Cavity Shaving plus Lumpectomy versus Lumpectomy Alone for Patients with Breast Cancer Undergoing Breast-Conserving Surgery: A Systematic Review and Meta-Analysis

Ke Wang, Yu Ren, Jianjun He*
Department of Breast Surgery, the First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi Province, China
* hejianjun811@sina.com

Abstract

The margin status is a well-established prognostic predictor for patients undergoing breast-conserving surgery (BCS). Recent data suggested that cavity shaving in addition to lumpectomy might be a promising approach for improving the clinical outcomes. We aimed to compare the efficacy and safety between cavity shaving plus lumpectomy and lumpectomy alone with a systematic review and meta-analysis. We searched the PubMed, Embase, and Cochrane CENTRAL databases for studies comparing cavity shaving with lumpectomy before June 10, 2016. Both comparative studies and self-control studies were included. A random-effects model was used to estimate the odds ratios (ORs) for positive margin rate, reoperation rate, recurrence rate, and weighted mean difference (WMD) for excised tissue volume. Twenty-six studies were included in the meta-analysis. The cavity shaving group had a significantly lower positive margin rate than the BCS-alone group (16.4% vs. 31.9%; OR = 0.41, 95% CI 0.32–0.53, P < 0.05). Cavity shaving was associated with a significantly decreased rate of reoperation (OR = 0.42, 95% CI 0.30–0.59, P < 0.05). The overall locoregional rate was low for cavity shaving and BCS-alone (3% vs. 4%). Cavity shaving had no significant effect on the risk of locoregional recurrence (OR = 0.86, 95% CI 0.32–2.35; P = 0.78). The excised tissue volume did not differ substantially between cavity shaving and BCS alone (WMD = −23.88, 95% CI −55.20 to 7.44, P = 0.14). For patients undergoing BCS, additional cavity shaving was an effective method to decrease the positive margin rate and avoid reoperation. The addition of cavity shaving did not appear to have excessive excised tissue volume compared with partial mastectomy alone.

Introduction

Breast cancer is the most common malignancy among women in the United States [1]. Nearly 270,000 women were diagnosed with operable breast cancer in 2015, approximately two-thirds
(180,000 women) of whom were suitable for breast-conserving surgery (BCS), namely partial mastectomy [2]. For early cases, BCS can yield an equivalent survival compared with radical mastectomy [3,4]. However, BCS has a higher lifelong local recurrence rate than total mastectomy, mandating adjuvant radiation therapy [5], and approximately 20–35% of patients who undergo BCS eventually require reoperation [6,7]. Margin status is a pivotal predictor for local recurrence [5,8,9]. The rate of positive margins after a partial mastectomy is as high as 20–40%. Patients with breast cancer with positive margins have a two-fold increase in the risk of tumor recurrence compared with those who have negative margins [10].

Cavity shaving (CS) was first introduced as a pathological biopsy technique to examine the residual tumor during or after partial mastectomy, and the incidence of residual tumor bed positivity reaches as high as 39.3% [11–13]. Later, several studies demonstrated that CS could be an easy and effective procedure to decrease the positive margin rate and re-excision rate. However, some authors have argued that the excision of selective margins might be sufficient [14,15]. The value of CS has been questioned because adjacent multifocal disease might outweigh margin status in causing BCS failure [16]. Thus, we conducted this systematic review and meta-analysis with the aim to compare the efficacy and safety between CS plus lumpectomy and lumpectomy alone.

Materials and Methods

We searched the PubMed, Embase, and Cochrane CENTRAL databases for eligible studies published before June 10, 2016. The following groups of key words or medical terms were used: (“cavity shave” or “cavity shaving” or “cavity margin” or “shave margin”) and (“lumpectomy” or “breast-conserving” or “partial mastectomy” or “breast cancer”). The detailed search strategy used for PubMed is listed in S1 File. The language was limited to English. Additionally, the reference lists of relevant studies were searched for potentially eligible records. This systematic review and meta-analysis was performed following the PRISMA guideline (S2 File) [17].

Study inclusion

The included studies could be comparative studies, including randomized controlled trials (RCTs) or non-randomized studies (NRS), or self-control studies, which compared CS with standard lumpectomy in patients with breast cancer undergoing breast-conserving surgeries. The breast cancer stage ranged from 0 to III. We preferred the margin assessed by the “no ink on tumor” criteria [10]. Other wider margins criteria were also accepted. However, studies assessing margins by imaging-guide techniques were excluded. We only selected studies that applied the CS procedure at the initial surgery. When multiple groups were presented in an individual studies, we selected the comparison between BCS plus CS and BCS alone. The outcomes of interest included positive margin rate, reoperation rate, locoregional or distant recurrence rate, volume of excised tissues, and cosmetic outcomes.

