical margin or <1 mm from the peripheral margin. Specimen with surgical margins less than 1 mm from the superficial (away from skin flap) or deep (away from pectoralis major muscle) layer of the fascia, where the fibroglandular boundary of the skin and chest wall was located, were not regarded as margin involvement.

IMAGE STUDY

Mammography

The mammograms were performed by using 1 of 3 digital mammography systems, a Hologic Selenia Dimension full-field digital mammography system (Hologic, Danbury, CT), Siemens Mammomat Inspiration (Siemens AG, Healthcare Sector, Erlangen, Germany) and the GE Senographe Essential digital mammography system (General Electric Medical Systems, Milwaukee, WI). All women received the standard mediolateral oblique (MLO) and craniocaudal (CC) views. Three radiologists who specialize in breast imaging independently interpreted the mammograms using a 5 MP premium diagnostic grayscale display system (Coronis 5MP Mammo, Barco, Kortrijk, Belgium) on a Picture Archiving and Communication System without using the aid of clinical information, physical examination, or sonography results.

Sonography

The ultrasound sonography procedures were performed with the patient in the supine position. A high-resolution 5 to 12 MHz linear array transducer, including color Doppler ultrasonography (Voluson 530D and 730D, Kretz Technik, Zipf, Austria), was used for imaging acquisition. Recorded images were reported according to the Breast Image Reporting and Data

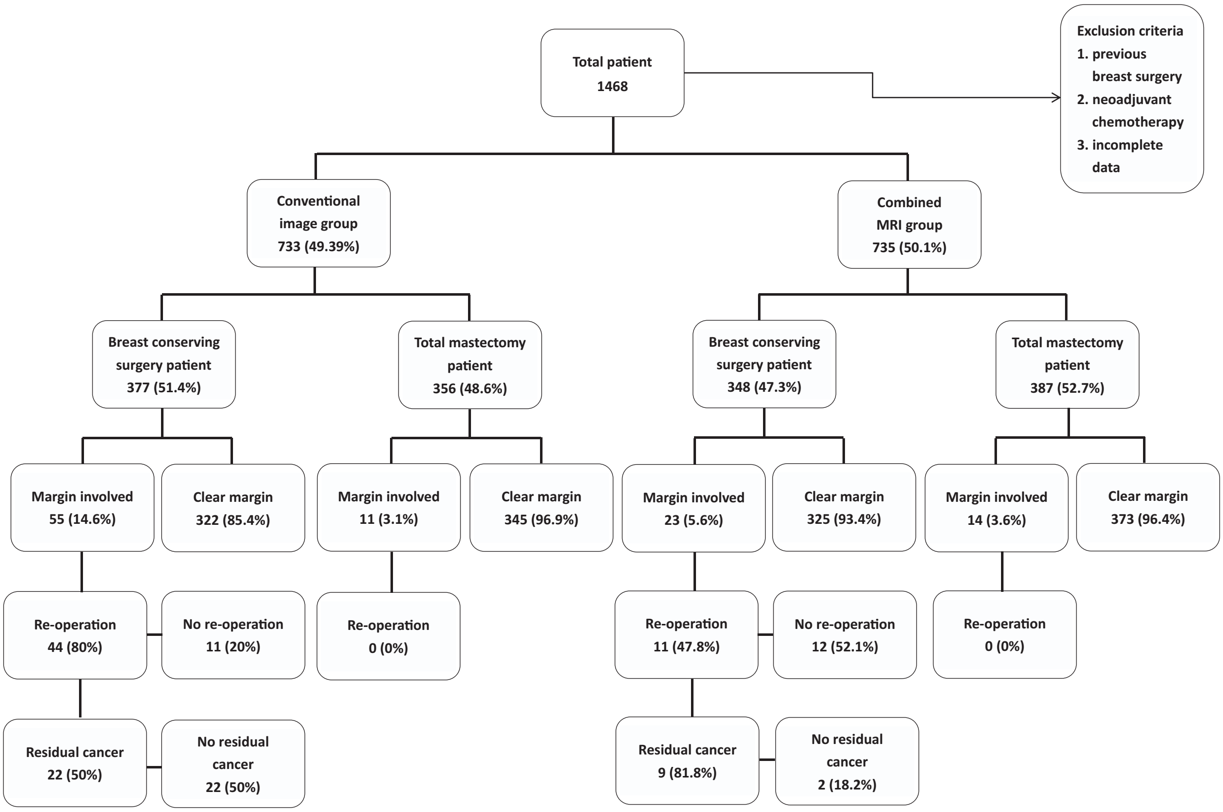

FIGURE 1. Flow chart of patients in the case-controlled comparative analysis.

