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Role of specimen US for predicting resection margin status in breast conserving therapy

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SUMMARY: **Role of specimen US for predicting resection margin status in breast conserving therapy.**

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Aim. *To assess the diagnostic accuracy of specimen ultrasound (US) for predicting resection margin status in women undergoing breast conserving therapy for US-detected cancer, having the histological findings as the reference standard.*

Patients and methods. *A total of 132 consecutive patients (age range, 34-87 years; mean, 51 years) underwent breast-conserving surgery for US-detected invasive breast cancer. All surgical specimens underwent US examination. The presence of lesion within the specimen and its distance from the specimen margins were assessed considering a threshold distance between the lesion and specimen margins of 10 mm. US findings were then compared with the pathological ones and specimen US. Sensitivity, specificity, diagnostic accuracy, positive (PPV) and negative predictive values (NPV) for predicting histological margin status were evaluated, having the histological findings as the reference standard.*

Results. *The histological examination detected invasive ductal carcinoma in 96/132 (73%) cases, invasive lobular carcinoma in 32/132 (24%), mucinous carcinoma in 4/132 (3%). The pathological margin analysis revealed 96/132 (73%) negative margins and 36 (27%) close/positive margins. US examination detected all 132 breast lesions within the surgical specimens. 110 (83%) negative margins and 22 (17%) positive margins were found on US. Sensitivity, specificity, diagnostic accuracy, PPV and NPV of 44%, 94%, 80%, 73% and 82%, respectively, were found for specimen US.*

Conclusions. *Specimen US represents a time and cost saving imaging tool for evaluating the presence of US detected-breast lesion within surgical specimen and for predicting the histological margin status.*

KEY WORDS: Breast cancer - US - Specimen - Resection margin.

Introduction

The widespread use of mammography and breast ultrasound (US) have increased the detection of clinically occult breast lesions, allowing an earlier diagnosis of breast cancer and a breast conserving surgery in women with early stage breast cancer (1, 2).

Non-palpable lesion management requires preoperative wire guided tumor localization and intra-operative imaging assessment of the surgical specimen in order to achieve a complete lesion surgical excision with negative resection margins (1, 2).

The resection margin assessment is required to prevent the risk of local recurrence and re-excision, including re-operative lumpectomy or mastectomy, in women undergoing breast conserving surgery (3-6).

The intra-operative surgical specimen imaging assessment includes radiography and US (4-6).

As regard to surgical specimen radiography, it has been reported that the comparison between the radiological and histological diagnoses had 66% sensitivity, 86% specificity, 74% positive predictive value and 81% negative predictive value. Therefore, specimen radiography was reliable for identifying clear margins (74% positive predictive value) and reduced the rate of re-operation from 31% to 20% (7, 8).

With regard to US specimen examination, no general consensus exists in the medical literature. In fact, some authors stated that US represents an effective procedure for identifying lesions within specimen; on the other hand, other authors reported a poor performance in the evaluation of surgical specimen margin status (9-11).

The aim of our study is to assess the diagnostic ac-

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curacy of specimen US for predicting resection margin status in women undergoing breast conserving therapy for US-detected cancer, having the histological findings as the reference standard.

Patients and methods

Between April 2010 and March 2015, a total of 132 consecutive patients (age range, 34-87 years; mean, 51 years) underwent breast-conserving surgery (wire-guided lumpectomy or quadrantectomy) for US-detected invasive breast cancer. Mammography, breast US, US-guided core-needle biopsies (CNB) were performed in all cases. CNB was performed under sonographic guidance by using a 13 MHz probe (Sonosite, Bothell, WA, US) and a 14-gauge needle.

In all patients, US-guided wire localization was performed approximately 6-12 hours before surgery by using a 20-gauge retractable hook-wire inserted into the lesion with a freehand technique. Accurate wire localization was confirmed with real-time ultrasound imaging and with additional radiographic images (two orthogonal views).

