Positional advantages of supine MRI for diagnosis prior to breast-conserving surgery

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Received November 7, 2022; Accepted December 21, 2022

DOI: 10.3892/mco.2023.2640

Abstract. The present study aimed to evaluate the rate of positive surgical margins for magnetic resonance imaging (MRI) performed in the supine position prior to breast-conserving surgery (BCS). The rate of positive surgical margins and the clinicopathological factors were examined in consecutive patients with BCS who underwent preoperative MRI performed in the supine position at Sapporo Medical University Hospital (Sapporo, Japan) and related hospitals and clinics between January 2012 and December 2013. Of 1,175 eligible patients, 1,150 were included after excluding 25 patients with either bilateral breast cancer or stage IV disease. Positive margin was defined as no cancer seen on the resected margin. The primary endpoint was the rate of positive surgical margins when preoperative MRI was performed in the supine position and the secondary endpoint was identification of the factors that predict positive margins. Of the 1,150 female patients (median age, 55 years; range, 29-97 years) who underwent BCS for breast cancer following MRI performed in the supine position, 215 (18.8%) had positive margins, which is similar to the rate with MRI in the prone position, and 930 (81.2%) had negative margins. The rate of positive surgical margins in patients of the human epidermal growth factor receptor 2 (HER2) type was significantly higher than that in the non-HER2 type group (6.5 and 2.9%; χ^2 P=0.0103). There was no increase in the rate of positive margins in breast cancers with a diameter of >T2. The rate of positive surgical margins following MRI performed in the supine position was 18.8%. Supine MRI appears to be suitable for informing on the extent of resection of breast cancer.

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Key words: breast cancer, supine MRI, surgical margin

Introduction

The number of breast cancer cases is increasing annually throughout the world and it has more than doubled from ~800,000 in 1990 to 1.68 million in 2016 (1). The 10-year survival rate for stage I primary breast cancer is >95% with good prognosis; however, that for metastatic/recurrent breast cancer is only ~5% (2). Proper definitive treatment is important to prevent metastasis and recurrence. Surgical treatment is known to have an important role as the initial treatment. The standard surgery for breast cancer is generally mastectomy or partial mastectomy; i.e., breast-conserving surgery (BCS), but it is important to obtain a negative surgical margin, particularly in BCS. A meta-analysis by the Early Breast Cancer Trialists' Collaborative Group reported that positive surgical margins in BCS increased breast cancer-related mortality (3). Accurate diagnosis of the spread of breast cancer is necessary to obtain negative surgical margins. The gold standard imaging examination for investigating the spread of breast cancer is ultrasound (US) (4). However, for diagnoses made by US, the rate of positive surgical margins is 24-27% (5,6), which is clearly insufficient and requires to be improved. As an alternative technique, magnetic resonance imaging (MRI) with the patient in the prone position has recently been used for this purpose. The prone position has the advantages of minimal deterioration of image quality due to respiratory movements and of improved ability to examine intraductal components of the mammary glands without distortion, as they are stretched when the breast is 'hanging' in this position (7,8). At present, US and MRI in the prone position are in widespread use as standard methods despite a lack of significant results from randomized controlled trials (RCTs) (6). An RCT conducted in 2001 compared the reoperation rate for BCS between a group with MRI in the prone position (n=816) and a triple assessment group of mammography (MG), US and core needle

biopsy (non-MRI group, n=807). There was no significant reduction in the reoperation rate in the MRI group (153/816, 19%) compared with the non-MRI group (156/807, 19%; odds ratio: 0.96, 95% CI: 0.75-1.24, P=0.77) (9). A disadvantage of MRI in the prone position is that it differs from the operating position (10,11). Even if spread of the lesion can be correctly diagnosed, it is considered that a certain shift occurs due to the change in posture between imaging and surgery. The present study was performed based on the notion that supine MRI has an advantage compared with prone MRI because the images are acquired in the same position as the surgical position. In addition, MRI image rendering technology has improved to the point that previous problems associated with supine MRI have been overcome. The aim of the present study was therefore to examine the rate of positive surgical margins for supine MRI.