System (BI-RADS).[32] The measurement of tumor size took the echo-poor center of the lesion and the echogenic halo into account. Experienced, board-certified breast physicians performed the whole sonographic examinations.

MRI

The MRI protocol is described in our previous study.[11] Briefly, a Siemens (Verio) 3.0 T magnet MR imaging was used. All patients were imaged with both breasts placed into a dedicated 16-channel breast coil in the prone position. Both breasts were examined with a 60-second interval between each dynamic phase image in the transverse plane. A commercially available MRI computer aid diagnosis (CAD) system (DynaCAD Version 2.1 for Breast MRI; Invivo, Gainesville, FL) was used to help analyzing MR images. Experienced, board-certified radiologist specializing in breast imaging (HKW) performed the whole breast MRI readings.

Statistical Analyses

Data are expressed as mean ± standard deviation (SD) for continuous variables. Differences in means of continuous measurements were tested by the Student *t* test. The Chi-square test was used for categorical comparisons of data. Univariate and multivariate analysis were used to find factors affecting margin involvement and to reduce the possible bias due to confounding variables. Propensity score matching analysis was performed with the package MatchIt in software R (version 3.2.2) to prevent bias from confounding factors. All tests were 2-tailed. A *P*-value of less than 0.05 was considered to indicate statistical significance. All statistical analyses were performed with the statistical package SPSS (IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp., Chicago) and accuracy of statistic results was confirmed by statistic expert (YJL).

RESULTS

There were no significant differences between patients who received conventional preoperative imaging alone (Group A, n = 733) and those who underwent preoperative MRI in addition to conventional imaging (Group B, n = 735) in age (52.2 ± 11.4 vs 52.7 ± 10.7, $P = 0.31$), tumor laterality, tumor size (2.2 ± 1.6 cm vs 2.3 ± 1.6 cm, $P = 0.17$), positive lymph node rate (33.0% vs 32.8%, $P = 0.96$), cancer stage, progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER-2) expression (Table 1).

Among the 733 patients in Group A, 377 (51.4%) received BCS and 356 (48.6%) received mastectomy. In Group B, 348 (47.3%) received BCS and 387 (52.7%) received mastectomy. There were no differences in surgical methods employed between the 2 groups of patients ($P = 0.13$, Table 2). However, the percentage of patients who underwent sentinel lymph node surgery and the percentage of patients who received breast reconstruction surgery were higher in Group B than in Group A ($P < 0.01$). The rate of detection of pathological multifocal/multicentric breast cancer was markedly higher in patients who received preoperative MRI than in those who underwent conventional imaging alone (14.3% vs 8.6%, $P < 0.01$, Table 2).

TABLE 1. Clinical Features of Patients of Current Case-Controlled Analysis

	Conventional Breast, Image Group, n = 733 (%)	Combined Breast, MRI Group, n = 735 (%)	*P*
Age, y	52.2 ± 11.4	52.7 ± 10.7	0.31
Location			
Right	363 (49.5)	341 (46.4)	0.23
Left	370 (50.5)	394 (53.6)	
Biopsy method			
CNB	566 (78.9)	634 (87.1)	<0.01
Stereotactic biopsy	61 (8.5)	83 (11.4)	
Excisional biopsy	82 (11.4)	5 (0.7)	
FNAC	8 (1.1)	6 (0.8)	
N/A	16	7	
Tumor size, cm	2.2 ± 1.6	2.3 ± 1.6	0.17
Lymph node			
Positive	242 (33.0)	241 (32.8)	0.96
Negative	491 (67.0)	494 (67.2)	
Stage			
0	123 (16.8)	117 (15.9)	0.29
I	221 (30.2)	240 (32.7)	
II	286 (39)	302 (41.1)	
III	99 (13.5)	73 (9.9)	
IV	4 (0.5)	3 (0.4)	
Grade			
I	128 (18.5)	118 (16.9)	<0.01
II	421 (60.8)	364 (52.0)	
III	144 (20.8)	218 (31.1)	
N/A	40	35	
ER			
Positive	538 (75.0)	576 (79.4)	<0.05
Negative	179 (25.0)	149 (20.6)	
N/A	16	10	
PR			
Positive	533 (74.3)	535 (73.8)	0.81
Negative	184 (25.7)	190 (26.2)	
N/A	16	10	
HER-2			
Positive	162 (23.2)	160 (22.9)	0.89
Negative	535 (76.8)	538 (77.1)	
N/A	36	37	

All data were presented as mean ± standard deviation (SD).
CNB = core needle biopsy, ER = estrogen receptor, FNAC = fine needle aspiration cytology, HER-2 = human epidermal growth factor receptor-2, N/A = not available, PR = progesterone receptor.