Data collection and quality assessment

Two reviewers independently extracted the data using a standardized form. When an outcome was followed at different intervals, the one with longest follow-up was selected. The following information was extracted: author, year, study design, country, sample size, age, proportion of ductal carcinoma in situ (DCIS), tumor size, outcomes of interest, and study period. To assess the quality of the RCTs, we used the Jadad score [18]. We used the modified Newcastle-Ottawa scale (NOS) to evaluate non-randomized or non-comparative studies [19]. The NOS evaluated four aspects including selection, comparability, exposure, and outcomes. The scores ranged
from 0–7 points, with 0–2 points indicating low quality, 3–5 points indicating medium quality, and >6 points denoting high quality.

**Statistical analysis**

The meta-analysis for comparative outcomes was performed using Stata 12.0 software (Stata Corporation, College Station, TX, USA). For pooling the single-arm event rate, we used Comprehensive Meta-Analysis software (version 2.2, Biostat, Englewood, NJ, USA). For dichotomous outcomes, we used odds ratios (ORs) and 95% confidence intervals (CI) as the effect estimate. The relative risk (RR) was only used in sensitivity analysis for pooling data from RCTs. For continuous measures, we used the weighted mean difference (WMD) with 95% CI as the effect estimate. The median value with range or interquartile range was transformed into the mean ± standard deviation (SD) by the established calculation method [20]. A random-effects model was used for data synthesis. Heterogeneity was assessed by the $I^2$ statistics. $I^2 <25\%$ was regarded as low heterogeneity, 25–75% was regarded as medium heterogeneity, and $\geq75\%$ was considered high heterogeneity [21]. Subgroup analysis was performed by the study design and region. Sensitivity analysis was performed by excluding the included studies one by one. Meta-regression was conducted according to the sample size and percentage of DCIS. The publication bias was examined by the funnel plot, and quantitatively by the Egger's test and Begg's test [22,23]. Two-sided $P < 0.05$ was considered statistical significant.

**Results**

**Selection process**

A total of 153 records were initially identified, including 95 records from the PubMed, 54 records from the Embase, and 4 records from the Cochrane CENTRAL databases. After removing duplicates and irrelevant publications, 56 full-text studies were assessed for eligibility. Thirty-nine studies were pooled into a qualitative synthesis. Further, we excluded 12 studies that did not compare CS with BCS alone, and 1 study in which CS was performed as a second surgery. Twenty-six studies were included into the meta-analysis. Fig 1 displays the study selection process.

**Study characteristics**

Twenty-six studies between 1994 and 2016 were included into the final meta-analysis, including 15 comparative studies (2 RCTs and 13 NRSs) [15,24–37], and 11 self-control NRSs [12,16,38–46]. Among the 24 NRSs, most had a retrospective design (21/24). The characteristics of the included studies are presented in Table 1. Eleven studies were conducted in Europe, 13 in North America, and 2 in China. The sample size ranged from 76–786. The median or mean age for the majority of included studies ranged from 50–60 years. Although early patients with breast cancer indicated for BCS were unanimously included, the percentage of DCIS varied greatly (0%-100%). The mean/median size of tumor ranged from 1–2.5 cm. In quality assessment, 2 RCTs achieved high-quality scores [25,27]. When assessing the NRSs by the NOS score, the scores ranged from 5–7. The items of representativeness of cases undergoing CS and adequate follow-up were least fulfilled. The quality evaluation is displayed in S1 and S2 Tables.

**Positive margin rate**

Twenty-two studies compared the positive margin rate between CS plus BCS with BCS alone. Because 2 studies by the same author had overlapping cohorts [40,41], the one with the largest sample size was selected for analysis [41]. Overall, the pooled positive margin rate for the CS
procedure was 16.4% (95% CI 12.8–20.7%, $I^2 = 87.7\%$), and the pooled rate for BCS alone was 31.9% (95% CI 26.1–38.4%, $I^2 = 93.4\%$). In comparative analysis, CS plus BCS could significantly reduce the positive margin rate compared to BCS alone (OR = 0.41, 95% CI 0.32–0.53, $P < 0.05$). High heterogeneity was present ($I^2 = 73.3\%; P < 0.05$) (Fig 2). The association remained significant for self-control studies (OR = 0.44, 95% CI 0.29–0.68, $P < 0.05$; $I^2 = 85.4\%$) and comparative studies (OR = 0.39, 95% CI 0.30–0.52, $P < 0.05$; $I^2 = 44.3\%$). When stratified by region (Europe, North America, and China), only 2 Chinese studies showed a non-significant pooling result (OR = 0.60, 95% CI 0.28–1.30, $P = 0.19$).

