SHOULD CAVITY SHAVE MARGINS BE PERFORMED AS A ROUTINE IN BREAST CONSERVING SURGERY? A REVIEW OF RANDOMISED CONTROLLED TRIALS

Zackariah Clement∗,1

∗Breast and Endocrine Surgery, Flinders Medical Centre, Adelaide, Australia.

ABSTRACT

Background: Breast-conserving surgery (BCS) is the standard of care for women with early breast cancer. The margin status is crucial in breast-conserving surgery and is an important determinant for local recurrence. Local recurrence is associated with decreased overall and disease-free survival. Several studies have shown that cavity shave margin reduces the rate of positive margins and local recurrence. This review analyses the randomised controlled trials to compare the role of cavity shave margin in breast conserving surgery and its effect on positive margins and re-excision rates.

Methods: A systematic search of literature published before December 2016 for randomised controlled trials in MEDLINE, Pubmed, EMBASE, Proquest, Cochrane central register of controlled trials and Google Scholar was performed. Out of 12 articles, two randomised controlled trials were eligible. Positive margins and re-excision rates were analysed using odds ratio and risk difference.

Results: Out of 12 studies, 2 were suitable for review. Overall positive margins were 18.3% and 36% in the CSM and No-CSM groups respectively, with an odds ratio of 0.373 (95% CI, 0.189 to 0.739, P= 0.232) and risk difference of -0.194 (95% CI, -0.336 to -0.053, P= 0.198). The re-excision rates were lower in the CSM group when compared to the No-CSM group (12.2% vs 31.3%) with an odds ratio of 0.28 (95% CI, 0.160 to 0.520, P=0.578) and risk difference was -0.199 (95% CI, -0.309 to -0.089, P=0.264).

Conclusion: Analysis of the randomised controlled trials showed that cavity shave margins significantly reduced the risk of positive margins and the need for re-excision. It is a beneficial technique in women undergoing lumpectomy and breast conserving surgery.

KEYWORDS: Early breast cancer, breast conserving surgery, cavity shave margins

HOW TO CITE THIS ARTICLE

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Background:

Breast-conserving surgery (BCS) is the standard of care for women with early breast cancer. BCS include lumpectomy and sentinel lymph node biopsy followed by adjuvant therapy and whole breast radiation therapy [1-3]. The aim of BCS is to completely excise the tumour with negative margins and maintain satisfactory and acceptable cosmetic outcome. The importance
of margin status of breast conserving surgery for breast cancer is well documented [3-8]. Although the overall survival rates for breast conversing surgery is equivalent to total mastectomy, margin status is an important determinant of local recurrence. It has been reported that approximately 20-40% of patients have positive margins after breast conserving surgery and require re-excision for clear margins [3,6-8]. Negative margin does not mean a complete absence of residual unrectected tissue in the treated breast, but it results in decreased tumour burden low enough to be treated with radiotherapy. Positive margins are associated with 2 to 3 times increased the risk of local recurrence [7-11].

It is reported that the local recurrence is associated with decreased overall and disease-free survival [6, 7, 11, 12]. The determination of negative margins on a lumpectomy specimen depends on the adequacy of excision and the method of margin assessment. Three commonly known techniques include perpendicular, tangential and cavity shave margin methods. Among those three methods cavity shave margin method has been shown to have the lowest positive margin rate [13]. Several RCT and retrospective studies have shown that additional tissue circumferentially around the cavity (cavity shave margin-CSM) reduces the rate of positive margins. CSM have also shown to be useful in identifying multifocal disease [1-11].

Some authors argue that routine cavity shaving is not required if adequate margins are taken around the tumour, and selective intraoperative resection of margins are sufficient to reduce the rates of positive margins [12]. This systematic review analysed the literature and randomised controlled trials to compare the role of cavity shave margin in breast conserving surgery and its effect on positive margins and re-excision rates.

Methodology

Literature search
A comprehensive literature search was performed. All relevant randomised controlled trials regardless of language or publication status were searched. Publications in the following databases were searched up to December 2016: MEDLINE, Pubmed, EMBASE, Proquest, Cochrane central register of controlled trials and Google scholar. The search strategies and keywords used were “cavity shave margin”, “breast cancer”, “positive margins”, “re-excision”, and “breast conserving surgery”. There was no language restriction applied.

