

Usefulness of Breast MRI for Safe Omission of Axillary Lymph Nodes Dissection in Sentinel Node-Positive Breast Cancer Patients

Hiromi Fuchikami, Naoko Takeda, Kazuhiko Sato

Department of Breast Oncology, Tokyo-West Tokushukai Hospital, Tokyo, Japan
Email: Hiromi.fuchikami@tokushukai.jp

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Abstract

Background: Preoperative identification of patients with extensive lymph node metastasis (LNM) is important for safe omission of axillary lymph node dissection (ALND) in sentinel node (SN)-positive (SN+) breast cancer patients. **Methods:** We evaluated retrospectively the collected data of 758 breast cancer patients who underwent axillary surgery between 2008 and 2017, excluding those who received neoadjuvant chemotherapy. **Results:** Of the 758 patients, 607 were not suspicious to have LNM by axillary ultrasound (AUS-), but 38 suspicious cases were found by breast magnetic resonance imaging (MRI). Of 15 patients undergoing axillary fine needle biopsy (AFNA) due to second-look axillary ultrasound (AUS), 9 underwent ALND because of a positive AFNA (AFNA+). Among 81 (10.9%) patients undergoing ALND due to SN+ findings, 6 (7.4%) had extensive LNM (LNM \geq 4). If MRI was not performed, among the 90 of 673 patients undergoing ALND who had SN+ findings, 12 (13.3%) had LNM \geq 4. **Conclusions:** The proportion of cases with LNM \geq 4 was reduced from 13.3% to 7.4% among patients undergoing SN biopsies combined with breast MRI. ALND might be omitted safely in SN+ cases according to detailed preoperative evaluations using additional breast MRI to ultrasound.

Keywords

Breast Cancer, Sentinel Node, Axillary Lymph Node Dissection, Breast MRI

1. Introduction

Omission of axillary lymph nodes dissection (ALND) is standard for sentinel node (SN)-negative (SN-) breast cancer patients, but issues remain for SN-positive (SN+) patients. The American College of Surgeons (ACOSOG) trial Z0011 [1]

and European Organization for Research and Treatment of Cancer (EORTC) 10981 [2] reported that ALND omission due to systemic therapy and radiation should be an option. The National Cancer Institute of Canada Clinical Trials Group MA.20 trial (NCIC-CTG MA20) [3] reported the significance of combining regional nodal irradiation (RNI) to ALND. Although lymph node metastasis (LNM) ≥ 4 should be considered for RNI [3] [4], propriety is unknown regarding ALND omission.

At present, ALND is desirable in cases with extensive LNM, and SN biopsy requires appropriate preoperative evaluations. We assessed the possibility of predicting LNM ≥ 4 for safe omission of ALND in SN+ patients.

2. Patients and Methods

We considered the usefulness of breast magnetic resonance imaging (MRI). We considered the accuracy of two types of examinations for axillary lymph node assessment: ultrasound only and ultrasound including a second-look axillary ultrasound (AUS) combined with MRI.

2.1. Patients

This retrospective study was done on 758 patients who underwent surgery between September 2008 and February 2017, excluding those who received neoadjuvant chemotherapy. **Figure 1** shows a flow diagram of the examinations and surgery process at our hospital. ALND was performed in patients who had axillary fine needle aspiration biopsy (AFNA) class V (AFNA+) and SN+ findings. However, since January 2016, ALND has been omitted even for SN+ breast cancer cases to conserve surgery. We performed axillary irradiation in these cases.

2.2. AUS Examination

In our practice, we routinely perform an ultrasound (Aplio XG, Toshiba Medical

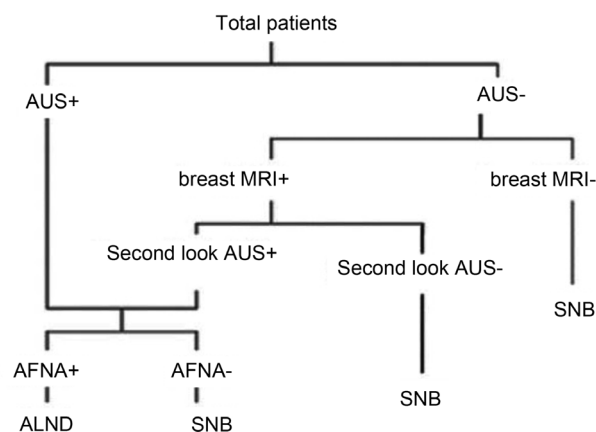


Figure 1. The flow diagram of the examinations and surgery process. AUS: axillary ultrasound, AFNA: axillary fine needle aspiration biopsy, SNB: sentinel lymph node biopsy, ALND: axillary node dissection.

Systems, Japan) survey of the axillary lymph nodes in breast cancer patients. Ultrasound results were considered positive if a detected lymph node showed cortical thickening and loss of hilum.