Fig 1. Flow Diagram Showing the Study Selection Process.

doi:10.1371/journal.pone.0168705.g001
Table 1. Characteristics of the Included Studies.

| Author (year)          | Country | Design    | No. of patients | Age (year) | DCIS, n (%) | Treatment regimens | Median size (cm) | Outcomes                              | Study period |
|------------------------|---------|-----------|-----------------|------------|-------------|-------------------|------------------|---------------------------------------|--------------|
| Macmillan et al. (1994)| UK      | Retrospective | 264            | Median: 55 | NA          | Shave-after vs. shave-before | 1.3              | Positive margin rate; recurrence rate  | 1988–1992    |
| Keskek et al. (2004)   | UK      | Retrospective | 301            | Mean: 55   | 20 (6.6%)   | Shave-after vs. shave-before | 2.0              | Positive margin rate; reoperation rate; recurrence rate | 1997–2002    |
| Camp et al. (2005)     | USA     | Retrospective | 257            | Median: 58 | 47 (17.6%)  | Shave vs. non-shave       | NA               | Reoperation rate; recurrence rate    | 1989–2001    |
| Cao et al. (2005)      | USA     | Retrospective | 126            | Mean: 58   | 23 (18.3%)  | Shave-after vs. shave-before | 1.4              | Positive margin rate                  | 2003–2004    |
| Janes et al. (2006)*   | UK      | Prospective  | 111            | Median: 59 | 1 (1%)      | Shave-after vs. shave-before | 1.9              | Positive margin rate; reoperation rate | 2001–2003    |
| Huston et al. (2006)   | USA     | Retrospective | 171            | Median: 59 | 29 (17%)    | Shave vs. non-shave       | 1.3              | Positive margin rate; reoperation rate; volume of excised tissue | 2000–2006    |
| Jacobson et al. (2008) | USA     | Retrospective | 125            | NA         | 26 (20.8%)  | Shave-after vs. shave-before | 1.8              | Positive margin rate; reoperation rate | 2002–2006    |
| Marudanayagam et al. (2008) | UK | Retrospective | 786            | Mean: 58   | 0           | Shave vs. non-shave       | 1.7              | Reoperation rate                     | 2000–2005    |
| Povoski et al. (2009)  | USA     | Retrospective | 204            | Median: 57 | 0           | Shave-after vs. shave-before | 1.6              | Positive margin rate; volume of excised tissue | 2003–2007    |
| Lovrics et al. (2009)  | Canada  | Retrospective | 489            | Mean: 59   | 0           | Shave vs. non-shave       | NA               | Positive margin rate; reoperation rate | 2000–2002    |
| Tengher-Barna et al. (2009) | France | Retrospective | 107            | Median: 57 | 15 (14%)    | Shave-after vs. shave-before | 1.6              | Positive margin rate; reoperation rate | 2003–2006    |
| Rizzo et al. (2010)    | USA     | Retrospective | 320            | Mean: 59   | 88 (44.2%)  | Shave vs. non-shave       | 1.6              | Positive margin rate; reoperation rate | 2004–2007    |
| Zavagno et al. (2010)  | Italy   | Retrospective | 508            | Mean: 58   | 0           | Shave vs. non-shave       | 1.6              | Positive margin rate; reoperation rate; volume of excised tissue | 2001–2008    |
| Coopey et al. (2011)   | USA     | Retrospective | 773            | Mean: 56   | 223 (28.8%) | Shave vs. non-shave       | 1.7              | Reoperation rate; recurrence rate     | 2004–2006    |
| Feron et al. (2011)    | France  | Prospective  | 96             | Mean: 56   | 0           | Shave-after vs. shave-before | 1.4              | Positive margin rate; reoperation rate | Jan-Dec 2007 |
| Hequet et al. (2011)   | France  | Retrospective | 99             | Median: 58 | 16 (16.1%)  | Shave-after vs. shave-before | 1.5              | Positive margin rate                  | 2007–2008    |
| Kobbermann et al. (2011) | USA | Retrospective | 138            | Median: 59 | 40 (29%)    | Shave vs. non-shave       | NA               | Positive margin rate; reoperation rate | 2004–2009    |
| Wolf et al. (2011)     | USA     | Retrospective | 356            | Mean: 58   | 356 (100%)  | Shave vs. non-shave       | NA               | Positive margin rate; reoperation rate; volume of excised tissue | 2004–2008    |
| Mook et al. (2012)     | USA     | Retrospective | 144            | Median: 59 | 42 (29.2%)  | Shave vs. non-shave       | 1.5              | Positive margin rate; reoperation rate; volume of excised tissue; complications | 2004–2009    |
| Unzeitig et al. (2012) | USA     | Retrospective | 522            | Mean: 57   | 384 (73.6%) | Shave vs. non-shave       | NA               | Reoperation rate                      | NA           |
| Yang et al. (2012)     | China   | Prospective  | 166            | Median: 49 | 24 (14.7%)  | Shave-after vs. shave-before | 2.1              | Positive margin rate                  | 2008–2009    |
| Hequet et al. (2013)   | France  | Retrospective | 294            | Median: 57 | 35 (12%)    | Shave-after vs. shave-before | 1.2              | Positive margin rate; recurrence rate | 2003–2008    |
| Bolger et al. (2015)   | Ireland | Retrospective | 188            | Mean: 54   | 0           | Shave vs. non-shave       | NA               | Positive margin rate; reoperation rate | 2008–2011    |
| Chagpar et al. (2015)  | USA     | RCT         | 235            | Mean: 61   | 56 (23.8%)  | Shave vs. non-shave       | 1.1              | Positive margin rate; reoperation rate; volume of excised tissue; complications | 2011–2013    |

(Continued)
In the sensitivity analysis, we specifically analyzed the 2 RCTs by using the relative risk (RR) as estimates [25,27], and this analysis still showed a significant correlation (RR = 0.53, 95% CI 0.44–0.64; $I^2 = 19.2\%$). When excluding the included studies one by one, no individual study accounted for a significant change in the pooled data. In the meta-regression, sample size and the proportion of DCIS did not appear to account for the source of heterogeneity ($P = 0.32$ and $P = 0.67$, respectively). The funnel plot was symmetrical (Fig 3A), and no publication bias was detected by the Begg’s test ($P = 0.45$) or Egger’s test ($P = 0.09$).