The overall rate of surgical margin involvement was significantly higher among patients who received conventional preoperative imaging alone (9%) than among those who combined with preoperative MRI (5%) ($P < 0.01$). There were no significant differences in rate of margin positivity between patients in Group A and those in Group B who received total mastectomy (3.1% vs 3.6%, $P = 0.84$) or breast reconstruction (4.9% vs 4.5%, $P > 0.99$). However, the rate of positive margin involvement was significantly lower in patients who received BCS and preoperative MRI than in those who received conventional imaging alone (6.6% vs 14.6%, $P < 0.01$, Table 2).

Two index surgeons (A and B), defined as surgeons who have performed more than 100 surgeries for breast cancer, were selected to evaluate whether breast MRI affected the surgeon's choice of operation and whether the imaging method was associated with margin positivity in resected specimens (Table 3). For surgeon A, there was no significant difference in number of BCS procedures performed between the conventional imaging group (158/316) and the MRI group (148/329) ($P = 0.21$). There were also no significant differences in overall rate of surgical margin involvement between the two groups (7.6% vs 4.9%, $P = 0.19$) and no significant differences in rates of margin involvement after total mastectomy (1.3% vs 2.2%, $P = 0.69$), or BCS (13.9% vs 8.1%, $P = 0.15$) between the 2 groups. For surgeon B, there was no significant difference in number of BCS procedures performed between the conventional imaging group (154/261) and the MRI group (127/216) ($P > 0.99$). There were also no significant differences in overall rate of surgical margin involvement between the 2 groups (9.2% vs 5.1%, $P = 0.11$) and no significant differences in rates of

TABLE 2. Operation Methods and Clinical Outcome According to Different Group of Image Survey

	Conventional Breast, Image Group, n = 733 (%)	Combined Breast, MRI Group, n = 735 (%)	*P*
Surgical treatment			
Mastectomy type			
Total mastectomy	356 (48.6)	387 (52.7)	0.13
BCS	377 (51.4)	348 (47.3)	
Lymph node surgery			
No surgery	72 (9.8)	16 (2.2)	<0.01
SLNB	282 (38.5)	426 (58.0)	
SLNB + ALND	177 (24.1)	159 (21.6)	
ALND	202 (27.6)	134 (18.2)	
Breast reconstruction			
Yes	61 (17.1)	154 (39.8)	<0.01
Pathology outcome			
Pathological multifocal			
Yes	63 (8.6)	105 (14.3)	<0.01
No	670 (91.4)	630 (85.6)	
Pathological nipple invasion			
Yes	47 (6.4)	61 (8.3)	0.19
No	686 (93.6)	674 (91.7)	
Pathology margin involvement			
Yes	66 (9.0)	37 (5.0)	<0.01
No	667 (91.0)	698 (95.0)	
Total mastectomy			
Margin involvement			
Yes	11 (3.1)	14 (3.6)	0.84
No	345 (96.9)	373 (96.4)	
BCS			
Margin involvement			
Yes	55 (14.6)	23 (6.6)	<0.01
No	322 (85.4)	325 (93.4)	
With breast reconstruction			
Margin involvement			
Yes	3 (4.9)	7 (4.5)	<0.99
No	58 (95.1)	147 (95.5)	

ALND = axillary lymph node dissection, BCS = breast-conserving surgery, SLNB = sentinel lymph node biopsy.

margin involvement after total mastectomy (6.2% (Group A) vs 6.7% (Group B), $P = 0.77$). However, the rate of margin positivity in resected specimens in patients who underwent BCS was significantly lower among patients who received MRI than among patients who received conventional preoperative imaging (3.9% vs 11.7%, $P = 0.03$, Table 3).

We also analyzed whether there were differences in the rates of reoperation for cases of margin involvement and the rates of residual cancer detection after reoperation between the 2 image study groups (Table 4). Of the 103 (7%) patients with margin involvement, 66 had undergone preoperative conventional image studies and 37 had undergone MRI as well as conventional imaging. The overall rate of reoperations in margin involved conditions was significantly higher among patients in the conventional imaging group (66.7%) than among those in the combined MRI group (29.7%, $P < 0.01$). None of the patients with margin involvement who received total mastectomy in either imaging group underwent a second surgery. The rate of reoperation for patients with margin involvement who received BCS was significantly higher among those who underwent conventional imaging alone (80%) than among those who received preoperative MRI in addition to conventional imaging (47.8%, $P < 0.01$). The overall BCS reoperation rates were 11.7% (44/377) in the conventional imaging group and 3.2% (11/348) in the combined MRI group ($P < 0.01$).