Inclusion and exclusion criteria
This review focused on the role of cavity shave margins in early breast cancer. All Published randomised controlled trials were included in women with the intervention as cavity shave margin in breast-conserving surgery versus breast-conserving surgery alone. Outcomes considered relevant for this review include positive margins, re-excision rates, recurrence, cosmetic outcome, and adverse events. The primary outcome was positive margin and re-excision rates. We excluded the articles if they were case reports, non-comparative studies, conference abstracts, duplicates, and reviews.

Methods of study selection, quality assessment and data extraction
The search identified the study titles and abstracts, and full-text articles were obtained and assessed for pre-specified inclusion criteria.

The quality of the included studies was evaluated using the following criteria: study design, the number of participants, outcome measures, and follow-up, withdrawal and loss to follow-up. Data extracted include author name, year of publication, the number of patients, recurrence, re-excision rates, cosmetic outcome, and adverse events.

Assessment of risk of bias
The studies were assessed for randomisation methodology, allocation concealment, blinding, incomplete outcome data, selective reporting, and other potential sources of bias. The Cochrane risk of bias tool was used to assess for the above bias.

Statistical analysis
Cochrane collaboration guidelines were used to analyse the studies. Dichotomous variables were evaluated using risk difference and odds ratio. Forest plot was generated using binary random effect and DerSimonian-Laird random-effects method with a confidence level of 95%. A P-value of less than 0.05 was considered statistically significant. Chi-square test was used to assess the heterogeneity. When the heterogeneity is high (I2 >50%), the random effect model was used. Analyses were done using the Open Meta- Analyst software.

Results

Search results
The database search identified 12 studies. 1 duplicate study was removed, and nine studies were excluded, as they were not randomised controlled trials. 2 randomised controlled trials were eligible, which was included in this comprehensive meta-analysis (Flow diagram).

Study characteristics
Table 1 shows the main feature of the included trials. 2 trials with a total of 311 patients were included. 164 patients underwent BCS with cavity shave margin (CSM), and 147 patients underwent BCS without cavity shave margins (No-CSM) (Table 1). The qualities of the included studies were good regarding sample size, random sequence generation, allocation concealment, blinding or participants and personnel, incomplete attrition, and selective reporting. Based on Cochrane risk of bias tool the risk of bias was graded as low, high, and unclear. Both the included studies had reported randomisation sequence generation, allocation concealment, blinding or participants and personnel, and selective reporting. However, it is unclear whether the assessment of outcome was blinded. Hence there is a possibility for
Table 1 Characteristics of included studies

| Study                | n   | CSM | No-CSM | Treatment arms             | Mean age | Node positive CSM | Node positive No-CSM | Recurrence CSM | Recurrence No-CSM | Follow-up |
|----------------------|-----|-----|--------|-----------------------------|---------|-------------------|----------------------|----------------|--------------------|-----------|
| Chapgar et al 2015   | 235 | 119 | 116    | BCS with CSM Vs BCS without CSM | 61 (33-94) | 11/98 (11%)       | 13/89 (15%)          | Ongoing evaluation | Ongoing evaluation | 60 months |
| Jones et al 2015     | 76  | 45  | 31     | BCS with CSM Vs BCS without CSM | 59.6 (37.8-80.9) | Not reported      | Not reported         | 3/45 (6.7%)      | 7/31 (22.6%)       | 22 months |

Detection bias in both the studies. There were no other potential sources of bias identified (Table 2).

**Tumour type**
In both the groups, the majority of the tumour was invasive carcinoma (78% in CSM and 72% in No-CSM groups respectively). Ductal carcinoma in situ (DCIS) was the only tumour found in 22% of the CSM and 28% in the No-CSM groups. A significant proportion of the participants had both DCIS and invasive components in their tumour (68% in CSM and 73% in No-CSM group respectively) (Table 3).