Reoperation rate
Thirteen comparative studies were available. The pooled reoperation rate was 15.0% (95% CI 9.3–23.3%; $I^2 = 94.5\%, P < 0.05$) for the CS group, and was 30.1% (95% CI 21.8–39.9%; $I^2 = 95.0\%, P < 0.05$) for BCS alone. CS plus partial mastectomy could significantly reduce the reoperation rate when compared to standard partial mastectomy (OR = 0.42, 95% CI 0.30–0.59, $P < 0.05$) (Fig 4). A significantly high heterogeneity was shown ($I^2 = 74.9\%, P < 0.05$). A sensitivity analysis by excluding one individual record at a time did not detect a significant change for any study. In the meta-regression analysis, neither the sample size ($P = 0.36$) nor the proportion of DCIS ($P = 0.91$) could explain the source of heterogeneity. The funnel plot was symmetrical (Fig 3B). No publication bias was revealed by Begg’s test ($P = 0.58$) or Egger’s test ($P = 0.44$).

Recurrence
Four studies reported data on locoregional recurrence [15,27,32,37]. The pooled incidence of locoregional recurrence for the CS group was 3.0% (95% CI 2.0–4.5%), and for the standard partial mastectomy group was 4.0% (95% CI 1.1–13.4%). The pooled result showed that CS in addition to BCS reduced the incidence of locoregional recurrence by 14% but this was not statistically significant (OR = 0.86, 95% CI 0.32–2.35; $P = 0.78$) (Fig 5). The heterogeneity was low and non-significant ($I^2 = 32.1\%, P = 0.22$). Only 2 studies compared additional CS with BCS alone on distal recurrence [15,27]. No significant result could be detected (OR = 1.75, 95% CI 0.18–17.04, $P = 0.63$; $I^2 = 60.0\%, P = 0.11$).

Excised tissue volume and cosmetic outcome
Eight studies compared the excised tissue volume between CS plus BCS and BCS alone [15,25,27,31–33,35,36]. Four studies were eligible for data synthesis [15,27,32,33]. The pooled data revealed that CS did not have a significantly increased volume of excised tissue compared with BCS alone, with a high level of heterogeneity (WMD = −23.88, 95% CI −55.20 to 7.44, $P = 0.14$;
I² = 77.7%, P < 0.05) (Fig 6). Two studies reported the cosmetic outcome. Mook et al. demonstrated that patients undergoing CS had improved cosmesis compared with those undergoing partial mastectomy [31]. Chagpar et al. showed a non-significant difference between the CS group and the BCS alone group in the patients’ perception of their cosmetic outcomes [25].

**Discussion**

In early years, cavity shave sampling was utilized as a pathological procedure to examine residual disease in the remnant cavity or tumor bed [13,47]. Frequently, residual tumor was
detected in the resected cavity specimen [11,13,48]. A positive margin was shown to be associated with a lower reoperation and re-excision rates than a negative margin [16,43,44,48–50]. However, the cavity biopsy differed from cavity resection in extent and width [16,48]. The variability of cavity sampling techniques has been elaborately summarized before [16]. In contrast, the technique of CS is relatively consistent, with complete resection of the surface and sufficient width of the cavity wall.

Our findings suggested that additional CS had a lower positive margin rate than BCS alone (16.4% vs. 31.9%). CS was associated with a 59% OR reduction in the tumor-involved margin. The precision of this association was reinforced by the narrow 95% CI of 0.32–0.53 [51]. The statistical significance was reinforced by stratified analysis of self-control or comparative

---

**Fig 3. The Publication Bias Shown by Funnel Plots.** (A) Funnel plot for studies comparing the positive margin rate; (B) Funnel plot for studies comparing the reoperation rate.

doi:10.1371/journal.pone.0168705.g003

**Fig 4. Forest Plot Comparing the Reoperation Rate for Lumpectomy With and Without Cavity Shaving.**

doi:10.1371/journal.pone.0168705.g004
studies, and by the pooled data from 2 RCTs. To date, the NCT01452399 trial represented
the most convincing evidence with regard to CS [25]. Notably, this trial demonstrated a
significant superiority for cavity shaving in univariate analysis ($P = 0.01$) but not in multivariate
analysis ($P = 0.06$). In this meta-analysis, we included a large number of studies with
greater statistical power and proved the advantage of CS.

