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Original article

Low re-excision rate for positive margins in patients treated with ultrasound-guided breast-conserving surgery

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ABSTRACT

Background: Re-excision is a necessary procedure in obtaining clean margins for breast-conserving surgery (BCS)-treated patients. Re-excision rates vary widely among different breast cancer management procedures. The aim of this study was to evaluate the efficacy of ultrasound (US)-guided BCS to decrease the re-excision rate in patients with US-detectable breast cancer, as well as the relationship between positive margins and ultrasonographic characteristics of tumor.
Methods: Between 2008 and 2009, we identified consecutive patients who underwent initial US-guided BCS for breast in situ or invasive carcinoma, which was preoperatively detected using US examination and on the basis of image-guided biopsy findings. The margins achieved after BCS were separately assessed by performing frozen section analysis of shaved margins. The negative margin and positive margin groups were compared for clinicopathological features and ultrasonographic findings.
Results: Of 381 patients undergoing US-guided BCS, 126 (33.1%) had palpable tumors and 255 (66.9%) had nonpalpable tumors. Positive margins were noted in 35 patients (9.2%). These patients underwent re-excision and were margin-free; no further surgery was required for these patients. There were no significant intergroup differences in clinicopathological features and ultrasonographic findings.
Conclusion: Breast US is an effective modality for intraoperative tumor localization and can thus help obtain clean margins and reduce the re-excision rate in cases in which breast-conserving therapy has been performed. Furthermore, frozen section analysis of cavity shaved margins is a feasible method for minimizing the need for further surgery.

Introduction

Breast-conserving surgery (BCS) plus adjuvant radiotherapy has become the alternative operative treatment to mastectomy for early-stage breast cancer, with evidence from randomized controlled trials showing equivalent survival.[1,2] Resection margin residual tumor is the most significant risk factor for local recurrence after BCS.[3–5] To obtain an adequate free pathologic margin, re-excision is commonly performed in patients who have undergone breast-conserving therapy. The re-excision varies widely among different treatments, varying from 4.2% to 59%.[6–11] In order to improve adverse event of cosmesis, save cost and time and to relieve patients' anxiety, it is necessary to reduce the additional procedures such as re-excision or repeat operations for positive or close margin after BCS.

There are several studies documented in the literature that demonstrate that the use of intraoperative US for either palpable[12–14] or nonpalpable breast cancers[6,15,16] can lower rates of re-excision following BCS. Additionally, several techniques for intraoperative margin assessment can be used to avoid positive margin in BCS, including frozen section analysis,[17] cavity shaving margin,[18] touch preparation cytology,[19–21] intraoperative specimen radiography,[5] intraoperative sonography[22] and gross examination of lumpectomy specimens.[23] The best procedure for intraoperative margin assessment is debatable, and it intraoperatively depends on equipment availability and surgical experience.

In our institution, breast US was routinely performed preoperatively for breast cancer patients. In cases in which US revealed cancerous lesions, BCS with US guidance was performed. With regard to intraoperative margin assessment of BCS, frozen section analysis was performed to assess shaved cavity margins.

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We hypothesized that the positive margin can be reduced in patients undergoing BCS by performing US-guided examination, leading to better surgical planning and more precise tumor localization, which in turn would result in low re-excision rates. The primary aim of this study was to assess the efficacy of US-guided BCS in obtaining clean margins and to determine whether some specific clinicopathological factors and ultrasonographic features could be predictors of positive margin. We also examined frozen section analysis of cavity shaving margins as a technique for accurate intraoperative margin assessment.

Patients and methods

Patients

The study was approved by the institutional review board. Between January 2008 and December 2009, we conducted a retrospective review of the data of breast cancer patients recorded in a database at Chang Gung Memorial Hospital. We identified 381 patients who underwent initial US-guided BCS for breast cancer in situ or invasive carcinoma that could be detected by US and confirmed by image-guided biopsy, and not excisional biopsy. Of 381 patients undergoing US-guided BCS, 126 (33.1%) had nonpalpable tumors and 255 (66.9%) had palpable tumors. Eighty-eight of the 381 patients (23%) had screen-detected tumors and the other 293 patients (77%) had symptomatic tumors. Demographic and pathologic data collected included data on age, tumor size, histology, histological grade, lymph node status, estrogen receptor (ER) status, progesterone receptor (PR) status, and human epidermal growth factor receptor 2 (HER-2) expression status.

