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Ductal carcinoma in situ diagnosed at US-guided 14-gauge core-needle biopsy for breast mass: Preoperative predictors of invasive breast cancer

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ABSTRACT

Objectives: To identify preoperative features that could be used to predict invasive breast cancer in women with a diagnosis of ductal carcinoma in situ (DCIS) at ultrasound (US)-guided 14-gauge core needle biopsy (CNB).

Methods: A total of 86 DCIS lesions that were diagnosed at US-guided 14-gauge CNB and excised surgically in 84 women were assessed. We retrospectively reviewed the patients' medical records, mammography, US, and MR imaging. We compared underestimation rates of DCIS for the collected clinical and radiologic variables and determined the preoperative predictive factors for upstaging to invasive cancer.

Results: Twenty-seven (31.4%) of 86 DCIS lesions were upgraded to invasive cancer. Preoperative features that showed a significantly higher underestimation of DCIS were palpability or nipple discharge ($p = 0.040$), number of core specimens less than 5 ($p = 0.011$), mammographic maximum lesion size of 25 mm or larger ($p = 0.022$), mammographic mass size of 40 mm or larger ($p = 0.046$), sonographic mass size of 32 mm or larger ($p = 0.009$), lesion size of 30 mm on MR ($p = 0.004$), lower signal intensity (SI) on fat-saturated T2-weighted MR images (FS-T2WI) ($p = 0.005$), heterogeneous or rim enhancement on MR images ($p = 0.009$), and apparent diffusion coefficient (ADC) values lower than 1.04×10^{-3} mm^2/s on diffusion-weighted MR imaging (DWI) ($p < 0.001$).

Conclusion: Clinical symptom of palpability or nipple discharge, number of core specimen, mammographic maximum lesion or mass size, SI on FS-T2WI, heterogeneous or rim enhancement on MR, and ADC value may be helpful in predicting the upgrade to invasive breast cancer for DCIS diagnosed at US-guided 14-gauge CNB.

1. Introduction

As the diagnostic breast imaging has been improved, the diagnosis of ductal carcinoma in situ (DCIS) has increased, which now accounts for almost 30% of newly diagnosed breast cancers [1]. DCIS is a preinvasive breast cancer wherein proliferating neoplastic cells are still confined by the mammary duct basement membrane [2]. Therefore, there should be no nodal metastasis theoretically and the use of sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND) is not routinely recommended for DCIS [1,3–7].

Percutaneous image-guided core needle biopsy (CNB) is performed as a reliable alternative to surgical biopsy for obtaining a histological diagnosis of breast lesions [8]. However, the major limitation of CNB is the possibility of histologic underestimation. In literatures, preoperative diagnosis of DCIS by CNB showed underestimation rates up to 52% of cases [1–7,9–16]. This is probably due to inherent sampling error in a lesion that contains both DCIS and invasive cancer. For this reason, several researchers have tried to determine the preoperative clinical, radiologic or pathologic risk factors predicting the upgrade to invasive cancer to avoid additional surgical procedures such as SLNB or ALND [1–7,9–16]. However, data were analyzed irrespective of imaging technique used for guidance (i.e., stereotactic, ultrasound [US], or MR imaging) or biopsy technique (i.e., gun biopsy or vacuum-assisted biopsy). Also, there is still little consensus among the described predictive factors from previous studies.

This study was performed to identify preoperative clinical and radiologic features that could be used to predict invasive breast

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cancer in women with a diagnosis of DCIS at US-guided 14-gauge CNB.

2. Materials and methods

This retrospective study was conducted with institutional review board approval and a waiver of patient informed consent.

2.1. Patients

Between January 2007 and March 2013, 3250 consecutive US-guided 14-gauge CNBs of breast masses were performed at our institute. After review of the pathologic results of these CNBs, we identified 107 DCIS lesions. Among these lesions, 21 lesions were excluded from this study due to complete remission of the lesion after neoadjuvant chemotherapy ($n = 1$) and no operation at our institute after CNB diagnosis ($n = 20$). A total of 86 DCIS lesions in 84 women who underwent surgical resection constituted the study population. All patients received curative surgery: breast conservative surgery ($n = 28$) and mastectomy ($n = 56$).

2.2. Biopsy procedure

CNBs were performed using high-resolution US units with 7.5–12 MHz or 4–15 MHz linear-array transducers (HDI 5000 or iU22, Philips Healthcare, Bothell, WA; Supersonic Imagine, Aix-en-Provence, France). An automated gun (Pro-Mag 2.2, Manan Medical Products, Northbrook, IL) and a 14-gauge Tru-cut needle with a 22-mm throw (SACN™ Biopsy Needle, Medical Device Technologies, Gainesville, FL) or 14-gauge dual-action semiautomatic core biopsy needle with 22-mm throw (Stericut with coaxial; TSK Laboratory, Tochigi, Japan) were used. Biopsies were performed by one of nine breast radiologists with fellowship training ($n = 5$) or clinical experience ($n = 4$), each of whom had 1–12 years of experience in breast imaging and biopsy with US guidance. Our standard protocol was that four or five core samples per lesion were obtained. In specific cases such as grossly inadequate tissue, targeting difficulty, non-cooperation or refusal of the patient to continue biopsy, or minor complications such as pain or bleeding, more or fewer core samples were occasionally obtained.