CS with BCS could approximately halve the reoperation rate compared with BCS alone
(15.0% vs. 30.1%). In accordance with the trial by Chagpar et al. [25], this meta-analysis

![Forest Plot Comparing the Locoregional Recurrence Rate for Lumpectomy With and Without Cavity Shaving.](doi:10.1371/journal.pone.0168705.g005)

![Forest Plot Comparing the Excised Tissue Volume for Lumpectomy With and Without Cavity Shaving.](doi:10.1371/journal.pone.0168705.g006)
showed that CS was associated with a significantly reduced reoperation rate (OR = 0.42). The statistical power was also reinforced by the narrow 95% CI of 0.30–0.59. CS had a non-significant impact on the rate of locoregional recurrence. However, the pooled local recurrence rate was low (3% vs. 4%). CS did not seem to correlate with decreased distant recurrence. Recurrence is an outcome that requires long-term follow-up and might be influenced by multiple clinicopathological factors, such as genetic mutation, histology type, and neoadjuvant chemotherapy (NAC). In addition, the very small number of studies limits the statistical power.

One of the major concerns related to CS is the excessive resection of tissue volume and the subsequent poor aesthetic result. However, we did not find that CS significantly excised more tissue volume than standard partial mastectomy. In fact, the excision extent was largely at the discretion of individual surgeons, some of whom might have decided to perform wide resection to ensure a negative margin when the cavity wall was not removed. Although data on cosmetic outcome are scarce, 2 related studies did not show compromised cosmetic satisfaction with CS [25,31].

Notably, multiple tumors and technical factors could influence the determination of margin status and these are generally beyond the control of surgeons. DCIS was a critical issue that deserved special attention owing to its tendency to be multifocal [49]. Margin-positive patients with DCIS had a worse prognosis compared with margin-positive patients with invasive ductal carcinoma [52]. NAC treatment might lead to tumor shrinkage in a mosaic or honeycomb pattern [53]. Consequently, surgical resection of the tumor mass in NAC-treated patients tends to leave more residual carcinoma in the cavity compared with resection in non-NAC-treated patients [49]. Chen et al. showed that the cavity margin status was significantly associated with locoregional recurrence in NAC-treated patients but not in non-NAC-treated patients [49]. In addition, tumor size [29,40,45], tumor grade [29,46,49], vascular invasion [29,46,49], and lymph node metastasis [15,29,40,45,49] have been suggested to be correlated with the cavity-shave margin status. These factors should be carefully considered when planning the extent of the cavity shave margin [29].

This meta-analysis has several limitations. Because retrospective studies or non-randomized studies were included [14,37,48], recall bias and selection bias were unavoidable. The definition of the positive cavity shave margin was not consistent, and the standard of positivity varied between studies with respect to the distance from the cut edge. Although the guideline defines no ink on tumor as an adequate margin [10], the inking method might lead to false-positive results owing to shrinkage of the specimen, ink seeping into the specimen, or dislocation of malignant cells towards the margins [36]. This criteria was recently criticized to result in increased positive CSM compared with the standard ≥2 mm margin in lumpectomy [54–56]. The thickness of the cavity shave and whether or not it was oriented were at the discretion of the surgeon [15]. In addition, it was rather difficult to standardize the excised volume of CSM [25]. The majority of studies did not perform intraoperative frozen section analysis of the shaved cavity margin [37]. Several confounding factors, such as post-BCS radiotherapy [57], have been suggested to be closely associated with future recurrence or survival. Lumpectomy specimens with narrower margins were more likely to have residual disease in two or more SCM [54]. In addition, the advancement of intraoperative imaging techniques could help eliminate re-excisions [58,59].

**Conclusion**

In conclusion, our meta-analysis confirmed that additional CS was effective in reducing margin involvement and the reoperation rate when compared with partial mastectomy alone. CS did not seem to be associated with an excessive excised tissue volume or poor cosmetic
outcomes. Although the included studies suffered from high heterogeneity, they represented the best evidence currently available. Reassuringly, our findings were consistent with the results from the largest single-center RCT on the cavity shave margin.

**Supporting Information**

S1 File. Search strategy used for PubMed database.
(DOCX)

S2 File. PRISMA 2009 Checklist.
(DOC)

S1 Table. Quality assessment of randomized controlled trials by the Jadad scale.
(DOCX)

S2 Table. Quality assessment of non-randomized studies by the modified Newcastle-Ottawa scale (NOS).
(DOCX)

**Author Contributions**

Conceptualization: JH.
Data curation: JH.
Formal analysis: KW.
Funding acquisition: JH.
Investigation: KW.
Methodology: YR.
Project administration: JH.
Resources: JH.
Software: JH.
Supervision: JH.
Validation: JH.
Visualization: JH.
Writing – original draft: KW.
Writing – review & editing: JH.