In patients with margin involved and undergone reoperations, further BCS could be performed in 68.2% (30/44) of patients in conventional image group and 81.8% (9/11) in combined with MRI group ($P = 0.48$, Table 4). There was no difference in rate of residual breast cancer found at reexcised specimens after BCS between the 2 imaging groups (50% vs 81.8%, $P = 0.09$). The results of rates about margin involvement, reoperations, mastectomy, and local recurrences in our case-controlled comparative study were compared with other literature reported series and summarized in Table 5.

The factors affecting margin involvement in patients received BCS were further analyzed with univariate and multivariate analysis. In Table 6 univariate analysis, excision biopsy (odds ratio = 2.08, $P = 0.04$), without MRI use (conventional breast image only) (odds ratio = 2.38, $P = 0.01$), and pathological multifocal/multicentric breast cancer (odds ratio = 2.16, $P = 0.04$) were risk factors for margin involvement in patients received BCS. In multivariate analysis, multifocal/multicentric breast cancer (odds ratio = 2.38, $P = 0.02$) and without MRI use

TABLE 3. Effect of Preoperative Breast MRI on Index Surgeons on Margin Involved Rate

Surgeon A	Conventional Breast Image (316)	Combined Breast MRI (329)	P
Operation type			
Total mastectomy	158 (50)	181 (55)	0.21
BCS	158 (50)	148 (45)	
Breast reconstruction	26 (16.5)	57 (31.5)	<0.01
Overall margin involvement	24/316 (7.6)	16/329 (4.9)	0.19
Margin involvement in BCS	22/158 (13.9)	12/148 (8.1)	0.15
Margin involvement in total mastectomy	2/158 (1.3)	4/181 (2.2)	0.69
Surgeon B	**Conventional Breast Image (261)**	**Combined Breast MRI (216)**	**P**
Operation type			
Total mastectomy	107 (41)	89 (41.2)	<0.99
BCS	154 (59)	127 (58.8)	
Breast reconstruction	34 (31.8)	40 (44.9)	0.08
Overall margin involvement	24/261 (9.2)	11/216 (5.1)	0.11
Margin involvement in BCS	18/154 (11.7)	5/127 (3.9)	0.03
Margin involvement in total mastectomy	6/107 (6.2)	6/89 (6.7)	0.77

BCS = breast-conserving surgery, MRI = magnetic resonance imaging.

(odds ratio = 2.35, $P < 0.01$) were the major predisposing factors for margin involvement.

To prevent bias from confounding factors, a propensity-score matching was also perform to select 2 groups of patients for further analysis of factors related to margin involvement in primary operable breast cancer patients (Table 7). We have 641 patients in conventional image group and combined with breast MRI group. The pathologic margin involvement was 8.3% in conventional image group, and 5% in combined with MRI group ($P = 0.03$). The margin involvement rate in patients received BCS was 13.5% in conventional image group versus 6.6% in combined with MRI group ($P = 0.01$). In multivariate analysis (Table 8), multicentric/multifocal breast cancer (odds ratio=2.53, $P = 0.03$), and without MRI use (odds ratio = 1.97, $P = 0.02$) remained the 2 major factors related to margin involvement in BCS patients.

DISCUSSION

Surgical resection with clear histologic margin remained the main task of surgeons either in BCS or mastectomy. Factors that influence local recurrence include patient age, tumor stage, tumor grade, lymphovascular invasion, molecular subtype, and positive surgical margins.[6,33–37] Positive surgical margin has been demonstrated to be the most important and preventable factor associated with recurrence of operable breast cancers.[6,35,37] Methods that show promise for minimizing the rate of positive margin involvement[10] include margin index,

TABLE 4. Margin Involved BCS Patients With Reexcision and Residual Cancer Found in Reexcised Specimens

	Conventional Breast Image	Combined Breast MRI	P
Margin involvement			
Yes	66 (9.0)	37 (5.0)	<0.01
No	667 (91.0)	698 (95.0)	
Reoperations in margin involved condition			
Yes	44 (66.7)	11 (29.7)	<0.01
No	22 (33.3)	26 (70.3)	
Reoperation in margin involved total mastectomy			
Yes	0 (0)	0 (0)	<0.99
No	11 (100)	14 (100)	
Reoperation in margin involved BCS			
Yes	44 (80)	11 (47.8)	<0.01
No	11 (20)	12 (52.1)	
Further BCS	30 (68.2)	9 (81.8)	0.48
Completion mastectomy	14 (31.8)	2 (18.2)	
Residual cancer found in reexcision specimen			
Yes	22 (50)	9 (81.8)	0.09
No	22 (50)	2 (18.2)	

BCS = breast-conserving surgery, MRI = magnetic resonance imaging.