Orienting surgical wires were placed on the edges of breast specimen at the time of surgery. All surgical specimens were accurately oriented and underwent US examination. Longitudinal and transverse US scans were performed in all cases by a single radiologist with more than 5 years experience in breast imaging.

The presence of lesion within the specimen and its distance from the specimen margins in four radial directions (superior, inferior, medial and lateral) were assessed. US findings were then compared with the pathological ones.

As reported by previous literature studies (9, 12-19), sonographic threshold distance of 10 mm between the tumor and the surgical specimen margins was adopted in our series in order to classify the margin status. In particular, a <10 mm distance between the tumor and the specimen margins was considered as positive margins. In these cases, cavity shaves of the inadequate margin was immediately performed and additional removed tissue (re-excision specimen) did not undergo radiography or sonography. Sonographic margin status (negative or positive) was compared with the surgical pathology results.

Histo-pathologic examination of the surgical specimens was performed by a pathologist with more than 20-years experience in breast disease, who examined both malignant specimen and re-excision tissue. The margin was considered positive/close if foci of DCIS or invasive carcinoma were found within the 2-mm thick shaved margin. Patients whose margins were involved were candidate for re-excision.

Sensitivity, specificity, diagnostic accuracy, positive (PPV) and negative predictive values (NPV) of specimen ultrasound in predicting histological margins were evaluated, having the histological findings as the reference standard.

True positives were represented by cases with sonographic margin of less than 10 mm, histologically confirmed as positive or close margin (2 mm); false positives by cases with sonographic positive margins, not confirmed at histology; true negatives by cases with sonographic margins of more than 10 mm, histologically confirmed as negative margin (>2 mm); false negatives by cases with sonographic negative margins who resulted positive (2 mm) at histology.

Results

The histological examination detected invasive ductal carcinoma in 96/132 (73%) cases, invasive lobular carcinoma in 32/132 (24%), mucinous carcinoma in 4/132 (3%). The mean lesion size was 14 mm (range 5-21 mm). Intraductal component was found in 16/132 (12%) cases. The pathological margin analysis revealed 96/132 (73%) negative margins and 36 (27%) close/positive margins.

US examination detected all 132 breast lesions within the surgical specimens. With regard to US margin classification, 110 (83%) negative margins (Figure 1) and 22 (17%) positive margins were found. By comparing US and histological margin analysis, 16 true positives, 90 true negatives, 6 false positives and 20 false negatives occurred in our series.

Sensitivity, specificity, diagnostic accuracy, PPV and NPV of 44%, 94%, 80%, 73% and 82%, respectively, were found.

Discussion

Although specimen radiography represents the traditional imaging tool for evaluating the presence of breast lesion within the surgical specimen and the margin status, an increasing role for specimen US has been reported in the medical literature especially due to the diffusion of high frequency transducers. This kind of method is particularly effective in many cases where the breast lesion is not visible at mammography but is only detected by means of breast US, as in case of young women with dense breasts (7, 9-11).

The possibility of using US imaging also for lesions visible at both mammography and in vivo US also exists. The main advantages are represented by the minimal time delay during surgical procedures as compared with mammography, the lower costs, the lower time requested for specimen evaluation and the possibility to

