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● *Original Contribution*

BETTER OVERALL SURVIVAL FOR BREAST CANCER PATIENTS BY ADDING BREAST ULTRASOUND TO FOLLOW-UP EXAMINATIONS FOR EARLY DETECTION OF LOCOREGIONAL RECURRENCE—A SURVIVAL IMPACT STUDY

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Abstract—We retrospectively reviewed patient records to evaluate the effectiveness of our 15 y of ultrasound (US) surveillance of recurrent breast disease in comparison with mammography (MM) and clinical examination. From 4796 stage 0–III breast cancer patients who had received surgical treatment, we identified locoregional recurrence (LRR) in 161 patients. The mean age of the 161 patients was 48 y (27–82 y), and the mean follow-up interval was 77.2 mo (11–167 mo). The methods of LRR detection, sites of LRR and overall survival (OS) were examined. Multivariate Cox survival analysis showed significantly better survival in groups detected by US (hazard ratio = 0.6, *p* = 0.042). The 10-y LRR OS by detection types for US (n = 69), clinical examination (n = 78) and MM (n = 8) were 58.5%, 33.1% and 100%, respectively (*p* = 0.0004). US was seen with better OS associated with the effective early detection of non-palpable LRR breast cancer, which is mostly not detectable on MM. (E-mail: wctsai@kfsyscc.org) © 2016 World Federation for Ultrasound in Medicine and Biology.

Key Words: Breast cancer, Follow-up, Ultrasound, Locoregional recurrence, Clinical examination.

INTRODUCTION

The combination of early diagnosis and effective treatment of breast cancer has led to a significant decrease in breast cancer–related mortality (Lu et al. 2009). However, irrespective of the surgical methods, breast cancer survivors still face long-term risks of locoregional recurrence (LRR) (Saphner et al. 1996), which could be a local recurrence (LR), regional recurrence (RR) or both. An LR is recurrent breast cancer in the ipsilateral breast or chest wall, while an RR is a recurrent metastasis through lymphatic pathways to the ipsilateral axillary, supraclavicular or internal mammary nodes. To manage the risks, routine follow-up history taking, clinical examination (CE) and annual mammography (MM) of the breast tissues are done as recommended surveillance protocol for detection of breast cancer recurrences (Khatcheressian et al. 2013).

In our institution, the follow-up surveillance protocol of locoregional condition after primary treatment of breast cancer calls for annual MM with a breast ultrasound (US) at 6 mo points for the first 5 y and alternating annual imaging between MM and US thereafter. The CE is done at each return visit in addition to the imaging examination (Table 1). We add US surveying to the follow-up protocol because 89% of women examined in our institution have breasts that are heterogeneous or extremely dense, which lowers the sensitivity on mammogram (Tsai et al. 2013). Also, women aged 40 y or younger with even denser breasts make up a large percentage (29.3%) of breast cancer population in our country (Cheng et al. 2000). Hence, US is routinely used for pre-treatment staging and post-treatment annual follow-up of breast cancer in our hospital.

Another reason for the routine US examinations is related to the RR. The axillary and supraclavicular lymph nodes are the most common sites of RR (Galper et al. 1999). When it comes to the detection of axillary lymph nodes, CE is associated with a 39% false-negative rate (Smart et al. 1978). MM cannot cover the entire axillary

Table 1. Post-treatment follow-up protocol for breast cancer patients

Time (OP)	0 < OP < 2 y				2 y < OP < 5 y				OP > 5 y			
	3 mo	6 mo	9 mo	1 y	3 mo	6 mo	9 mo	1 y	3 mo	6 mo	9 mo	1 y
CE	○	○	○	○		○		○				○
MM				○				○				○*
US		○				○						

CE = clinical examination; MM = mammography; OP = operation for primary breast cancer; US = ultrasound.
* Alternated annual US or mammography.

area, nor can it evaluate the supraclavicular or internal mammary nodes. On the other hand, US is known for its effective detection of RR (Iyengar et al. 2012).

The role of US and its impact on OS, compared with CE and MM, in detecting occult malignancy in asymptomatic, treated women has been reported but with limited reviews of relatively low LRR numbers (10–81) and short follow-up study intervals (2–3 y) (Kim et al. 2010, 2011; Lee et al. 2013; Moon et al. 2009). We were curious to see if our US utilization for LRR detection has achieved any significant survival benefit compared with two other detection methods, CE and mammogram, for early detection of clinical occult LRR of breast cancer.

MATERIALS AND METHODS

This retrospective study was approved with a waiver of the requirement to obtain informed consent by Koo Foundation Sun Yat-Sen Cancer Center Institutional Review Board.

Patient selection

From January 2000 to September 2009, 4796 breast cancer patients with stage 0–III disease underwent breast conserving surgery (n = 1554; 32.4%) or mastectomy (n = 3242; 67.6%) in our cancer center. Those with bilateral breast cancer, distant metastasis at diagnosis and second primary breast cancer were excluded. During the follow-up period ending in October 2013, a total of 25,990 US examinations, 24,785 MM examinations, 2220 US-guided fine-needle aspirations or biopsies and 116 stereotactic vacuum-assisted biopsies were performed for our study cohort (n = 4796). Two hundred sixteen (4.5%) patients were diagnosed with contralateral breast cancer and 161 (3.36%) patients with LRR (Fig. 1). These 161 patients with LRR were selected and their data were analyzed. In our institution, a data manager in the department of clinical research entered and annually updated the clinical data of our breast cancer patients receiving treatment. Among the 161 patients, 34 patients refused our suggested treatment or were lost to follow-up after their LRR diagnosis in our hospital. To avoid selection bias, we still include the overall survival data and detection methods that we had from these 34 patients

for analysis. The date of death of these 34 patients were obtained (with Institutional Review Board approval) from the national mortality profile in our National Ministry of Health and Welfare.

CE method

The CE is performed by a physician during each clinic visit on both breasts (or chest wall after mastectomy), bilateral axillary fossa and supraclavicular regions for any suspicious signs of LRR.

MM examination and quality control

MM examinations are performed using several mammographic scanners: Senographe DMR+ and Senographe DS, (GE Medical, BUC, Cedex, France); Mammomat 1000, (Siemens, Erlangen, Germany); Selenia, (Hologic, Bedford, MA, USA). The two-view (medial-lateral oblique and cranial-caudal) MM was performed on all patients. For post-mastectomy patients, we only performed the MM of the contralateral breast. In the event of any suspicious MM finding, a diagnostic US would be performed before tissue diagnosis. We sought to maintain the highest possible imaging quality level by implementing the quality control according to the American College of Radiology regulation.

US examination methods, interpretation and quality control

The US examinations were performed by breast technologists who have more than 3 y of experience using digital sonographic scanners (iU22 and HDI 5000, Philips Medical, Bothell, WA, USA; V730 Expert, GE Medical, Zipf, Austria) for US examination in our institution. The probes used were broadband linear array transducers with a 5–12 MHz or 6–12 MHz extended operation frequency range. The scanning areas covered the bilateral breasts (or the chest wall after mastectomy), axillar and supraclavicular, internal mammary nodes of the original cancer side. The scanning was performed in a clockwise direction for bilateral breasts, from the nipple to the outer quadrants. At each clock direction when moving away from the nipple, the scanning would cover the inner rings of scanning. If there were any suspicious lesions, the radial and anti-radial images would be taken. Color Doppler