Accuracy of Intraoperative Margin Investigation by Frozen-Section in Breast Conservative Surgery

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ABSTRACT

Background: Now the vast majority of breast tumors are treated using Breast conservation therapy (BCT) method, including lumpectomy and radiotherapy. This study aimed to evaluate the effects of intraoperative frozen section in patients undergoing breast conservation surgery.

Methods: Totally 237 women who included in the category for breast conservative or oncoplastic surgery and post-operative radiotherapy (Early breast cancer Stage I, II and Stage IIIA after neoadjuvant chemotherapy and down staging) were enrolled in this prospective study from March 2009 to June 2011.

Results: In frozen section, totally 88 margins (6.1%) in 60 patients (25%) was positive (1-5 positive margins/ patients) that all of these patients were re-excised. In precise pathologic view the margins in 7 patients (2.9%) was positive that comprised 4% of all margins, furthermore the results showed closed margin in 4 patients. false negative in our study occurred in 0.8% of patients and in 0.1% of margins (sensitivity 100% and specificity 99.2%).

Conclusion: we designated intraoperative margin assessment by frozen section as an effective method in decreasing the rate of additional operations for margin control. Additionally, adequate margin width is accessible during same operation.

Keywords: Intraoperative Frozen-Section Analysis, margin, Breast conservative surgery.
Introduction

The most frequently diagnosed malignancy in Iranian women is breast cancer. During the last decade, development of mammography, sonography and other diagnostic technologies, moreover education to physicians and women have led to rapid increase of small no palpable breast cancer diagnosis in Iran.

Breast conservation therapy (BCT) including lumpectomy and radiotherapy is the leading treatment in the vast majority of breast tumors, and previous studies designated it as efficient therapy in properly selected patients with breast cancer. However, several previous studies divulged local recurrence frequently occurred after breast conservation surgery, and patients may need reoperation and radiation therapy. Several complications as anesthesia risks, delay on beginning of oncological therapy, poor cosmetic appearance and additional cost occur in case of reoperation in patients. All mentioned complications can be averted by intraoperative margin assessment and surgeons can make a repeated excision in the same operation if necessary. So, many authors have claimed local recurrence after breast conservation surgery is expressively lower when clean surgical margins of at least 2 mm are achieved. Furthermore, achievement of clear margins in patients undergoing breast conservation surgery leads to increase in disease free-survival. To address these concerns, we have steered this prospective study evaluating the possible long-term effects of intraoperative frozen section in patients undergoing breast conservation surgery.

Methods and materials

This prospective study was performed in one center under supervision of cancer research center of Shahid Beheshti Medical University (SBUM) Tehran, Iran, from March 2009 to June 2011 . The study was approved by ethical committee of Shahid Beheshti Medical University . Moreover, informed written consent were taken from all patients.

Totally 237 women who included in the category for breast conservative or oncoplastic surgery and post-operative radiotherapy (Early breast cancer Stage I, II and Stage IIIA after neoadjuvant chemotherapy and down staging) were enrolled. The patients were excluded in case of; diffuse suspicious microcalcification, multicentric / multifocal disease, and the patients who had contra-indication for radiotherapy, stage IIIB-C and metastatic breast cancer.

We recorded on a computerized database the patients demographic data, family history, menopausal status, radiological findings, operative records, tumor type localization, size and grade, estrogen/progesterone receptor status, C-erbB2, lymphovascular invasion, perineural invasion, necrosis, calcification, extensive intraductal component (EIC), axillary pathologic nodal status, stage, frozen section and permanent section results, follow-up, recurrence and mortality.

The operations were performed by one experienced surgical team. During the operation, the breast tumor was excised with 1-2 cm macroscopic margin, and surgical specimen was immediately marked with orienting sutures for intraoperative pathologic examination by frozen section. The pectoral fascia was the deep margin of excision.

Negative surgical margin was defined if tumor cells were > 2 mm from the inked surface of the lumpectomy specimen. Moreover, tumor positive margin was specified as tumor cells were present at the inked edge of specimen. Close margin was defined as tumor cells were ≤ 2 mm from the inked surface.

In pathologic department the margins were marked using multicolor Indian ink. Then the samples were sliced at one cm intervals, the tumor size and the distance of margins were measured. If the distance of margin from the edge of tumor in macroscopic view was <1cm, at least 2 slices (vertical and horizontal) from margin were obtained, and if was >1 cm, one slice was achieved. All margins of the resected specimens were assessed microscopically by frozen section which executed experienced pathologist. And embedded on a cryostat (Leica CM1850 UV) and placed on slides and stained with hematoxylin and eosin (H & E). After taking the result of frozen section, we placed metallic clips at the edge of lumpectomy cavity. Then to perform oncoplastic surgery in most lumpectomies, local advancement flaps can be created by mobilization of the edges of the lumpectomy cavity off the pectoralis fascia for 2 to 3 cm on all sides, with the option of additional mobilization of skin from breast pa-
renchyma at the superficial cavity edges. Tissue can be advanced and sutured to close at least part of the lumpectomy defect without creating skin dimpling. For lumpectomies in patients with large breasts, more advanced oncoplastic approaches that incorporate large volume excisions with mastopexy and reduction mammoplasty was performed. Then the reports of surgeon and pathologist were retrospectively reviewed for patients who had BCT.

