Original Investigation

Shear Wave Speed of the Lesion in Preoperative Breast Ultrasonography: Association with Disease-free Survival of Patients with Primary Operable Invasive Breast Cancer

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Rationale and Objectives: We aimed to investigate the relationship between shear wave speed (SWS) of the lesion on preoperative breast ultrasonography (US) and disease-free survival of patients with primary operable invasive breast cancer.

Materials and Methods: This retrospective study was approved by our Institutional Review Board. The requirement for informed consent was waived. A total of 195 consecutive newly diagnosed invasive breast cancer patients (age 33–83 years; mean 54.0 years) with preoperative breast US with SWS measurement of the lesion were identified. They underwent surgery between May 2012 and May 2013. SWS was measured at the center and three marginal zones in the main tumors, and the maximum value was used for analyses. For 35 patients who underwent primary systemic therapy (PST), the maximum SWS before PST was used. Cox proportional hazards modeling was used to identify the relationship between clinical-pathologic factors and disease-free survival.

Results: Fourteen recurrences occurred at 6–47 months (mean 22.3 months) after surgery. On multivariate analysis, a positive history of PST (hazard ratio [HR] = 4.93; 95% confidence interval [CI]: 1.66, 14.70; $P = .004$), adjuvant chemotherapy (HR = 3.67; 95% CI: 1.11, 12.1; $P = .033$), and higher maximum SWS (HR = 1.55; 95% CI: 1.07, 2.23; $P = .020$) were associated with poorer disease-free survival.

Conclusion: Higher maximum SWS on preoperative US, in addition to a positive history of PST and adjuvant chemotherapy, was significantly associated with poorer disease-free survival of patients with invasive breast cancer.

Key Words: Breast cancer; ultrasound; shear wave; recurrence; disease-free survival.

INTRODUCTION

Breast cancer is one of the most common malignancies and a leading cause of cancer mortality among women. Although a multidisciplinary approach including the development of screening and adjuvant therapy has improved the mortality rate (1,2), there are still more than 500,000 women who die from this malignancy per year worldwide (3). In planning therapeutic options for each breast cancer patient, it is beneficial to develop a prognosis. Studies have shown that information acquired from preoperative images including breast magnetic resonance imaging (MRI) can be used as prognostic factors (4–7).

Shear wave elastography is a method of quantitatively measuring tissue elasticity during breast ultrasonography (US) examinations. Focused acoustic radiation force pushing pulses of short duration and the speed of the shear waves that are propagated in a direction orthogonal to the direction of the tissue are measured (8). The shear wave speed (SWS) of the lesion reflects tissue stiffness. SWS can easily be measured in clinical settings, and its use has been reported to improve accuracy in differentiating breast cancers and benign lesions (9–17) when used in addition to B-mode ultrasound during breast screening and diagnosis. In addition, several studies have shown

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that shear wave elastography of breast cancer lesions is significantly associated with prognostic factors, including tumor size, immunohistochemical biomarkers, lymph node metastasis, and vascular and lymphovascular invasion (18–22). From these results, it is plausible that shear wave elastography could be useful for predicting outcomes, including tumor recurrence and metastasis, although these correlations have not been evaluated in previous investigations.

Therefore, the purpose of our current study is to investigate the relationship between SWS of the lesion on preoperative breast US and disease-free survival of patients with primary operable invasive breast cancer.

MATERIALS AND METHODS

Study Population

This retrospective study was approved by our Institutional Review Board. The requirement for informed consent was waived. In total, 324 consecutive patients who were newly diagnosed with breast cancer and underwent surgery from May 2012 to May 2013 were identified through a review of the medical records. Among them, 129 patients were excluded from the analysis because preoperative breast US with SWS measurements of the breast lesion was not performed ($n = 98$) or surgery was performed for noninvasive breast cancer ($n = 31$). As a result, 195 patients with invasive breast cancer were enrolled in this study (Fig 1). This population includes 35 patients who had undergone primary systemic therapy (PST) before surgery.

