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IS PRE-OPERATIVE AXILLARY STAGING WITH ULTRASOUND AND ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION RELIABLE IN INVASIVE LOBULAR CARCINOMA OF THE BREAST?

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Abstract—Axillary ultrasound (US) with US-guided fine-needle aspiration (US-FNA) for suspicious lymph nodes is important for pre-operative staging and planning of surgical management. Invasive lobular carcinoma (ILC) metastases were previously thought to be difficult to detect, but with a limited amount of evidence. This study investigated the ability of US and US-FNA to detect ILC metastases by assessing 142 patients with ILC. The sensitivity of US in detection of metastasis was 52.3%, and US was able to exclude 96% of N2 and N3 axillary metastases. The false-negative rate of US-FNA in detection of metastasis for suspicious lymph nodes on US was 34.8%, and lymph nodes with longer maximal dimensions were associated with false-negative US-FNA results. Multiplicity of breast lesions and maximal cortical thickness ≥3.1 mm of lymph nodes were independently associated with metastasis. Although pre-operative US in ILC can reliably exclude advanced axillary nodal disease, US-FNA results should be carefully interpreted. (E-mail: mines@yuhs.ac)   © 2016 World Federation for Ultrasound in Medicine & Biology.

Key Words: Breast, Lobular carcinoma, Ultrasound, Fine-needle aspiration, Axillary lymph node metastasis.

INTRODUCTION

Pre-operative, imaging-based staging of the axilla in breast cancer patients consists of ultrasound (US) with selective US-guided fine-needle aspiration (US-FNA) for morphologically suspicious lymph nodes (Bonnema et al. 1997; Houssami et al. 2011; Verbanck et al. 1997). Axillary lymph nodes are found with US, and US-FNA is performed on the most suspicious lymph node. When the US-FNA finding is positive, sentinel lymph node biopsy (SNLB) can be skipped, with the patient undergoing axillary lymph node dissection (ALND). Neoadjuvant chemotherapy can also be considered before surgery. When the US-FNA finding is negative, the patient undergoes SLNB for further evaluation. (Bonnema et al. 1997; Houssami et al. 2011; Verbanck et al. 1997). The American College of Surgeons Oncology Group Z0011 trial report suggested that early-stage (clinical T1/T2 N0 M0) breast cancer

patients with limited sentinel lymph node metastasis may be appropriately treated with breast conservation surgery and whole-breast radiation therapy in lieu of completion ALND (Giuliano et al. 2010, 2011). The ability to confidently exclude N2 and N3 disease with pre-operative US could obviate the need for completion ALND in certain patients, potentially decreasing patient morbidity (Neal et al. 2010). Neal et al. reported that although pre-operative axillary US excluded 96% of N2 and N3 metastases in invasive ductal carcinoma (IDC), it missed 17% of N2 and N3 metastases in invasive lobular carcinoma (ILC).

ILC constitutes approximately 5% to 15% of all breast cancers and is the second most common histologic breast cancer type after IDC (Li et al. 2003). ILCs are often poorly delineated because of a lack of a desmoplastic reaction (Fisher and Fisher 1977; Martinez and Azzopardi 1979) and can be more difficult to detect than IDC by palpation or by mammography (Le Gal et al. 1992; Urban and Castro 1971). This may delay diagnosis, which may explain why ILCs are larger than IDCs, and patients with ILCs are older than those with IDCs at diagnosis (Arpino et al. 2004; Sastre-Garau et al. 1996; Silverstein et al. 1994b). However, larger

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ILC size does not absolutely lead to an increased probability of lymph node metastasis, based on similar or lower rates of lymph node metastasis compared to IDC (Arpino et al. 2004; Sastre-Garau et al. 1996; Toikkanen and Pylkkänen 1997; Topps et al. 2014; Yeatman et al. 1995). This discrepancy may be explained by the low histologic grade (Arpino et al. 2004; Sastre-Garau et al. 1996; Toikkanen and Pylkkänen 1997) and high ER positivity of ILC (Arpino et al. 2004; Sastre-Garau et al. 1996; Topps et al. 2014). Because ILC is relatively rare compared with IDC, studies addressing the reliability of pre-operative axillary US and US-FNA in detection of lymph node metastasis are limited and report conflicting results (Boughey et al. 2007; Hackney et al. 2013; Sankaye et al. 2014; Topps et al. 2014). One study reported decreased US sensitivity in the axillary staging of ILC compared with IDC (Hackney et al. 2013), whereas other studies did not find significant differences (Boughey et al. 2007; Sankaye et al. 2014; Topps et al. 2014). Several studies also reported that, compared with IDC, US-FNA or core-needle biopsy (CNB) had decreased sensitivity in ILC (Hackney et al. 2013; Topps et al. 2014), whereas other studies did not find significant differences (Boughey et al. 2007; Sankaye et al. 2014).