**References**

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin 2016; 66: 7–30. doi: 10.3322/caac.21332 PMID: 26742998

2. Cody HS 3rd, Van Zee KJ. Reexcision—The Other Breast Cancer Epidemic. N Engl J Med 2015; 373: 568–569. doi: 10.1056/NEJMe1507190 PMID: 26244311

3. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. N Engl J Med 2002; 347: 1227–1232. doi: 10.1056/NEJMoa020989 PMID: 12393819
4. Barton MK. Mastectomy and breast-conserving therapy confer equivalent outcomes in young women with early-stage breast cancer. CA Cancer J Clin 2015; 65: 335–336. doi: 10.3322/caac.21289 PMID: 26173435

5. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, et al. Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. N Engl J Med 2002; 347: 1233–1241. doi: 10.1056/NEJMoa022152 PMID: 12393820

6. McCaighill LE, Single RM, Aiello Bowles EJ, Feigelson HS, James TA, Barney T, et al. Variability in re-excision following breast conservation surgery. JAMA 2012; 307: 467–475. doi: 10.1001/jama.2012.43 PMID: 22298678

7. Wanis ML, Wong JA, Rodriguez S, Wong JM, Jabo B, Ashok A, et al. Rate of re-excision after breast-conserving surgery for invasive lobular carcinoma. Am Surg 2013; 79: 1119–1122. PMID: 24160812

8. Silverstein MJ, Lagios MD, Groshen S, Waisman JR, Lewinsky BS, Martino S, et al. The influence of margin width on local control of ductal carcinoma in situ of the breast. N Engl J Med 1999; 340: 1455–1461. doi: 10.1056/NEJM199905133401902 PMID: 10320383

9. McCaighill LE, Single R, Ratliff J, Sheehy-Jones J, Gray A, James T. Local recurrence after partial mastectomy: relation to initial surgical margins. Am J Surg 2011; 201: 374–378; discussion 378. doi: 10.1016/j.amjsurg.2010.09.024 PMID: 21367382

10. Moran MS, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton J, et al. Society of Surgical Oncology-American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. JCO Oncol 2014; 32: 1507–1515. doi: 10.1002/jco.2013.53.3935 PMID: 24516019

11. Macmillan RD, Purushotham AD, Mallon E, Love JG, George WD. Tumour bed positivity predicts outcome after breast-conserving surgery. Br J Surg 1997; 84: 1559–1562. PMID: 9393279

12. Macmillan RD, Purushotham AD, Mallon E, Ramsay G, George WD. Breast-conserving surgery and tumour bed positivity in patients with breast cancer. Br J Surg 1994; 81: 56–58. PMID: 8313122

13. Umpleby HC, Herbert A, Royle GT, Taylor I. Wide excision of primary breast cancer: the incidence of residual carcinoma at the site of excision. Ann R Coll Surg Engl 1998; 70: 246–248.

14. Gibson GR, Lesnikoski BA, Yoo J, Mott LA, Cady B, Barth RJ Jr. A comparison of ink-directed and traditional whole-cavity re-excision for breast lumpectomy specimens with positive margins. Ann Surg Oncol 2001; 8: 693–704. PMID: 11597009

15. Coopey SB, Buckley JM, Smith BL, Hughes KS, Gadd MA, Specht MC. Lumpectomy cavity shaved margins do not impact re-excision rates in breast cancer patients. Ann Surg Oncol 2011; 18: 3036–3040. doi: 10.1245/s10434-011-1909-7 PMID: 21947583

16. Povoski SP, Jimenez RE, Wang WP, Xu RX. Standardized and reproducible methodology for the comprehensive and systematic assessment of surgical resection margins during breast-conserving surgery for invasive breast cancer. BMC Cancer 2009; 9: 254. doi: 10.1186/1471-2407-9-254 PMID: 19635166

17. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009; 6: e1000097. doi: 10.1371/journal.pmed.1000097 PMID: 19621072

18. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996; 17: 1–12. PMID: 8721797

19. Wells GA, Shea B, O'Connell D, Peterson J, Welch V. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. http://wwwohric.ca/programs/c clinical_epidemiology/oxfordasp.

20. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol 2014; 14: 135. doi: 10.1186/1471-2288-14-135 PMID: 25524443

21. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003; 327: 557–560. doi: 10.1136/bmj.327.7414.557 PMID: 12958120

22. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. Biometrics 1994; 50: 1088–1101. PMID: 7786990

23. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997; 315: 629–634. PMID: 9310563

24. Bolger JC, Solon JG, Khan SA, Hill AD, Power CP. A comparison of intra-operative margin management techniques in breast-conserving surgery: a standardised approach reduces the likelihood of residual disease without increasing operative time. Breast Cancer 2015; 22: 262–268. doi: 10.1007/s12282-013-0473-3 PMID: 23649303
25. Chagpar AB, Killelea BK, Tsangaris TN, Butler M, Stavris K, Li F, et al. A randomized, controlled trial of cavity shave margins in breast cancer. N Engl J Med 2015; 373: 503–510. doi: 10.1056/NEJMoA1504473 PMID: 26028131