Patients and methods

Patients. Enrolled in this multi-center retrospective study were 1,150 consecutive patients with a diagnosis of breast cancer who underwent BCS between January 2012 and December 2013 at Sapporo Medical University Hospital, Sapporo Breast Surgical Clinic, Sapporo-Kotoni Breast Clinic, Shin-Sapporo Breast Clinic or Higashi Sapporo Hospital (Sapporo, Japan). Inclusion criteria were as follows: Patients with BCS who underwent preoperative MRI performed in the supine position at the above-mentioned hospitals between January 2012 and December 2013. Patients with bilateral and stage IV breast cancer were excluded. For all patients, surgeries were performed by certified surgeons and BCS was performed in all cases based on the decision of each surgeon. Surgical margin-negative was defined as no microscopically observable tumor at the margin. MRI was performed using the GE SIGNA Excite 1.5T, GE SIGNA HGX 1.5T (Cytiva) or PHILIPS Ingenia 1.5T Ver.4.3 (Philips Medical Systems, Inc.). There was no standardized technique for partial resection at any of the institutions and the operative method was selected based on curative ability and adaptability. All patients underwent MG, US and clinical best examination. At Sapporo Medical University Hospital (Sapporo, Japan), but no other institution, rapid intraoperative pathological examination was performed in four directions and additional resection was performed if the result was cancer-positive. The final pathological diagnoses were obtained by an individual pathologist at the respective institution or by a dedicated pathologist at an affiliated pathology laboratory. If either non-invasive or invasive cancer was identified, the patient was considered cancer-positive. Furthermore, the margin was compared between patients with different HER2 status.

Statistical analysis. The clinicopathological parameters were compared between the margin-positive and -negative groups using the χ^2 test. P<0.05 was considered to indicate statistical significance. JMP11 software (SAS Institute, Inc.) was used for statistical analysis.

Results

Patients' background. After excluding 25 cases of bilateral breast cancer and stage IV cancer, 1,150 of the 1,175 patients were enrolled in the study (Fig. 1). All of these women (median age, 55 years; range, 29-97 years) underwent MRI in the supine position prior to BCS for breast cancer.

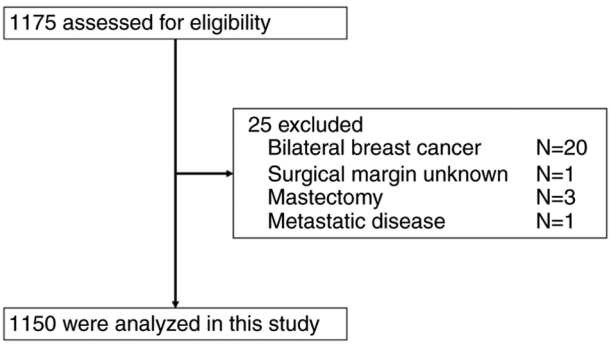

Figure 1. Flowchart of patient selection.

Patients' characteristics. The patient characteristics, rate of positive surgical margins and clinicopathological factors are listed in Table I. Regarding the rate of positive surgical margins determined by supine MRI (primary endpoint), 215/1,150 patients (18.8%) had positive and 930/1,150 (81.2%) had negative margins.

Positive margin rate. The rate of positive surgical margins was substantially higher in patients of the HER2-positive type than in those with HER2-negative type breast cancer (6.5 and 2.9%, respectively; χ^2 P=0.0103; Table II).

Discussion

The rate of positive surgical margins for MRI in the supine position in the present study was 18.8%, which is similar to 19.7-20.0%, the rates reported for MRI in the prone position (6,12-14). US may also be used for preoperative imaging and has the advantages of being simple and inexpensive. It may be performed in the operating position; however, it has the disadvantage that only part of the breast may be visualized at a time. For this reason, MRI imaging in the prone position has been employed for preoperative assessment (15). The present results indicated comparable rates of positive margins for supine- and prone-position MRI. As the present data were obtained between 2012 and 2013, it is possible that the current positive margin rate is further reduced when examined by MRI using the most advanced technology. In the present subgroup analysis of tumors with a diameter of 2 cm or less, the positive rate was almost comparable between supine and prone MRI, similar to the results of previous studies (16,17). However, only the tumor size cannot be deduced from the positive rate. The present study indicated an increased rate of positive margins for prone MRI in the case of tumors >2 cm, but this was not the case for supine MRI in the current study. It may be difficult to determine the extent of resection in larger tumors imaged with prone-position MRI, as the relationship of the resection line to the complex tumor differs considerably between the prone imaging and supine surgical positions. By contrast, spatial variation is minimized with supine MRI due to its similarity with the supine surgical position. A total of

Table I. Characteristics of the patients of the present study (n=1,150).

Parameter	Value
Age, years	55 (29-97)
cT	
0	181 (15.8)
1	738 (64.6)
2	213 (18.6)
3	6 (0.5)
4	5 (0.4)
pN	
0	888 (81.8)
1-3	197 (18.2)
ER	
Positive	975 (85.3)
Negative	168 (14.7)
PgR	
Positive	825 (73.2)
Negative	302 (26.8)
HER2	
Positive	121 (11.4)
Negative	944 (88.6)
ER/HER2 status	
ER- and HER2+	41 (3.6)
Any	1,104 (96.4)
NG	
1	592 (67.8)
2	80 (9.2)
3	201 (23.0)
Ly	
Positive	423 (40.5)
Negative	622 (59.5)
Margin	
Positive	215 (18.8)
Negative	930 (81.2)

Values are expressed as the median (range) or n (%). cT, clinical tumor stage; pN, pathological node stage; ER, estrogen receptor; PgR, progesteron receptor; HER2, human epidermal growth factor receptor 2; NG, nuclear grade; Ly, lymphatic invasion.