TABLE 5. Literature Review of Comparative Studies of Preoperative MRI on Rates of Margin Involvement, Reoperation, Mastectomy, and Local Recurrence

Author	Journal	Study Design	Number of Cases	Margin Involved Rate	Reoperation Rate	Mastectomy Rate	Local Recurrence
Fischer et al[25]	Eur Radiol 2004	Comparative study (follow-up time, MRI 40.3 and no MRI 41 months)	MRI = 121, no MRI = 225	—	—	MRI 28.9% vs no MRI 38.7%, $P = 0.08$	MRI 1.2% vs no MRI 6.8%, $P < 0.01$. Contralateral carcinoma MRI 1.7% vs no MRI 4%, $P < 0.01$
Bleicher et al[12]	J Am Coll Surg 2009	Comparative study	MRI = 130, no MRI = 447	MRI 21.6% vs no MRI 13.8%, $P = 0.20$	—	MRI vs no MRI for mastectomy OR = 1.8	—
Hwang et al[26]	Ann Surg Oncol 2009	Comparative study, invasive breast carcinoma patients	MRI = 127, no MRI = 345	No difference in negative margin	MRI 11.8% vs no MRI 13.3%, $P = 0.50$	—	At 8 years MRI 1.8% vs no MRI 2.5%, $P = 0.67$
Mann et al[23]	Breast Cancer Res Treat 2010	Comparative study, invasive lobular carcinoma patients	MRI = 99, no MRI = 168	—	MRI 9% vs no MRI 27%, $P = 0.01$ (overall 5% vs 15%, $P = 0.01$)	MRI 48% vs no MRI 59%, $P = 0.1$	—
Itakura et al[27]	Clin Breast Cancer 2011	Comparative study, ductal carcinoma in situ patients	MRI = 38, no MRI = 111	Negative margin MRI 84% vs no MRI 89%, $P = 0.42$	Number of reexcision MRI = 0.58 vs no MRI = 0.42, $P = 0.31$	MRI 45% vs no MRI 14%, $P < 0.01$	—
Miller et al[29]	Ann Surg 2012	Comparative study	MRI = 219, no MRI = 195	—	MRI 14% vs no MRI 18%, $P = 0.34$	MRI 43% vs no MRI 28%, $P < 0.01$	MRI 1.6% vs no MRI 5%, $P = 0.13$
Obdeijn et al[22]	AJR 2013	Case-controlled study	MRI = 123, no MRI = 119	MRI 15.8% vs no MRI 29.3%, $P < 0.01$	MRI 18.9% vs no MRI 37.4%, $P < 0.01$	—	—
Fancellu et al[30]	Clinical Breast Cancer 2014	Comparative study	MRI = 109, no MRI = 128	—	MRI 4.1% vs no MRI 8.6%, $P = 0.9$	MRI 13.7% vs no MRI 7%, $P = 0.05$	—
Sung et al[24]	AJR 2014	Matched control comparative study	MRI = 174, no MRI = 174	Negative margin MRI 89% vs no MRI 90%, $P = 0.29$	MRI 29% vs no MRI 45%, $P = 0.02$	—	No difference in local or regional recurrence ($P = 0.33$) or distant disease-free survival ($P = 0.73$)
Vos et al[28]	Br J Surg 2015	Population-based cancer registry study	MRI = 1637, no MRI = 3164	MRI 18.1% vs no MRI 15.1%, OR = 1.2 (95% CI: 1.0–1.45)	MRI 9.8% vs no MRI 7.2%, OR = 1.33, (1.04–1.7)	MRI 38.8% vs no MRI 24.2%, OR = 2.13, (1.87–2.41)	—
Lai	Present study	Case-controlled comparative study	MRI = 735, no MRI = 733	Overall: MRI 5% vs no MRI 9%, $P < 0.01$; BCS group: MRI 6.6% vs no MRI 14.6%, $P < 0.01$	BCS reoperation rates: MRI 3.2% vs no MRI 11.7%, $P < 0.01$	MRI 52.7% vs no MRI 48.6%, $P = 0.13$	—

Only cases comparative or case-controlled analysis was included in the literature review, and metaanalysis was not included in the current literature review.
BCS = breast-conserving surgery, CI = confidence interval, MRI = magnetic resonance imaging, OR = odds ratio, vs = versus.

