Rates of margin positive resection with breast conservation for invasive breast cancer using the NCDB

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ABSTRACT

Background: Previous studies suggest the rate of positive surgical margin (PSM) after lumpectomy for breast cancer is approximately 20 %. The risk of PSM at time of resection is often a source of fear for patients, driving some to elect to undergo mastectomy. This study describes rates and predictors of positive margins for invasive breast cancers in the National Cancer Database (NCDB).

Materials and methods: From 2004 to 2013, patients with non-metastatic invasive breast cancers who underwent breast conservation surgery were identified from the NCDB. Patients’ demographic, clinical, and facility of treatment characteristics were collected and compared. Per SSO-ASTRO-ASCO criteria, margin negative is defined as no gross or microscopic disease (i.e. no tumor on ink). Bivariate tests and multivariate logistic regression were conducted to identify independent predictors of patients with PSM at the time of resection.

Results: A total of 707,798 patients were identified with non-metastatic invasive breast tumors who underwent lumpectomy. Rate of PSM across the entire cohort was 5.02 %. Over time, the rate of PSM decreased significantly from 6.54 % in 2004 to 3.91 % in 2013 (p < 0.001). Pure lobular histology predicted for the highest rate of PSM compared with IDC (8.63 vs 4.55 %; p < 0.001). In adjusted analysis, high grade, non-ductal histology and HER2 amplification were significantly associated with PSM with breast conservation while estrogen and progesterone status were not.

Conclusion: This study demonstrates a 5 % risk of PSM at time of breast conservation surgery using a large, modern national database. Patients with invasive lobular and mixed histology have a nearly two-fold risk of PSM compared to invasive ductal cancers. These results provide important data points to help appropriately counsel patients regarding the risk of PSM.

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1. Introduction

Breast cancer remains the most common malignancy among women with recent studies estimating 276,480 new cases of invasive breast cancer diagnosed among women in one year [1]. Treatment options for women with early-stage invasive breast cancer (IBC) may include undergoing total mastectomy or breast conservation therapy (BCT) plus whole breast radiation therapy (WBRT). Multiple randomized phase III trials have shown survival for BCT followed by WBRT to be equivalent to mastectomy for treatment of stage 1 and 2 (early stage) IBC [2–4]. Since long-term survival is comparable for both therapies, the major benefit of BCT plus WBRT is conservation of as much healthy breast tissue as possible allowing maintenance of a sensate and cosmetically appealing breast. However, a risk to choosing BCT plus WBRT is positive surgical margin (PSM), defined as tumor on ink for IBC, which results in 2-fold increased risk of ipsilateral breast tumor recurrence [5]. As a result, most patients with PSM will undergo re-excision requiring additional surgery, discomfort, health-related costs, and emotional stress.

Of the factors that influence local recurrence, margin resection is one of the few modifiable risk factors, prompting surgeons to seek novel approaches to lower rates of PSM [6]. Previous studies suggest the rate of PSM with BCT plus WBRT is approximately 20 % [7].
The risk of PSM at time of resection is often a source of fear for patients, which may be driving many to elect to undergo mastectomy rather than BCT plus WBRT. In fact, recent studies have shown an increase in the rates of mastectomy since the year 2000 [8].

At initial consultation, patients should have appropriate counseling regarding risks of positive margin resection, to aid in treatment decision making. For patients with early stage IBC, it is possible that histology, grade, and receptor status could influence the rate of PSM. With more information about these rates, patients could receive optimal counseling from their oncologists to help in making an informed decision about their treatment plan. The purpose of this study is to describe rates and predictors of PSM at time of resection with breast conservation therapy for early-stage IBC using a large modern patient cohort from the National Cancer Database (NCDB).

2. Materials and methods

2.1. Study design

From (2004–2013) patients with non-metastatic invasive breast cancers who underwent breast conservation surgery were identified from the NCDB. Our patient cohort included patients with non-metastatic stage (M0 or MX), invasive disease on pathology, and breast conservation surgery with or without radiation treatment (Fig. 1). Patients who received radiation therapy prior to surgery or with unknown margin status were excluded from the analysis. Patients’ demographic, clinical, and facility of treatment characteristics were collected for analysis of treatment variables. Patients were stratified by histology, grade, and receptor status. These variables were used to detect predictors for rates of positive margin resections. Per the SSO-ASTRO-ASCO consensus criteria [5], margin negative is defined as no gross or microscopic disease at the margin (i.e. no tumor on ink).

2.2. Statistical methods

Using the patient cohort as defined in Fig. 1, patients’ treatment variables were compared using two-sided t-tests and chi-square tests. Multivariate logistic regression was used to identify independent predictors of patients with positive margin at the time of resection adjusting for histology, grade, and receptor status. Odds ratios compared predictors of positive margin, with a p-value of 0.01 defined as statistically significant.

3. Results

Between 2004 and 2013, 707,798 patients were identified from the NCDB that met the study criteria. Patient and tumor characteristics are described in Table 1. The rate of margin positive resection across the entire cohort was 5.02 %. Of note, rates of positive margin resection decreased significantly from 6.54 % in 2004 to 3.91 % in 2013 (p < 0.001) as shown in Fig. 2.