**Positive margin**
Overall positive margins were 18.3% and 36% in the CSM and No-CSM groups respectively. The rate of positive margin was significantly lower in the CSM group when compared to the No-CSM group with an odds ratio of 0.373 (95% CI, 0.189 to 0.739, P = 0.232). The risk difference was also in favour of the CSM group with an estimated risk difference of -0.194 (95% CI, -0.336 to -0.053, P = 0.198) (Table 4, Figures 1&2).

**Neoadjuvant chemotherapy**
Table 6 shows 7.3% and 8.2% participants received neoadjuvant chemotherapy in the CSM and No-CSM groups respectively with an odds ratio of 0.719 (95% CI, 0.297 to 1.743, P=0.341) (Figure 5). The risk difference between the groups was -0.013 (95% CI, -0.103 to 0.076, P=0.238) (Figures 6).

**Adverse events and cosmetic outcome**
Chapgar et al. reported three postoperative haematomas and all of them were in the No-CSM group. Jones et al. did not report any complications. Chapgar et al. reported that their patient perceived cosmetic outcome between both the groups were not significantly different.

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**Figure 1:** Positive margins - Odds Ratio

**Figure 2:** Positive margins - Risk Difference

**Figure 3:** Re-excision - Odds Ratio

**Figure 4:** Re-excision - Risk Difference

**Figure 5:** Neoadjuvant therapy - Odds Ratio
Table 2 Evaluation of study quality

| Study      | Random sequence generation (selection bias) | Allocation concealment (selection bias) | Blinding of participant and personnel (performance bias) | Blinding of outcome assessment (detection bias) | Incomplete outcome data (attrition bias) | Selective reporting (reporting bias) | Other bias |
|------------|---------------------------------------------|----------------------------------------|----------------------------------------------------------|-----------------------------------------------|----------------------------------------|-----------------------------------|------------|
| Chapgar et al 2015 | +                                           | +                                      | ?                                                       | +                                             | ?                                       | 11/98 (11%)                     | ?          |
| Jones et al 2015    | +                                           | +                                      | ?                                                       | +                                             | Not reported                          | ?                                 | ?          |

+ Low risk, - high risk, ? Unclear risk

Table 3 Tumour type

| Groups                          | Total Invasive carcinoma | DCIS only | DCIS +Invasive |
|---------------------------------|--------------------------|-----------|----------------|
| Study                           | n                        | CSM       | No-CSM         | CSM | No-CSM | CSM | No-CSM | CSM | No-CSM |
| Chapgar et al 2015              | 235                      | 119       | 116            | 95/119 (80%) | 84/116 (72%) | 24/119 (20%) | 32/116 (28%) | 83/119 (70%) | 87/116 (75%) |
| Jones et al 2015                | 76                       | 45        | 31             | 33/45 (73%)  | 22/31 (71%)   | 12/45 (27%)  | 9/31 (29%)   | 28/45 (62%)  | 17/31 (55%)  |
| Total                           | 311                      | 164       | 147            | 128/164 (78%) | 106/147 (72%) | 36/164 (22%) | 41/147 (28%) | 111/164 (68%) | 107/147 (73%) |

Figure 6: Neoadjuvant therapy - Risk Difference

different (P=0.69). Jones et al. did not report their cosmetic outcome.

Recurrence

Jones et al. reported a local recurrence rate of 6.7% in the CSM group when compared to 22.6% in the No-CSM group. Chapgar et al. are evaluating their recurrence, and their follow-up is still ongoing at the time of this study.

Discussion

This meta-analysis was performed to assess the role of cavity shave margin in breast conserving surgery in women with early breast cancer. Both the included studies had good sample size, high-quality reporting and minimal risk of bias.