TABLE 6. Risk Factors for Margin Involvement in Patients Received Breast-Conserving Surgery

	Univariate Analysis			Multivariate Analysis		
Parameters	**Odds Ratio**	**95% CI**	***P***	**Odds Ratio**	**95% CI**	***P***
Age	1.00	−0.02 to 0.02	0.85			
Pathologic tumor size (invasive, cm)	1.16	−0.43 to 0.32	0.11			
Biopsy method (excision biopsy)	2.08	−0.02 to 1.40	0.04	1.43	−0.42 to 1.06	0.34
Without MRI (conventional breast image only)	2.38	0.38 to 1.39	<0.01	2.35	0.33 to 1.40	<0.01
Pathological multifocal/multicentric (yes)	2.16	−0.02 to 1.468	0.04	2.38	0.07 to 1.59	0.02
Lymph node (positive)	0.78	−0.85 to 0.31	0.41			
Grade (II, III)	0.89	−0.69 to 0.51	0.71			
ER (positive)	1.20	−0.43 to 0.88	0.58			
PR (positive)	0.98	−0.58 to 0.57	0.93			
HER-2 (positive)	0.66	−1.21 to 0.26	0.26			

CI = confidence interval, MRI = magnetic resonance imaging, ER = estrogen receptor, PR = progesterone receptor, HER-2 = human epidermal growth factor receptor-2.

nomograms, intraoperative ultrasound-guided resection, wire-guided localization, radioactive seed localization, standardize cavity shaving, frozen section analysis, and MRI.

In a systematic review and meta-analysis, MRI was determined to be the most sensitive preoperative imaging tool for detection of additional or occult disease.[15] In our study, the rate of detection of pathological multifocal/multicentric breast cancer was markedly higher in patients who received preoperative MRI than in those who underwent conventional imaging alone (14.3% vs 8.6%, $P < 0.01$, Table 2). Similar findings have been reported elsewhere.[15,38] Adding breast MRI to conventional breast imaging did increase the findings of more multifocal/multicentric breast cancer or disease extent more severe than expected, and therefore might increase the decision to perform a mastectomy. In our case-controlled comparison analysis, the combination of preoperative breast MRI did increase 4.1% mastectomy rate, however, it was statistically nonsignificantly ($P = 0.13$). In Killelea et al's study,[39] they found that ''when compared with the women who did not have an MRI, the women with a normal MRI or a benign biopsy actually had an increased lumpectomy rate (66% and 62%). Thus, some women who were considering mastectomy may have chosen lumpectomy based on the MRI results. This may explain why the use of MRI had a relatively modest effect overall on the lumpectomy rate.'' Our study also supported this finding that when breast MRI showed unifocal breast cancer, which was consistent with previous mammography and/or sonographic findings, then patients and surgeons were more convinced to receive BCS.

From Table 2, about 7.9% (4.1%/51.4%) of patients would change their surgery from BCS to mastectomy due to the addition of breast MRI. The margin involved rate in patients received BCS decreased from 14.6% (conventional breast image group) to 6.6% (combined with preoperative MRI group) ($P < 0.01$). About 54.8% (8%/14.6%) of previous margin involved BCS patients was prevented after combining preoperative breast MRI to conventional breast images. Combining with preoperative breast MRI could help us to find a group of patients with higher risk of margin involvement for BCS. The allocation of this high-risk group of patients to mastectomy (with or without breast reconstruction) would greatly decrease margin involved rate for patients receiving BCS. We found that a 54.8% decrease ratio of margin involvement in BCS patients was derived from the change of 7.9% patients, who might not be suitable for BCS. The development of nipple sparing type of mastectomy[40] did increase patients' will to perform mastectomy with reconstruction when preoperative MRI revealed disease extent larger than expected (39.8% breast reconstruction rate in combined MRI group vs 17.1% in conventional image group, $P < 0.01$, Table 2). From the observation of this case-controlled comparison analysis, we speculated that adding preoperative breast MRI to conventional breast images could help physicians to pick up a group of patients who were not suitable for BCS and allocate them to receive mastectomy could greatly decrease the surgical margin involved rate.

