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Preoperative clinicopathologic factors and breast magnetic resonance imaging features can predict ductal carcinoma in situ with invasive components

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ABSTRACT

Purpose: Ductal carcinoma in situ (DCIS) is a non-invasive cancerous breast lesion; however, from 10% to 50% of patients with DCIS diagnosed by core needle biopsy (CNB) or vacuum-assisted core biopsy (VACB) are shown to have invasive carcinoma after surgical excision. In this study, we evaluated whether preoperative clinicopathologic factors and breast magnetic resonance image (MRI) features are predictive of DCIS with invasive components before surgery.

Materials and methods: Patients comprised 128 adult women with a diagnosis of DCIS as determined by pathological analysis of CNB or VACB specimens and positive MRI findings who underwent breast surgery during the period January 2011 to December 2013 at the Changhua Christian Hospital. Clinicopathologic and breast MRI factors were compared between patients with postoperative pathology indicative of true DCIS and those with postoperative pathology showing DCIS with invasive components.

Results: Of the 128 patients with a preoperative diagnosis of DCIS, 73 (57.0%) had postoperative histopathologic evidence of true DCIS and 55 (43.0%) showed evidence of DCIS with invasive components. Results of statistical analyses revealed that MRI evidence of a mass-like lesion ($P = 0.025$), nipple-areolar complex (NAC) invasion ($P = 0.029$), larger tumor volume ($P = 0.010$), larger maximum measurable apparent diffusion coefficient (ADC) area ($P = 0.039$), heterogenous or rim enhancement pattern ($P = 0.010$), as well as immunohistochemical evidence of human epidermal growth factor receptor 2 (HER-2) overexpression ($P = 0.010$) were predictive of DCIS with an invasive component in postoperative surgical specimens.

Conclusion: Invasive component should be considered in biopsy proven DCIS patients with preoperative MRI evidence of a mass-like lesion, nipple-areolar complex invasion, large tumor volume, a larger maximum measurable ADC area, or a rim or heterogenous enhancement pattern, as well as in patients with immunohistochemical evidence of HER-2 overexpression.

1. Introduction

Breast cancer is the most common type of cancer in women in most Western countries and is the leading cause of cancer death in many Asian countries, including Taiwan [1]. Breast cancer screening programs as well as improvements in diagnostic imaging [2] have resulted in a dramatic increase in the diagnosis of early stage breast cancer, particularly ductal carcinoma in situ (DCIS) [3],

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thereby allowing treatment regimens to be adopted before cancer progresses to invasive or metastatic stages.

DCIS is characterized histologically by the proliferation of malignant epithelial cells that are bounded by the basement membrane of the mammary duct [3]. Sentinel lymph node biopsy (SLNB) is not routinely performed in patients with DCIS because, in theory, DCIS does not metastasize to adjacent lymph nodes [3]. In clinical practice, however, a preoperative diagnosis of DCIS as determined by pathologic analysis of biopsy specimens does not preclude invasive disease in excised specimens. In fact, studies have shown that up to 50% (range, 3.5–56%) of excised DCIS specimens that were initially diagnosed preoperatively by core needle biopsy (CNB) or vacuum-assisted core biopsy (VACB) have an invasive component [4–26]. Therefore, methods that could detect or at least predict DCIS with invasive component before surgery would allow for more comprehensive care planning.

In this study, we investigated whether certain preoperative clinicopathologic factors and breast magnetic resonance image (MRI) features are predictive of DCIS with invasive component before surgery.

2. Materials and methods

2.1. Patients

Patients with primary DCIS as diagnosed by CNB or VACB and positive MRI findings who underwent breast surgery during the period January 2011 to December 2013 at the Changhua Christian Hospital were retrospectively recruited from the breast cancer database, which is maintained by the Comprehensive Breast Cancer Center of the Hospital. Patients who had received neoadjuvant chemotherapy and patients without detailed clinicopathologic data were excluded (Fig. 1). The study was approved by the hospital's institutional review board (IRB) (IRB No. 140404).

The clinicopathologic factors gathered from the database included age, sonographic tumor size, biopsy method, tumor grade, and status of estrogen receptor (ER), progesterone receptor (PR), and human epithelial growth factor receptor 2 (HER-2) expression. MRI-related factors included tumor size, nipple-areolar complex (NAC) status, enhancement pattern, and signal intensity on T2-weighted images, dynamic curves, enhancement peak, apparent diffusion coefficient (ADC) value, and measureable ADC area. Patients were separated into two groups, namely a DCIS group comprising patients with postoperative histopathologic evidence of true DCIS and a DCIS-IC group comprising patients with postoperative evidence of DCIS with invasive component (i.e., basement membrane invasion, characterized immunohistochemically by the lack of p63 staining in myoepithelial cells).