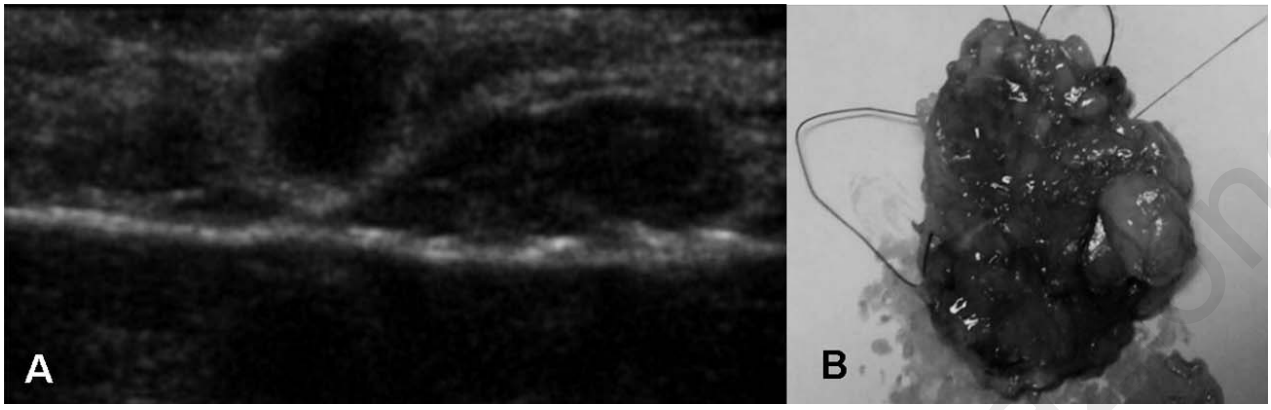

Fig. 1 - Specimen US (A) and corresponding surgical specimen (B) of a breast invasive ductal carcinoma with negative margins at US as confirmed at histological examination.

be performed in either the radiology department or the operative room (9-11).

Several studies supporting the use of surgical specimen US have been reported in this field (12-20).

Mesurolle et al. stated that specimen US represents an effective tool for indentifying the lesion within the specimen even if the margin assessment is limited by the presence of false negative and false positive cases with sensitivity, specificity, NPV and PPV respectively of 75%, 80.5%, 76.7% and 79%. Usually, US false negative cases were represented by small hypo-echoic lesions within a fatty background or by entities known to be difficult to diagnose on US such as DCIS. US false positives could be caused by the specimen flattening which can occur applying the US transducer directly on the specimen surface, especially when the lesion is not perfectly centrally located in the specimen (11, 20). According to Mesurolle, specimen US can be an alternative tool of specimen imaging in case of non fatty breasts and for lesions of more than 5 mm in diameter (11). Similarly, in our series, all breast lesions had a diameter of more than 5 mm and sensitivity, specificity, diagnostic accuracy, PPV and NPV values of 44%, 94%, 80%, 73% and 82%, respectively, were found. In particular, by comparing US and histological margin analysis, 6 false positives and 20 false negatives occurred. False positive cases were represented by lesions located close to specimen margins which seemed to be involved when the US transducer was directly applied on the specimen surface. The same phenomenon, called "pancake phenomenon", typically and more strongly occurs during specimen radiography compression having significant implications for margin assessment (9). False negative cases were due to breast cancer intra-ductal components, difficult to recognize on US, in 16 cases and probably due to lesion echo-texture compared with background in the remaining cases.

On the other side, Londero et al. reported a poor potential of US for evaluating specimen margin status with sensitivity, specificity, PPV and NPV values of 28.5%, 84.6%, 25% and 86.8% considering a sonographic threshold of 10 mm and of 7.1%, 96.8%, 28.2% and 85.3% considering a threshold of 4 mm. They considered 4 mm as the minimal tumor-margin distance measurable using their US equipment (9). However, in our series, as reported in previous studies, we used a threshold of 10-mm in order to reduce the false negative rate (12, 13, 21).

Our study had some limitations mainly represented by the small number of the enrolled patients, the lack of a comparison with radiographic findings, the lesion diameter which was more than 5 mm in all cases, the absence of mixed lesions with a fluid component which may be difficult to detect on specimen US.

Conclusions

Specimen US represents a time and cost saving imaging tool for evaluating the presence of US detected-breast lesion within surgical specimen and for predicting the histological margin status. Its main limitation is represented by breast cancer intra-ductal components, difficult to recognize on US.

Conflict of interest

The Authors declare that they have no conflict of interest to the publication of this article.

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