Lobular histology, histologic grade, and HER2+ receptor status were significantly associated with margin-positive resection with breast conservation. However, estrogen and progesterone status were not significantly associated with margin status. Pure lobular histology predicted for the highest rate of positive margin compared with IDC (8.63 % vs 4.55 %; p < 0.001). Mixed histology vs IDC also predicted for positive margin 7.22 % with an odds ratio of 1.57 (95 % CI 1.3–1.91). Her2+ was associated with increased PSM (4.8 % vs 4.1 % OR 1.16). Increasing grade was associated with PSM (Grade 1: 4.0 %; Grade 2: 5.2 %; Grade 3: 5.4 %). Odds Ratio for grade 2 was 1.18 (p < 0.03) and grade 3 was 1.29 (p < 0.01) compared to grade 1. On multivariable adjusted analysis, grade, histology and amplified HER2 status were significantly associated with PSM while estrogen and progesterone status were not (Table 2).

Increasing clinical T stage at diagnosis was correlated with increased PSM after BCS (T1:4.05 %, T2:6.99 %, T3:18.4 %, T4: 27.4 %, p < 0.01) as well as increasing clinical N stage (N0: 4.42 %, N1:7.07 %; N2:10.45 %, N3:11.79 %, p < 0.01).

4. Discussion

Using a large modern national database, this study demonstrates breast conservation surgery carries only a 5 % risk of positive margin resection.
Table 1
Patient characteristics.

| Patient characteristic | Absolute number±1 sd (Percent) |
|------------------------|--------------------------------|
| Age                    | 62 ± 12.8                      |
| Race                   |                                 |
| White                  | 573,316 (81.9 %)               |
| Hispanic               | 30,081 (4.25 %)                |
| African American       | 69,364 (9.8 %)                 |
| Other                  | 22, 366 (3.16 %)               |
| Histology              |                                 |
| Ductal                 | 611,357 (86.4 %)               |
| Lobular                | 54,430 (7.69 %)                |
| Mixed                  | 41,830 (5.91 %)                |
| Clinical stage         |                                 |
| T1                     | 532,264 (75.2 %)               |
| T2                     | 146,514 (20.7 %)               |
| T3                     | 10,033 (1.46 %)                |
| T4                     | 3610 (0.51 %)                  |
| N0                     | 641,264 (90.6 %)               |
| N1                     | 55,491 (7.84 %)                |
| N2                     | 10,616 (1.15 %)                |
| N3                     | 2831 (0.4 %)                   |
| Pathologic stage       |                                 |
| T1                     | 543,589 (76.8 %)               |
| T2                     | 174,222 (20.8 %)               |
| T3                     | 6157 (0.87 %)                  |
| T4                     | 2194 (0.31 %)                  |
| N0                     | 414,770 (58.6 %)               |
| N1                     | 38,929 (5.5 %)                 |
| N2                     | 5875 (0.83 %)                  |
| N3                     | 1982 (0.28 %)                  |
| Grade                  |                                 |
| 1                      | 174,826 (24.7 %)               |
| 2                      | 297,583 (42.1 %)               |
| 3                      | 193,937 (27.4 %)               |
| Estrogen receptor      |                                 |
| Positive               | 586,764 (82.9 %)               |
| negative               | 121,033 (17.1 %)               |
| Progesterone receptor  |                                 |
| Positive               | 512,446 (72.4 %)               |
| Negative               | 196,060 (27.7 %)               |
| HER 2 receptor         |                                 |
| Amplified              | 95,598 (12.8 %)                |
| Non-amplified          | 617,200 (87.2 %)               |

Table 2
Multivariable analysis of predictors of positive margins.

| Factor                        | Odds ratio | Confidence interval (95 %) | P-value |
|-------------------------------|------------|----------------------------|---------|
| Ductal histology              | 1.0        | (reference)                | NA      |
| Lobular histology             | 1.96       | (1.66–2.31)                | <0.01   |
| Mixed histology               | 1.57       | (1.3–1.91)                 | <0.01   |
| Grade 1                       | 1.0        | (reference)                | NA      |
| Grade 2                       | 1.18       | (1.02–1.37)                | 0.03    |
| Grade 3                       | 1.29       | (1.1–1.51)                 | <0.01   |
| Estrogen receptor positive    | 1.03       | (0.91–1.19)                | 0.6     |
| Progesterone receptor negative| 0.93       | (0.83–1.05)                | 0.26    |
| HER 2 receptor positive       | 1.16       | (1.06–1.29)                | <0.01   |

Fig. 2. The trend in PSM over time (line graph).
5. Conclusion

This large national database study demonstrates only 5% risk of positive margin at time of breast conservation surgery. Patients with invasive lobular histology have a nearly two-fold risk of margin positive resection compared to invasive ductal cancers. HER2 amplified disease increases patients’ risk of margin positive resection, while grade, estrogen and progesterone status did not significantly predict for positive margin. These results provide important data points to help appropriately counsel patients regarding the risk of positive margins, and possible need for re-excision in patients desiring breast conservation therapy in the modern era.

Author contributions

WJH, AE, CP, and DHB contributed to the study conception. All authors contributed to design and drafting of manuscript. JR provided statistical expertise. WJH, AE, and DHB made critical revisions to the paper. DHB supervised the submission of the manuscript.

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Declaration of competing interest

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