26. Huston TL, Pigalarga R, Osborne MP, Toussimis E. The influence of additional surgical margins on the total specimen volume excised and the reoperative rate after breast-conserving surgery. Am J Surg 2006; 192: 509–512. doi: 10.1016/j.amjsurg.2006.06.021 PMID: 16978962

27. Jones V, Linebarger J, Perez S, Gabram S, Okoli J, Bumpers H, et al. Excising Additional Margins at Initial Breast-Conserving Surgery (BCS) Reduces the Need for Re-excision in a Predominantly African American Population: A Report of a Randomized Prospective Study in a Public Hospital. Ann Surg Oncol 2016; 23: 456–464. doi: 10.1245/s10434-015-4789-4 PMID: 26254169

28. Kobbermann A, Unzeitig A, Xie XJ, Yan J, Euhus D, Peng Y, et al. Impact of routine cavity shave margins on breast cancer re-excision rates. Ann Surg Oncol 2011; 18: 1349–1355. doi: 10.1245/s10434-010-1420-6 PMID: 21046260

29. Lovrics PJ, Cornacchi SD, Farrokhyar F, Garnett A, Chen V, Franic S, et al. The relationship between surgical factors and margin status after breast-conservation surgery for early stage breast cancer. Am J Surg 2009; 197: 740–746. doi: 10.1016/j.amjsurg.2008.03.007 PMID: 18789424

30. Marudanayagam R, Sinhal R, Tanchel B, O’Connor B, Balasubramanian B, Paterson I. Effect of cavity shaving on reoperation rate following breast-conserving surgery. Breast J 2008; 14: 570–573. doi: 10.1111/j.1524-4741.2008.00649.x PMID: 19000040

31. Mook J, Klein R, Kobbermann A, Unzeitig A, Euhus D, Peng Y, et al. Volume of excision and cosmesis with routine cavity shave margins technique. Ann Surg Oncol 2010; 17: 228–234. doi: 10.1245/s10434-009-0643-x PMID: 19636625

32. Pata G, Bartoli M, Bianchi A, Pasini M, Roncali S, Ragni F. Additional Cavity Shaving at the Time of Breast-Conserving Surgery Enhances Accuracy of Margin Status Examination. Ann Surg Oncol 2016; 23: 2802–8. doi: 10.1245/s10434-016-5210-7 PMID: 27034079

33. Zavagno G, Dona M, Orvieto E, Mocellin S, Pasquali S, Goldin E, et al. Separate cavity margins excision as a complement to conservative breast cancer surgery. Eur J Surg Oncol 2010; 36: 632–638. doi: 10.1016/j.ejso.2010.05.018 PMID: 20542659

34. Unzeitig A, Kobbermann A, Xie XJ, Yan J, Euhus D, Peng Y, et al. Influence of surgical technique on mastectomy and reexcision rates in breast-conserving therapy for cancer. Int J Surg Oncol 2012; 2012: 725121. doi: 10.1155/2012/725121 PMID: 22312542

35. Wolf JH, Wen Y, Axelrod D, Roses D, Guth A, Shapiro R, et al. Higher Volume at Time of Breast-Conserving Surgery Reduces Re-Excision in DCIS. Int J Surg Oncol 2011; 2011: 785803. doi: 10.1155/2011/785803 PMID: 22312524

43. Cao D, Lin C, Woo SH, Vang R, Tsangaris TN, Argani P. Separate cavity margin sampling at the time of initial breast lumpectomy significantly reduces the need for reexcisions. Am J Surg Pathol 2005; 29: 1625–1632. PMID: 16327435

45. Feron JG, Nguyen A, Bezu C, Antoine M, Darai E, Coutant C, et al. Interest in cavity shaving in breast conservative treatment does not depend on lumpectomy technique. Breast 2011; 20: 358–364. doi: 10.1016/j.breast.2011.01.014 PMID: 21324697

46. Hequet D, Bricou A, Delpech Y, Barranger E. Surgical management modifications following systematic additional shaving of cavity margins in breast-conservation treatment. Ann Surg Oncol 2011; 18: 114–118. doi: 10.1245/s10434-010-1211-0 PMID: 20628283

47. Hequet D, Bricou A, Koundal M, Ziol M, Feron JG, Rouzier R, et al. Systematic cavity shaving: modifications of breast cancer management and long-term local recurrence, a multicentre study. Eur J Surg Oncol 2013; 39: 899–905. doi: 10.1016/j.ejso.2013.05.012 PMID: 23773800

48. Jacobson AF, Asad J, Booolbol SK, Osborne MP, Boachie-Adjei K, Feldman SM. Do additional shaved margins at the time of lumpectomy eliminate the need for re-excision? Am J Surg 2008; 196: 556–558. doi: 10.1016/j.amjsurg.2008.06.007 PMID: 18809063

49. Janes SE, Stankeata M, Singh S, Isgar B. Systematic cavity shaves reduces close margins and re-excision rates in breast conserving surgery. Breast 2006; 15: 326–330. doi: 10.1016/j.breast.2005.10.006 PMID: 16337123
44. Keskek M, Kothari M, Ardehali B, Betambe au N, Nasiri N, Gui GP. Factors predisposing to cavity margin positivity following conservation surgery for breast cancer. Eur J Surg Oncol 2004; 30: 1058–1064. doi: 10.1016/j.ejso.2004.07.019 PMID: 15522551