The data were analyzed using Statistical Package for Social Studies version 16.0 (SPSS Inc, Chicago, Ill). Data were expressed as mean ± SD. P<0.05 was considered as significant.

Results

Totally we evaluated 237 women with mean age 48.6 ±10.35 and 1422 margins (6 margins/ specimen: superficial, deep, medial, lateral, superior and inferior). The mean tumor size was 2.25±0.22; the mean number of axillary nodes was 10.5±6.1 and the mean number of positive axillary nodes was 2.26±4.3. Type of tumor in 182 patients (76%) was ductal carcinoma, in 43 patients (18%) lobular carcinoma and in 12 patients (5%) was mixed tumor. 88 margins (6.1%) in 60 patients (25%) was positive (1-5 positive margins/ patients) in frozen section that all of these patients were re-excised (Table 1).

In precise pathologic view the margins in 7 patients (2.9%) was positive that comprised 4% of all margins, furthermore the results showed closed margin in 4 patients. In two patients with negative margin in frozen, result of pathologic reports were DCIS in margin. In this case false negative in our study occurred in 0.8% of patients and in 0.1% of margins (sensitivity 100% and specificity 99.2%). Finally, we performed modified radical mastectomy for these patients.

Discussion

Some papers emphasized frozen section is not a suitable technique and declared that frozen section especially when use in smaller specimens may causes loss of tissue for permanent section, and frozen section has sampling errors and artifacts due to fat or calcifications. However in a large sample review on 672 cases, Bianchi et al. in a study divulged no technical conflicts mentioned above. Moreover, Caruso et al. designated frozen section with oncoplastic resections led to a proper control of local disease and decreased more surgical investigations for margins revision. Additionally, Osborn et al. specified that routine use of frozen-section analysis of lumpectomy margins is a cost effective method and decreases reoperation rate for margin control.

We revealed 88 positive margins (6.1%) in 60 patients (25%) in frozen section that all of these patients were re-excised. Moreover, we divulged that intraoperative evaluation of margin status has a major advantage because immediate re-excision can be carried out during the same operation and additional operations are prevented. Our results were in line with several previous studies that indicated lumpectomy followed by radiotherapy is an alternative to mastectomy. Though, these studies revealed that BCS is related to a higher risk of local recurrence than mastectomy. In this regard intraoperative evaluation to obtain free negative margins is very helpful to avoiding local recurrence, and two methods for intraoperative evaluation of lumpectomy margins are frozen section analysis (FSA) and touch imprint. Recent studies have implied frozen section is accurate and reliable, these reports hinted sensitivity and specificity about 97% and 100% respectively. In line with these studies specificity and sensitivity in our study were 99.2% and 100% respectively. Moreover false negative in our study was 0.8 and in previous reports was 0.4 to 3.4.

The most important advantage of FSA is lower re-

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<th>Table 1. Descriptive characteristics of study population</th>
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<td>Age(Mean ± SD) 48.6±10.35</td>
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<tr>
<td>Tumor size (Mean ± SD) 2.25±0.22</td>
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<tr>
<td>Axillary nodes (Mean ± SD) 10.5±6.1</td>
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<td>Positive axillary nodes (Mean ± SD) 2.26±4.3</td>
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<tr>
<td>Ductal carcinoma 182(76%)</td>
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<td>Lobular carcinoma 43 (18%)</td>
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<td>Mixed tumor 12(5%)</td>
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<tr>
<td>Positive margins 88(6.1%)</td>
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<tr>
<td>Positive margins to pathology report 4%</td>
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<td>False negative 0.1% of margins</td>
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excision rate in comparison with permanent section technique. In our study the rate of re-excision was 6.1% and was in agreement to previous study by camp et al that specified re-excision rate about 6.3% in their review. Furthermore recent reports disclosed intraoperative evaluation of margin status has a major benefit because immediate re-excision can be performed during the same operation that decreases the rate of reoperation. In line with this fact, reoperation in our survey was very low and occurred only in two patients.

Briefly, in current study we designated intraoperative margin assessment by frozen section as an effective method in decreasing the rate of additional operations for margin control. Additionally, adequate margin width (> 2 mm negative margin in our cases) was obtained during same operation. Moreover, 25% of our patients were underwent re-excision during initial operation because of close or positive margins, so we kept them from risks of additional operations risks as anesthesia, poor cosmetic appearance, anxiety, delay on starting oncological treatments and higher cost.

The interpretation of our results is subjected to limitation as lack of control group. So, we could not compare the frozen section method with other intraoperative techniques. Further comparative investigations are recommended to validate the findings reported here.

Conclusion

We recommend intraoperative analysis of margins by frozen section in breast conserving surgery for breast cancer patients to reduce the probability of reoperation.

Acknowledgment

We would like to thank the nursing, administrative and secretarial staff of the surgery and pathology department and clinic at our hospital for their contribution to the maintenance of our patient record without which this project would have been impossible.

References