Therefore, the purpose of this study was to investigate the diagnostic performance of pre-operative axillary US and US-FNA and to evaluate the clinicopathologic and US features associated with lymph node metastasis in ILC.

METHODS

This retrospective study was approved by the institutional review board, and the requirement for informed consent was waived.

Patients

Since 2007, bilateral axillary US has been performed along with breast US for all patients undergoing breast US at our institution. Between July 2007 and January 2014, 3951 consecutive patients underwent surgery for breast cancer at our institution. Of these patients, 144 (3.6%) were diagnosed with pure ILC by surgery. Two patients who had a recurrence at the chest wall after a previous mastectomy were excluded. Therefore, 142 patients diagnosed with pure ILC by surgery were included. All included patients had undergone pre-operative breast and axillary US examinations.

US and US-FNA

Pre-operative US was performed by 1 of 11 breast radiologists (4 faculty members with 6 to 16 y of experience and 7 fellows with 1 to 2 y of experience) using 5- to 12-MHz linear transducer US machines (Phillips ATL HDI, iU22, Phillips Advanced Technology Laboratories, Bothell, WA, USA; or GE LOGIQ 9, GE Medical Systems, Milwaukee, WI, USA). Suspicious US features for metastasis were a round shape, an eccentric thick or irregular nodular cortex and an eccentric or absent fatty hilum (Alvarez et al. 2006; Choi et al. 2009; Koelliker et al. 2008). Lymph nodes were regarded as suspicious when one or more of these US features were observed by the radiologist. US-FNA was performed for all patients with one or more suspicious lymph nodes. If a patient had two or more suspicious lymph nodes, the most suspicious lymph node was aspirated. US-FNA was performed with a 23-gauge needle and a 2-mL syringe using the to-and-fro method without local anesthesia and without an aspirator.

Patient treatment and reference standard

Neoadjuvant chemotherapy was administered when indicated, at the discretion of the medical oncologist. Patients with axillary lymph node (ALN) metastases confirmed by US-FNA proceeded directly to ALND. Other patients (e.g., patients with no suspicious lymph nodes at US or negative cytology at US-FNA) underwent SLNB. If metastasis was confirmed at SLNB, ALND was performed. Final surgical histopathologic results of either SLNB or ALND were used as reference standards.

Data and statistical analysis

Clinicopathologic and US features were collected through a review of medical records, and features were categorized as follows: age (<50 y or ≥50 y); location of the main tumor (right or left); palpability of the main tumor and ipsilateral ALN; tumor size, defined as the largest diameter on US (clinical T stage); tumor size, defined as the invasive tumor size on surgical pathology (pathologic T stage); pathologic N stage of ALNs (N0 = no metastasis, N1 = micrometastasis defined as a small cluster of cells >0.2 mm and/or >200 cells but none >2.0 mm or metastases in 1–3 ALNs with at least one metastasis >2.0 mm, N2 = metastases in 4–9 ALNs, and N3 = metastases in ≥10 ALNs) categorized according to the current American Joint Committee on Cancer recommendations (Edge and Compton 2010); multiplicity of breast lesions determined by imaging finding (single or multiple, defined as the presence of two or more tumor foci within a single quadrant of the breast [multifocal] or within different quadrants of the same breast [multicentric]); histologic grade reported on surgical pathology reports (low, intermediate or high) (Bloom and Richardson 1957); and estrogen receptor (ER), progesterone receptor (PR) and HER-2 status. Multiplicity of breast lesions was prospectively determined from imaging findings by the radiologist who