Preoperative US Examinations

Preoperative US examinations were performed by one of five ultrasound technologists with 3–10 years' experience in breast ultrasound. Conventional US was performed using the ACUSON S2000 ultrasound system (Siemens Medical Solutions, Mountain View, CA) equipped with a linear array transducer with a bandwidth of 6–18 MHz, and SWS measurements were conducted with a linear array transducer with a bandwidth of 4–9 MHz.

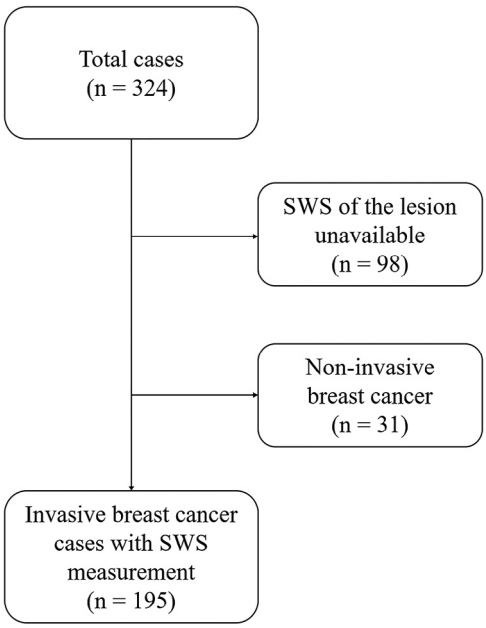

Figure 1. The patients' enrollment criteria. SWS, shear wave speed.

SWS was measured first at the center of the lesion, and then at three (superficial and two lateral) marginal zones of the lesion using a 5×5 mm region of interest (ROI) (Fig 2). To measure SWS at each spot, technologists placed the ROI onto a target and held the probe to prevent it from moving. They then pressed a button to start the SWS measurement. Upon completion of the measurement, the ultrasound system was stopped automatically and placed on hold during a cooling time, which is required to avoid an excessive increase in temperature at the surface of the probe and inside of the body. SWS measurements were conducted three times at each spot (corresponding to a total of 12 SWS measurements for each lesion), and the maximum value was used for analyses. During SWS measurement, a result of "X.XX m/s" sometimes occurred, and this phenomenon was presumably associated with several factors: the measurements were outside the tolerable range of the system for shear wave velocity calculation, the tissue inside the ROI was heterogeneous, or a liquid component was present in the ROI (17). Maximum SWS was confirmed among scores that were successfully measured after discarding "X.XX m/s" results (eg, when "X.XX" display was acquired for 2 of a total of 12 SWS measurements, the maximum SWS was chosen among the 10 remaining successfully acquired scores). Maximum diameter of the breast tumor and presence and/or absence of ipsilateral axillary lymphadenopathy were also evaluated during the same examination. In 18 cases with multifocal or multicentric cancers and 15 cases with bilateral breast cancers, the maximum SWS of the lesion with the largest diameter was used so that the analyses could be performed on a per-patient basis; for patients who underwent PST, maximum SWS was measured before PST was administered.

Clinical-Pathologic Evaluation

Information including patient age, type of surgery (mastectomy or lumpectomy), history of PST, and adjuvant therapies including chemotherapy, hormone therapy, and radiation therapy were obtained through medical records. Estrogen receptor status, progesterone receptor (PgR) status, human epidermal growth factor receptor-2 (HER2), and nuclear grade (1 or 2 vs 3) were assessed based on the results of percutaneous biopsy before treatment. HER2 staining status was scored as 0, 1+ , 2+ , or 3+ , and tumors with scores of 3+ were considered to be HER2 positive, whereas those with scores of 0 or 1+ were considered to be HER2 negative. Tumors with scores of 2+ were further evaluated with in situ hybridization. Recurrence included breast cancer recurrence (local-regional or distal) or new primary contralateral breast cancer (invasive or ductal carcinoma in situ).