45. Tengher-Barma I, Héquet D, Reboldi-Leffler A, Frassati-Biaggi A, Seince N, Rodrigues-Faure A, et al. Prevalence and predictive factors for the detection of carcinoma in cavity margin performed at the time of breast lumpectomy. Mod Pathol 2009; 22: 299–305. doi: 10.1038/modpathol.2008.186 PMID: 18997732

46. Yang H, Jia W, Chen K, Zeng Y, Li S, Jin L, et al. Cavity margins and lumpectomy margins for pathological assessment: which is superior in breast-conserving surgery? J Surg Res 2012; 178: 751–757. doi: 10.1016/j.jss.2012.05.030 PMID: 22683081

47. Guidi AJ, Connolly JL, Harris JR, Schnitt SJ. The relationship between shaved margin and inked margin status in breast excision specimens. Cancer 1997; 79: 1568–1573. PMID: 9118040

48. Barthelmes L, Al Awa A, Crawford DJ. Effect of cavity margin shavings to ensure completeness of excision on local recurrence rates following breast conserving surgery. Eur J Surg Oncol 2003; 29: 644–648. PMID: 14511610

49. Chen K, Jia W, Li S, He J, Zeng Y, Yang H, et al. Cavity margin status is an independent risk factor for local-regional recurrence in breast cancer patients treated with neoadjuvant chemotherapy before breast-conserving surgery. Am Surg 2011; 77: 1700–1706. PMID: 22273234

50. Besana-Ciani I, Greenall MJ. The importance of margins status after breast conservative surgery and radiotherapy in node positive patients: a follow-up of 10–15 years. Int Semin Surg Oncol 2008; 5: 13. doi: 10.1186/1477-7800-5-13 PMID: 18498621

51. Guyatt GH, Oxman AD, Kunz R, Brozek J, Alonso-Coello P, Rind D, et al. GRADE guidelines 6. Rating the quality of evidence—imprecision. J Clin Epidemiol 2011; 64: 1283–1293. doi: 10.1016/j.jclinepi.2011.01.012 PMID: 21839614

52. Singletry SE. Surgical margins in patients with early-stage breast cancer treated with breast conservation therapy. Am J Surg 2002; 184: 383–393. PMID: 12433599

53. Akashi-Tanaka S, Fukutom T, Sato N, Iwamoto E, Watanabe T, Katsumata N, et al. The use of contrast-enhanced computed tomography before neoadjuvant chemotherapy to identify patients likely to be treated safely with breast-conserving surgery. Ann Surg 2004; 239: 238–243. doi: 10.1097/01.sla.0000109157.15687.d9 PMID: 14745332

54. Merrill AL, Tang R, Plichta JK, Rai U, Coopey SB, McEvoy MP, et al. Should New "No Ink On Tumor" Lumpectomy Margin Guidelines be Applied to Ductal Carcinoma In Situ (DCIS)? A Retrospective Review Using Shaved Cavity Margins. Ann Surg Oncol. 2016; 23: 3453–8 doi: 10.1245/s10434-016-5251-y PMID: 27207096

55. Merrill AL, Coopey SB, Tang R, McEvoy MP, Specht MC, Hughes KS, et al. Implications of New Lumpectomy Margin Guidelines for Breast-Conserving Surgery: Changes in Reexcision Rates and Predicted Rates of Residual Tumor. Ann Surg Oncol 2016; 23: 729–734. doi: 10.1245/s10434-016-4916-2 PMID: 26467498

56. Rubio IT, Ahmed M, Kovacs T, Marco V. Margins in breast conserving surgery: A practice-changing process. Eur J Surg Oncol 2016; 42: 631–640. doi: 10.1016/j.ejso.2016.01.019 PMID: 26880017

57. Iacucancho G, Pinnaro P, Landoni V, Marzi S, Soriani A, Giordano C, et al. Single fraction partial breast irradiation in prone position. J Exp Clin Cancer Res 2007; 26: 543–552. PMID: 18365551

58. Zysk AM, Chen K, Gabrielsson E, Tafra L, May Gonzalez EA, Canner JK, et al. Intraoperative Assessment of Final Margins with a Handheld Optical Imaging Probe During Breast-Conserving Surgery May Reduce the Reoperation Rate: Results of a Multicenter Study. Ann Surg Oncol 2015; 22: 3356–3362. doi: 10.1245/s10434-015-4665-2 PMID: 2620553

59. Tang R, Coopey SB, Buckley JM, Attreth OP, Fernandez LJ, Brachtel EF, et al. A pilot study evaluating shaved cavity margins with micro-computed tomography: a novel method for predicting lumpectomy margin status intraoperatively. Breast J 2013; 19: 485–489. doi: 10.1111/tbj.12146 PMID: 23773680