Table II. Comparison of clinicopathological factors between margin-positive and margin-negative cases.

Parameter	Margin positive (n=218)	Margin negative (n=932)	P-value
Age, years	53 (29-83)	55 (30-97)	0.5109
cT			0.6903
0	33 (15.4)	148 (16.0)	
1	142 (66.0)	596 (64.2)	
2	38 (17.7)	175 (18.7)	
3	2 (0.9)	4 (0.4)	
4	0 (0)	5 (0.5)	
pN			0.5561
0	174 (83.3)	714 (81.5)	
1-3	35 (16.7)	162 (18.5)	
ER			0.7555
Positive	184 (86.0)	791 (85.2)	
Negative	30 (14.0)	138 (14.8)	
PgR			0.5662
Positive	160 (74.8)	665 (72.8)	
Negative	54 (25.2)	248 (27.2)	
HER2			0.1624
Positive	28 (14.2)	93 (10.7)	
Negative	169 (85.8)	775 (89.3)	
ER/HER2 status			0.0103
ER- and HER2+	14 (6.5)	27 (2.9)	
Any	201 (93.5)	903 (97.1)	
NG			0.5513
1	112 (68.3)	480 (67.7)	
2	18 (11.0)	62 (8.7)	
3	34 (20.7)	167 (23.6)	
Ly			0.0857
Positive	71 (35.2)	352 (41.8)	
Negative	131 (64.8)	491 (58.2)	

Values are expressed as the median (range) or n (%). cT, clinical tumor stage; pN, pathological node stage; ER, estrogen receptor; PgR, progesteron receptor; HER2, human epidermal growth factor receptor 2; NG, nuclear grade; Ly, lymphatic invasion.

three RCTs (6,9,12) of perioperative procedures using supine MRI reported percentages of positive margins, although the positive margin rates were different for ductal carcinoma *in situ* and invasive ductal carcinoma. The combined positive margin rate of 19.7-20.0% is comparable to the 18.8% reported in the present study.

Higher positive margin rates have been reported with both supine- and prone-position MRI for the HER2-positive type compared with non-HER2 type breast cancer (18). In the latter study, there are reports of a higher rate of positive margins in HER-positive breast cancer, while this does not appear to be the case for ER-positive patients. A previous RCT (6) has reported that positive margins are more likely to occur in cases of *in situ* HER2-positive breast cancer because ductal spread is poorly detected even by MRI. Expected improvements in MRI image-rendering technology should increase iability to detect ductal carcinoma *in situ* (16,19). Prospective cohort studies will then be required to evaluate the efficacy of the new technology. Previous studies have reported a difference in tumor size between positive and negative surgical margin rates (12-14), but in the present study, no such difference was found.

There are certain limitations to the present study. As its retrospective design may have introduced bias, the results should be interpreted with caution. In the present study, there was no prone position group included, so there was no direct

comparison between prone- and supine-position patients. Furthermore, as it appears that there were differences in procedures among the different hospitals included, this may have introduced heterogeneity. However, it may be assumed that the data are meaningful because of the relatively large size of the study cohort. The correlation between phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit α gene mutation and positive resection margins or between PI3K/AKT/mTOR pathway-related mutations and positive resection margins is important in the analysis of clinicopathological factors, but lack of preparation, including informed consent, made it difficult to examine this in the present study.

In conclusion, the rate of positive surgical margins in patients who underwent preoperative imaging with supine MRI prior to BCS was 18.8%, which is similar to the 20% reported previously (6). Supine MRI may provide useful information for determining the extent of resection.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

GK, HS, DK, TMiz and IT conceived and planned the present study in detail. FS, AW, YK, MO, AO, HM, TMik, YY, TMat, TO and HK extracted the entirety of patient data, performed the data collation and put the data into a form in which it could be entered into statistical software. AW, YK and DK performed analysis and interpretation of the patient data. HM, TMiz, HK and TO critically revised the manuscript for important intellectual content. GK drafted the manuscript. IT provided overall supervision and gave final approval for the version to be published. All authors read and approved the final manuscript. GK and HS confirmed the authenticity of all the raw data.

Ethics approval and consent to participate

This study adhered to ethical tenets of The Declaration of Helsinki and Ethical Principles for Medical Research Involving Human Subjects, and was approved by the Clinical Trial Center of Sapporo Medical University, Japan (342-179).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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