The clinicopathologic factors and MRI features were then compared between the two groups to better understand the variables that might be predictive of DCIS with invasive component.

2.2. Diagnostic imaging equipment

2.2.1. Sonography

Patients were imaged in the supine position with both arms over the head. Imaging was performed with a high resolution 5–12 MHz linear array transducer (Voluson 530D and 730D, Kretz Technik, Austria). Both breasts were examined in transverse and radial planes, and specific locations were targeted if there was a known lesion. Imaging reports were recorded according to the American College of Radiology (ACR) Breast Image Reporting and Data System (BI-RADS). Measurement of tumor size took the echo-poor center of the lesion and the echo-genic halo into account. The sonographic examinations were carried out by experienced, board-certified breast surgeons.

2.2.2. Magnetic resonance imaging and protocol

MR imaging was performed with a Siemens MAGNETOM Verio 3.0 Tesla MRI machine. All patients were imaged in the prone position with both breasts placed into a dedicated 16-channel breast coil. MR imaging protocols included the following: bilateral axial turbo-spin-echo fat-suppressed T2-weighted imaging (TR/TE 4630/70 ms; field of view 320 mm; slice thickness 3 mm; number of excitations 1), axial turbo-spin-echo T1 weighted imaging (TR/TE 736/9.1 ms; field of view 320 mm; slice thickness 3 mm; number of excitations 1), and diffusion weighted imaging (DWI) (TR/TE 5800/82 ms; field of view 360 mm; slice thickness 3 mm, with b values of 0, 400, and 800 sec/mm^2).

Dynamic contrast enhanced MR images (DCE-MRI) were obtained with a three-dimensional fat-suppressed volumetric interpolated breath-hold examination (VIBE) sequence with parallel acquisition once before and five times after a bolus injection of gadobenate dimeglumine (0.1 mmol/ kg). Both breasts were examined in the transverse plane at 60 s intervals in each phase of the dynamic studies. The dynamic MRI parameters were as follows: TR/TE 4.36/1.58 ms; field of view 320 mm; slice thickness 1 mm.

ADC maps were acquired from diffusion-weighted images with b values of 0, 400, and 800 sec/mm^2. The region-of-interest (ROI) was manually selected on the ADC maps corresponding as closely as possible to the location and size seen on DCE-MR images. Necrotic areas seen on contrast-enhanced images were avoided. The ADC value was calculated as the mean of the voxels in the ROI. The ADC value and ROI area of each lesion in the same patient were obtained, and the lesion with the lowest ADC value was recorded. The following characteristics on MR images were used to define NAC invasion: dilatation and enhanced lactiferous duct, nipple inversion or retraction, periareolar skin thickening, and NAC enhancement.

Measurements of tumor size and tumor volume on MR images were calculated using a commercially available MRI computer aid diagnosis (CAD) system (DynaCAD, Version 2.1, In vivo, Gainesville, FL.). To avoid underestimating the tumor volume due to a blooming effect and early periductal enhancement, the result was manipulated by an experienced radiologist after computer-based tumor segmentation. All of the MRI readings were interpreted by an experienced, board-certified breast imaging radiologist (HKW), who had a 29-years radiologist career and 10 years' experience of breast MRI.

2.3. Vacuum-assisted core biopsy (VACB) procedure

VACB was performed in patients in whom sonographic examination was unable to detect microcalcification lesions. After locating the lesion using a stereotactic technique, a 10-gauge EnCor needle or a 9-gauge ATEC needle was placed inside the microcalcification lesion and multiple core specimens were obtained from different sites via vacuum assistance by rotating the needle aperture. In general, 12 samples were harvested in each patient (mean 16, range 10–20). When sufficient tissue had been harvested, the needle was removed. A radio-opaque marker was then placed at the site from which the specimens had been obtained and the core tissue samples were sent to the department of pathology for histological evaluation. Mammography was performed after the biopsy procedure to confirm the presence or absence of hematoma at the biopsy site.

2.4. Core needle biopsy (CNB) procedure

The CNB procedures were performed using a free hand technique with a 14-gauge automated or 16-gauge Tru-Cut needle and a spring-loaded biopsy gun (Magnum, Bard, Covington, GA, USA)