Studies that have investigated whether preoperative MRI results in lower rates of margin involvement, and local recurrence have provided conflicting results (Table 5).[12,15,25,28,30,41] Obdeijn et al[22] in a case-controlled study showed that the margin positive rate was significantly decreased in MRI group compared with controlled no MRI group (15.8% vs 29.3%, $P < 0.01$). However, other studies have failed to show that breast MRI is associated with improved margin status.[12,24,26–28] Fischer et al[25] showed that the ipsilateral tumor recurrence and the development of new breast cancer on the contralateral side were decreased in cased who received preoperative breast MRI evaluation. Other studies did not show adding preoperative MRI to conventional breast imaging would statistically decrease local recurrence.[24,26,29] In our present study, without MRI use (conventional breast image only) was associated with increased risk (Odds ratio = 2.35, $P < 0.01$, Table 6) of margin involvement in patients received BCS in multivariate analysis. To reduce the bias from possible confounding factors, the propensity score matching were performed and we repeat the analysis (Tables 7 and 8). In multivariate analysis, multicentric/multifocal breast cancer (odds ratio = 2.53, CI = 0.02–1.75, $P = 0.03$), and without MRI use (odds ratio = 1.97, CI = 0.10–1.28, $P = 0.02$) remained the 2 major factors related to margin involvement in BCS patients. An increased rate of mastectomy were observed in some studies,[12,25,27–30] however, other studies showed MRI was not associated with increased mastectomy rate.[23,25] In contrast to the ''negative impact'' results,[12,27,28] which found that MRI was associated with an increased mastectomy rate but was not

TABLE 7. Clinical Features of Patients After Propensity Score Matching

	Conventional Breast, Image Group, n = 641 (%)	Combined Breast, MRI Group, n = 641 (%)	*P*
Age, y	52.25 ± 11.45	52.83 ± 10.93	0.35
Location			
Right	317 (49.5)	294 (45.9)	0.22
Left	324 (50.5)	347 (54.1)	
Biopsy method			
CNB	514 (81.2)	586 (92.3)	<0.01
Stereotactic biopsy	49 (7.7)	48 (7.6)	
Excision	65 (10.3)	1 (0.2)	
FNAC	5 (0.8)	0 (0.0)	
Tumor size, cm	2.16 ± 1.65	2.38 ± 1.59	0.01
Lymph node			
Positive	228 (35.6)	214 (34.2)	<0.01
Negative	413 (64.4)	412 (65.8)	
Stage			
0	95 (9.7)	106 (10.8)	0.01
I	197 (20.1)	196 (20.0)	
II	257 (26.3)	283 (28.9)	
III	84 (8.6)	56 (5.7)	
IV	4 (0.4)	0 (0.0)	
Grade			
I	119 (19.4)	90 (14.2)	<0.01
II	376 (61.2)	330 (52.2)	
III	119 (19.4)	212 (33.5)	
ER			
Positive	483 (76.2)	517 (81.4)	0.07
Negative	151 (23.8)	118 (18.6)	
PR			
Positive	476 (75.1)	472 (74.3)	0.92
Negative	158 (24.9)	163 (25.7)	
HER-2			
Positive	141 (22.5)	146 (24.0)	0.01
Negative	487 (77.5)	463 (76.0)	

CNB = core needle biopsy, ER = estrogen receptor, FNAC = fine needle aspiration cytology, HER-2 = human epidermal growth factor receptor-2, MRI = magnetic resonance imaging, N/A = not available, PR = progesterone receptor.
Mean ± standard deviation (SD).

TABLE 8. Risk Factors for Margin Involvement in Patients Received Breast-Conserving Surgery After Propensity Score Matching

	Univariate Analysis			Multivariate Analysis		
Parameters	**Odds Ratio**	**95% CI**	***P***	**Odds Ratio**	**95% CI**	***P***
Age	1.01	−0.02 to 0.03	0.7			
Pathologic tumor size (invasive, cm)	1.16	−0.06 to 0.333	0.13			
Biopsy method (excision biopsy)	2.28	−0.01 to 1.57	0.04	1.50	−0.47 to 1.19	0.34
Without MRI (conventional breast image only)	2.21	0.25 to 1.37	0.01	1.97	0.10 to 1.28	0.02
Pathological multifocal/multicentric (yes)	2.65	0.08 to 1.77	0.02	2.53	0.02 to 1.75	0.03
Lymph node (positive)	0.18	−0.98 to 0.20	0.21			
Grade (II, III)	0.62	−0.90 to 0.03	0.03	0.70	−0.78 to 0.10	0.11
ER (positive)	0.69	−0.91 to 0.23	0.20			
PR (positive)	0.67	−0.92 to 0.15	0.13			
HER-2 (positive)	0.79	−0.86 to 0.36	0.45			

CI = confidence interval, ER = estrogen receptor, HER-2 = human epidermal growth factor receptor-2, PR = progesterone receptor.

associated with improved margin status, we found that preoperative MRI was associated with a lower rate of margin involvement without an apparent increase in mastectomy rate.