2.3. Data analysis

After review of the postoperative pathologic result, the final diagnoses of all lesions were categorized as two groups: DCIS group and invasive cancer group which includes microinvasive cancer, and the rate of upgrade to invasive cancer was assessed (i.e., the proportion of lesions yielding DCIS at CNB that were found at surgery to be invasive cancer). The recorded pathologic diagnoses from both the CNB and the surgical procedures were accepted for this study; the pathologic slides were not reviewed. The patients' medical records were reviewed and data on age, symptoms (i.e., palpable mass or bloody or nonbloody nipple discharge), and the procedural characteristics (the experience of US-guided 14-gauge CNB of the radiologist and the number of core specimens per lesion) were compiled.

To collect radiologic variables, each image was reviewed retrospectively in consensus by two radiologists with 3 and 8 years of experience in breast imaging, who were blinded to the upgrade to invasive carcinoma. The BI-RADS was adapted to describe the mammographic, US and MR imaging features [17]. Regarding mammography, the following features were evaluated: breast density, lesion visibility, lesion characteristics (mass, asymmetry, calcifications, or combined), and lesion size (the longest dimension of mass only, calcification only, and maximum lesion size whether it was mass, calcification, or combined). For a mass on mammography, its shape, margin, and density were determined. Regarding US, the following features were evaluated: lesion size, shape, margin, orientation, lesion boundary, echo pattern, posterior acoustic features, ductal change, and calcifications. Regarding MR imaging, dynamic contrast-enhanced MR imaging (DCE-MRI), fat-suppressed T2-weighted MR images (FS-T2WI), and diffusion weighted-image (DWI) with apparent diffusion coefficient (ADC) map were reviewed. On DCE-MRI, lesion size, lesion characteristics (mass or nonmass), lesion morphology (shape, margin, and internal enhancement in mass lesion; distribution and internal enhancement in non-mass lesion), and time–signal intensity curve pattern were evaluated. Time–signal intensity curve patterns were categorized into three patterns for the initial rise (fast, medium, slow) and the delayed phase (persistent, plateau, or washout). On FS-T2WI, the signal intensity (SI) of the lesion was visually evaluated to determine whether the SI of the lesion was lower than, equivalent to, or higher than that of the surrounding breast tissue. On the ADC map automatically acquired on the base of DWI with a b value of 0 and 1000 s/mm^2, the region-of-interest (ROI) was drawn manually with reference to DCE-MRI to include the entire tumor on the section including the largest tumor area. Areas of necrotic tissue, as identified from the morphologic and contrast-enhanced images, were avoided. The lesion ADC value was calculated as the mean of the voxels in the ROI using a monoexponential fitting model, and the average ADC was calculated for each lesion [18].

2.4. Statistical analysis

The predictive factors of DCIS underestimation were determined by comparing the upgrade rate for each clinical and radiologic variable. Statistical comparisons were performed by using the χ^2 or Fisher exact test or two-sample t-test. Regarding the number of core specimens, lesion size, and ADC values, results were compared by using a cut-off value for increasing likelihood of invasion which was decided by a receiver operating characteristic curve analysis and Youden index. Differences were considered to be statistically significant at $p < 0.05$. All statistical analyses were performed using statistical software (SAS, version 9.2; SAS institute, Cary, NC).

3. Results

Among 86 DCIS lesions at CNB, 27 (31.4%) were upgraded to invasive cancer after surgery.

Table 1 summarizes the comparison of clinical variables according to the upgrade to invasive cancer. Thirty-seven lesions (43.0%) were associated with the following symptoms: palpable mass ($n = 24$), bloody nipple discharge ($n = 10$), nonbloody nipple discharge ($n = 1$), or palpable mass with nonbloody ($n = 1$) or bloody ($n = 1$) nipple discharge. The presence of symptom showed a significantly higher upgrade rate (43% vs 22%; $p = 0.040$). Lesions from which core specimens less than five were obtained showed a significantly higher upgrade rate than five or more (45% vs 20%; $p = 0.011$). However, patient's age and the biopsy experience of radiologists showed no statistical significance.

Mammography was available for 78 lesions (Table 2). Masses that were at least 40 mm in size showed a significantly higher upgrade rate than masses that were smaller than 40 mm (53% vs 20%; $p = 0.046$). Lesions showing the maximum lesion size of 25 mm or larger showed a significantly higher upgrade rate than those smaller than 25 mm (44% vs 14%; $p = 0.022$). However, there was no significant difference in upgrade rate according to the other mammographic features (Table 2). Regarding US features, lesion that was 32 mm or larger in size showed a significantly higher upgrade rate than lesion that was smaller than 32 mm (55% vs 24%;