Pre-operative breast ultrasonography examination

All patients underwent preoperative US examination with either Philips IU22 or Philips HDI 5000 US machine equipped with a 5–12 MHz linear array transducer (Bothell, WA). A US examination helps assess lesions in terms of size, shape, margin, presence of a lateral refraction sign, anteroposterior (AP)/width (W) ratio, presence of changes in the surrounding tissue changes, and presence of a mass with or without microcalcification.

Surgical procedure

The surgeon performed US-guided tumor localization with the same devices as those used for preoperative US examination. The ultrasonographic transducer was placed in a radial and anti-radial plane over the center of the tumor, and the skin was marked depending on the extent of tumor. The skin flap was designed to cover the part of the tumor that was closest to the overlying skin and the previous needle puncture hole and was marked on the skin. The distance between the planned incision margin and the tumor edge was 1 cm. BCS was performed along the skin markers, and the pectoralis fascia was routinely removed as the deep margin. The excision specimen was marked with silk stitches for orientation at the medial, lateral, superior, and inferior boundaries. Four pieces of breast tissue were excised by taking less than 0.5-cm–thick shavings from the walls of the cavity and were labeled as medial, lateral, superior, and inferior cavity margins. Frozen section analysis of these cavity shaving margins was immediately performed by a pathologist. If intraductal or invasive carcinoma was detected, re-excision of the involved margin would be carried out to achieve negative cavity margin status during the same operation. Negative margin was defined as at least 2 mm for both ductal carcinoma in situ (DCIS) and invasive carcinoma .A tumor-free margin of less than 2 mm was termed as close margin. Re-operation was considered to be performed for either a cavity shaving margin that was proven negative on frozen section analysis but positive on permanent pathology, or if permanent pathology identified a positive or close margin in the excision specimen.

Final pathologic examination

After formalin fixation and staining with hematoxylin and eosin, all frozen sections were examined by microscopy. True margin was inked for the re-excision specimen, which was also sutured with silk for orientation. The permanent pathology of tumor specimens was examined for tumor size in 3 dimensions, histological type, ER status, PR status, HER-2 expression status, histological grade, and the tumor margin distance (distance between the tumor and cut edge of the specimen) from 6 sites.

Statistical methods

To assess the association between the documented variables and the existence of a positive margin, categorical variables were compared by Pearson's chi-square test and continuous variables were assessed using *t* test. The logistic regression model was used for multivariate analysis. The dependent variable was the existence of positive margin (no/yes). Independent variables were age, tumor size, axillary lymph node status (negative/positive), tumor histological type (DCIS, invasive ductal carcinoma, invasive lobular carcinoma, or others), tumor grade (low/high), ER status (negative/positive), PR status (negative/positive), HER-2 expression status (negative/positive), tumor shape (smooth/irregular), tumor margin (circumscribed/non-circumscribed), lateral refraction sign (none, mild, or marked), AP/W ratio ($\leq 0.7 / > 0.7$), change of surrounding tissue (no/yes), and mass with microcalcification finding (no/yes). In tumor grade classification, low- and intermediate-grade DCIS and grade I and II invasive carcinoma were classified as low-grade carcinomas, whereas high-grade DCIS and grade III invasive carcinoma were classified as high-grade. A P value equal to or less than 0.05 was considered statistically significant. All statistical analyses were carried out using SPSS software, version 13.0 (SPSS Inc., Chicago, IL, USA).

Results

From January 2008 to December 2009, a total of 381 patients consecutively undergoing breast conserving surgery with ultrasound guidance for breast in situ or invasive carcinoma. The mean age of the patients was 49.7 years (range 29–94 years). The mean tumor size was 1.58 cm (range 0.03–5.50 cm) and was highly correlated with the mean tumor diameter measured by US ($P < 0.0001$). The mean tumor diameter measured by US was 1.88 cm (range 0.51–8.5 cm). By histological type of preoperative image-guided biopsy, 274 (71.9%) were IDC, 75 (19.7%) were DCIS and 8 (2.1%) were ILC.

Of the 381 patients, 346 patients (90.82%) underwent BCS with negative margin and 35 patients (9.18%) underwent BCS with re-excision for positive margin. The mean age of BCS with negative margin group was 49.6 years (range 24–94 years) and BCS with positive margin group was 51.1 years (range 34–89 years). One of the 35 patients underwent re-excision twice during the operation to achieve negative margin status. The remaining 34 patients underwent re-excision once because of a finding of positive cavity shaving margin on frozen section analysis. Frozen section analysis of initial positive cavity shaving margin sites indicated that a single margin was involved in 28 (80%) patients who underwent re-excision and multiple margins were involved in 7 (20%). Permanent pathology of excision specimens revealed that in 5 patients only one margin site was involved. Overall of these 5 patients had