2.3. Breast MRI

In our practice, we routinely perform breast MRI (1.5T scanner; Excite GE Healthcare, Milwaukee, WI) in breast cancer patients. Intravenous contrast was administered; agents used were gadobutrol, gadoterate meglumine, or gadoteridol. MRI results were considered positive (MRI diagnostic criteria) if significantly swollen axillary lymph nodes were detected, based on axillary lymph node size > 4 mm, long-to-short axis ratio, cortical thickness-to-anteroposterior diameter ratio, and contrast enhancing patterns.

2.4. Preoperative Evaluations

Second-look AUS was performed if axillary LNM was not suspected on the initial AUS but was suspected on breast MRI. Patients with suspected axillary LNM on AUS or second-look AUS underwent active AFNA. First, AUS+ cases were divided into two groups, AFNA+ and AFNA-. Second, we evaluated cases with LNM ≥ 4 in the two groups: patients who underwent ALND due to AFNA+ and due to SN+. Third, to consider the usefulness of axillary evaluation by breast MRI, cases with findings on MRI but not on AUS were examined.

This retrospective study was approved by the research ethics committee (TGE00606-060).

2.5. Statistical Analysis

The results were analyzed using descriptive statistical methods. The statistical significance of differences in proportions was assessed using the χ^2 test. P values < 0.05 were considered significant.

We examined the factors that have affected MRI result using multiple regression analysis.

3. Results

A total of 758 patients with breast cancer were enrolled into this study (stage Tis = 71, stage T1 = 526, stage T2 = 145, stage T3 = 16). Mean age of the entire group was 55.7 years (range, 26 - 95). **Table 1** shows the characteristics of all 758 patients. **Table 2** shows the results of every operative procedure. Of 758, 193 (25%) patients had axillary lymph node metastasis. The average number of positive axillary lymph nodes was 1.9 and 6.6 in the patients who underwent ALND due to SN+ and AFNA+ findings, respectively. Among the patients with LNM ≥ 4 , 664 with preoperative AUS- or AUS+/AFNA- findings underwent SN biopsy. A total of 81 patients (10.9%) underwent ALND due to SN+ findings. Of these, six patients (7.4%) had LNM ≥ 4 . However, among the patients who underwent ALND due to AUS+/AFNA+ findings, 46 (48.9%) had LNM ≥ 4 (P < 0.0001).

Table 1. Patients characteristics.

Age	Median age (y)	55.7 (26 - 95)
	≤40	72 (9%)
	41 - 50	250 (33%)
	51 - 60	167 (22%)
	61 - 70	152 (20%)
	71≤	117 (16%)
AUS	Negative	626 (83%)
	Positive	132 (17%)
MRI	Negative	647 (85%)
	Positive	111 (15%)
AFNA	Not done	609 (80%)
	AFNA+	94 (63%)
	AFNA-	55 (37%)
Pathological tumor stage	Median size (mm)	16.8
	pTis	71 (9%)
	pT1	526 (69%)
	pT2	145 (19%)
	pT3	16 (2%)
Operation	Breast conserving surgery	527 (70%)
	Mastectomy	231 (30%)

AUS: axillary ultrasound, AFNA: axillary fine needle aspiration biopsy.

Table 2. The results of every operative procedure.

	BCS or Mastectomy + SNB (SN-)	BCS or Mastectomy + SNB → ALND	BCS or Mastectomy + SNB (SN+)	BCS or Mastectomy + ALND
Number of the patients	565	81	18	94
Median age	56.1	53.6	56.2	59.5
Median invasion size	14.5	17.2	26.8	31.0
Median number of axillary lymph node metastasis	0	1.9		6.8
Median number of SN metastasis	1.4	1.8	1.8	
Median number of non-SN metastasis		0.8		
Median number of non SN removed		10.4		
Median number of SN and non SN removed		12.2		16.8

SNB: sentinel node biopsy, BCS: breast conserving surgery, ALND: axillary lymph node dissection, SN: sentinel lymph node.

Then we considered the usefulness of MRI. First, we considered the accuracy of three types of examinations; ultrasonography excluding second look AUS without MRI, ultrasonography including a second look AUS combination of MRI, and MRI alone. Sensitivity and specificity of MRI were 44% and 96%. There was no difference in these three evaluations (**Table 3**). Multivariate analyses showed axillary lymph nodes metastasis, and tumor size were significantly associated with MRI in patients (both of two; $P < 0.01$) (**Table 4**). Of the 607 AUS- cases, 38 were MRI+, and 15 patients underwent AFNA due to second-look AUS. Of these 15 patients, 9 with AFNA+ and 6 with AFNA- results underwent SN biopsy. Two of the latter six patients had SN+ results and one had $LNM \geq 4$. However, of the nine AFNA+ cases, five had $LNM \geq 4$ (**Figure 2**). In addition, considering the

Table 3. Accuracy of examinations.