No consensus exists among surgeons as to what constitutes a safe surgical margin (1–2, >5, or >1 cm).[42] There is increasing evidence that a negative margin should be defined in samples with no tumor on the inked margin.[3,43] However, in this study, we defined a positive margin as one in which tumor cells were seen within 1 mm from peripheral inked margins because many studies have shown that margins <1 mm are associated with high risk of residual disease.[9,44,45]

Patients with positive margins are usually advised to receive further surgery to prevent local recurrence.[7,8,44] However, up to 50% of specimens taken during reoperation do not show evidence of residual breast cancer.[8,9,45] Some studies showed that preoperative breast MRI could reduce reexcision rates,[22–24] but other studies did not revealed a reduction in reoperations[26–30] (Table 5). In our study, we found that the use of preoperative breast MRI was associated with a significantly lower rate of reoperation than conventional imaging among patients with positive margins after BCS (47.8% vs 80%, $P < 0.01$). This decreased of reoperation in combined with MRI group might be that the surgeons would suppose that the residual cancer would be less as preoperative MRI did not show other multifocal or multicentric lesions for patients selected for BCS. Thus the overall rates of reoperation among patients who underwent BCS were 11.7% (44/377) in the conventional imaging group and 3.2% (11/348) in the MRI group ($P < 0.01$). Although we found that combining MRI with mammography and sonography was associated with a reduction in the number of reoperations, there was no significant difference in the rate of residual cancer detection in the reexcised specimens between patients who received conventional imaging only and those who received MRI preoperatively (50% vs 81.8%, $P = 0.09$).

In present study, we tried to understand the impact of adding breast MRI to conventional breast images on the effect of individual breast surgeons. In the past, most studies reported the impact of breast MRI was derived from a mixture of different experience of surgeons and disease severity of patients. This could mask the real effect of adding preoperative breast MRI upon physicians and their performance on patients' outcome. Fortunately, we had 2 index surgeons, defined as having more than 100 breast cancer operations in each of 2 imaging survey periods, for evaluation. During the study period in our hospital, more than 10 surgeons were found for the operations done in the 1468 patients. Index surgeon was chose to prevent the bias of inadequate surgical techniques or inexperience about breast imaging tools (either conventional breast images or combined with breast MRI) on the outcome of margin involvement. From these 2 index breast surgeons, we could see the impact of breast MRI on the practice or medical behavior on the breast cancer patients (Table 3). We found that for experienced breast surgeons, adding breast MRI did not increase mastectomy rate significantly, and a decrease of surgical margin involved rate in BCS patients were observed.

Limitations in this study include its retrospective nature and possible selection bias. Designing a case-controlled comparison analysis, we try to have 2 groups of patients with comparable characteristics, like patients' age, tumor size, lymph node status, and stages. However, as most of the retrospective cases collective analysis, we could not have all the characteristics (or variables) comparable or equal. The related lower estrogen receptor (ER) expression (75% vs 79%, $P < 0.05$), and higher histologic grade in conventional image group than combined with breast MRI group might be also selection bias related (Table 1). Furthermore, patients diagnosed and treated during 2009 to 2010, would have slightly higher proportion of patients diagnosed with excision biopsy or less percentage of patients received sentinel lymph node biopsy than patients diagnosed after January 2011. To prevent bias derived from confounding factors, we had performed the propensity score matching to reduce possible selection bias in this retrospective study. The lack of long-term follow-up results in present study could not answer whether preoperative MRI would decrease ipsilateral tumor recurrence or prolong disease-free survival. Nonetheless, our results clearly demonstrate that preoperative MRI combined with mammography and sonography results in a lower rate of positive surgical margins and reoperations than conventional preoperative imaging.

In conclusion, we found that preoperative breast MRI combined with conventional breast imaging would detect more multifocal/multicentric breast cancer, which was the major predisposing factor for margin involvement. The combination of breast MRI resulted in a lower rate of surgical margin involvement in patients who underwent BCS but not in patients who underwent mastectomy. Breast MRI was also associated with a higher rate of breast reconstruction in patients who underwent mastectomy and a lower rate of reoperation in patients with margin involvement who underwent BCS. MR images obtained preoperatively, however, were not sufficient for predicting residual cancer after excision.

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