After comparing the outcomes between the two groups, we found that excision of CSM significantly reduced the risk of positive margins and the need for re-excision. The positive margin in the CSM group was consistently lower than the No-CSM group. Despite a clear reduction in the positive margin, these findings were not statistically significant as the P value was 0.198. The re-excision rates were also much lower in the CSM group, but the result was not statistically significant with a P value of 0.264. The risk of local recurrence depends on the tumour biology, genetic composition, ER status-higher risk in ER-negative patients and the patients requiring neoadjuvant chemotherapy, and positive margins [8,10,12]. Positive margins can increase the possibility of recurrence of the loco-regional disease. Local recurrence is also associated with poor prognosis with overall decreased disease-free survival [8,11,13]. Several retrospective studies have reported lower rates of positive margins in patients who underwent breast-conserving surgery with cavity shave margin and also lower re-excision rates in those patient groups. Positive margins can lead to re-excisions, which causes significant psychological distress and anxiety for the patients and creates the need for another operation. This can affect patient’s confidence and trust in the treatment and the treating health professionals. This can also lead to increased cost for the health service provider [4-8,11].

Some authors argue that the use of cavity shave margin may be associated with a larger volume of tissue being excised and this can lead to the poor cosmetic outcome. However, some authors have suggested that CSM not only halves the rate of re-excision but also improves cosmetic results [4,14]. Chapgar et al. (2015) found that the volume of tissue excised in the CSM group was directly proportional to the volume of tissue.
Table 4 Positive margins

| Study            | n  | CSM | No-CSM | Positive margin CSM (%) | Positive margin No-CSM (%) |
|------------------|----|-----|--------|-------------------------|----------------------------|
| Chapgar et al 2015 | 235| 119 | 116    | 23/119 (19%)            | 39/116 (34%)               |
| Jones et al 2015 | 76 | 45  | 31     | 7/45 (15.6%)            | 14/31 (45.2%)              |
| Total            | 311| 164 | 147    | 30 (18.3%)              | 53 (36%)                   |

Table 5 Re-excision

| Study            | n  | CSM | No-CSM | Re-excision- CSM (%) | Re-excision-No-CSM (%) |
|------------------|----|-----|--------|----------------------|------------------------|
| Chapgar et al 2015 | 235| 119 | 116    | 13/119 (11%)         | 32/116 (28%)           |
| Jones et al 2015 | 76 | 45  | 31     | 7/45 (15.6%)         | 14/31 (45.2%)          |
| Total            | 311| 164 | 147    | 20/164 (12.2%)       | 46/147 (31.3%)         |

Table 6 Neoadjuvant chemotherapy

| Study            | n  | CSM | No-CSM | Neoadjuvant CSM | Neoadjuvant No-CSM |
|------------------|----|-----|--------|-----------------|-------------------|
| Chapgar et al 2015 | 235| 119 | 116    | 4/119 (3%)      | 3/116 (3%)        |
| Jones et al 2015 | 76 | 45  | 31     | 8/45 (17.8%)    | 9/31 (29%)        |
| Total            | 311| 164 | 147    | 12/164 (7.3%)   | 12/147 (8.2%)     |

excised before randomisation. The volume of tissue excised in the CSM group was significantly larger when compared to the No-CSM group (median 115.1 cm³ vs. 74.2 cm³). However, there was no reported difference in the patient-reported cosmetic outcome. However, several other studies have reported although the larger volume of tissue excision there is no inferior cosmetic outcome in patients who undergo cavity shave margin [3]. This may be due to the surgeon being more comfortable excising closer to the tumour during the initial excision, as they know a CSM will be performed after the initial excision to excise cavity margins [6]. Chapgar et al. (2015) reported postoperative three hematomas (2.5%), and no patients required drainage. This shows that CSM is associated with minimal adverse effects and complications and there is no difference when compared with traditional BCS alone [3]. It is reported that there is a minimal increase in the pathology cost with the cavity shave margin specimens and the benefits of decreased re-excision rates outweighs the cost of the pathologist. They also found that the overall cost was not significantly different between the CSM and the No-CSM groups [1].

Overall this study shows that the CSM plays a beneficial role in BCS in women with early breast cancer. Compared to patients who undergo BCS alone, BCS with CSM is associated with a substantial decrease in the rates of positive margin and re-excision rates. Due to a limited number of publication and study heterogeneity, the results should be interpreted with caution. Further high quality randomised controlled trials and meta-analysis are needed to further assess the role of CSM in the management of early breast cancer.

Authors’ Statements

Competing Interests
The authors declare no conflict of interest.

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