		Pathology		
		positive (193)	negative (565)	sum
AUS (before MRI)	positive	90 (47%)	35 (7%)	125
	negative	103 (53%)	530 (93%)	633
MRI	positive	85 (44%)	21 (4%)	106
	negative	108 (57%)	544 (96%)	652
AUS (second look)	positive	116 (53%)	39 (7%)	155
	negative	77 (47%)	526 (93%)	603

Table 4. Multivariate analysis.

	P-value	95% CI
Age	0.2835	-0.0025 - 0.0007
Tumor size	<0.001	0.0055 - 0.0089
Axillary lymph node metastasis	<0.001	0.0306 - 0.0429
AUS	0.1638	-0.0984 - 0.0167

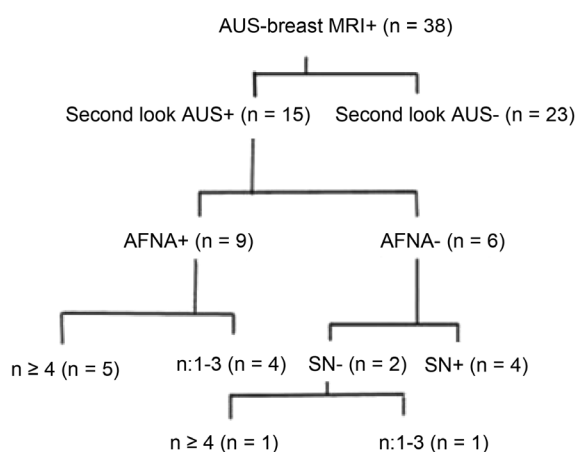


Figure 2. Axillary lymph node management in breast cancer patients. AUS: axillary ultrasound, AFNA: axillary fine needle aspiration biopsy, SNB: sentinel lymph node biopsy, SN: sentinel lymph node.

use of breast MRI by the proportion of cases with LNM ≥ 4 , if MRI and second-look AUS had not been performed, we would have performed SN biopsy in 673 patients, 12 of whom (13.3%) had LNM ≥ 4 . The proportion of cases with LNM ≥ 4 was reduced from 13.3% to 7.4% among those in which a SN biopsy was performed combined with breast MRI.

4. Discussion

ALND has been a standard treatment method for patients with LNM; however, it is associated with complications, such as lymphedema, shoulder stiffness, breast edema, seroma formation, upper limb numbness, and brachial plexopathy [5] [6]. Regarding ALND omission, issues remain for patients with SN+ findings. Although LNM ≥ 4 should be considered for RNI [7], propriety is unknown regarding ALND omission. The omission of ALND in surgical procedures for tumors with LNM has been considered, but remains controversial [8]. Various attempts have been made to predict axillary LNM to avoid ALND safely [9] [10]. Several predicting models have been developed [8] [11]-[18], and many studies have been done to select the best preoperative method for predicting axillary LNM [14] [15] [17] [18]. However, the best method to do so has not been established. Therefore, we evaluated the possibility of predicting LNM ≥ 4 for safe omission of ALND in SN+ cases. First, we reviewed each examination for axillary LNM. Accuracies of each examination were reported [9], with ultrasound found to be a suitable diagnostic tool for determining lymph node morphologic characteristics in the axilla, and histologic examination of lymph nodes, as well as sonographically guided AFNA [10]. AFNA is a simple, inexpensive, and minimally invasive technique that makes possible reduction in the numbers of SN biopsies performed [19] [20]. Previous studies have reported that the sensitivity of AFNA was low and the false-negative rate was high [7] [10] [19] [20]. In this study, all patients with AFNA+ findings had metastatic disease at ALND. On the other hand, many breast cancer patients currently undergo breast MRI as part of their initial preoperative workup. Though MRI is not recommended as a preoperative axillary evaluation method according to guidelines such as NCCN 2017 [4], integrating the information already gathered with regard to primary lesions and occult axillary lymph node risk will come at minimal additional cost. The capacity of breast MRI to predict additional axillary lymph node status is highly relevant for care of patients with SN+ findings [15]. Although AUS has been reported to have a similar specificity but better sensitivity than MRI [14], AUS is a subjective examination and it has some problems. Preoperative surgical examination of axillary lymph nodes by AUS itself has good specificity. However, AUS alone is characterized by low sensitivity in defining the presence of metastasis [21] [22]. We decided to perform second-look AUS in patients with AUS- and axillary MRI+ results. The additional cytological assessment of axillary lymph nodes using AFNA improves sensitivity and reaches an absolute specificity of 100% for the diagnosis of metastasis [23] [24]. Incidentally, we reviewed the flow of surgery, and since January 2016, ALND has been omitted even in SN+

breast cancer cases to conserve surgery. We decided to perform axillary irradiation in these cases. The proportion of cases with LNM ≥ 4 was 13.3% if the SN biopsy was performed after active AFNA due to ultrasound findings. Further, when combined with MRI findings, the ratio decreased to 7.4%. By case selection according to detailed preoperative evaluations and intentional AFNA, ALND might be omitted safely in SN+ cases.

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