Effectiveness of cavity shave margin versus standard partial mastectomy in early stage breast cancer patients

Ahmed Salah Arafa, Abdelwahab S. Almoregy, Alaa Fiad

Department of General Surgery, Zagazig University Hospital, Zagazig University, Sharkia Province, Egypt

Correspondence to Ahmed S. Arafa, Department of General Surgery, Zagazig University Hospital, Zagazig University, Sharkia Province, Egypt. Tel: +20 102 524 4965; e-mail: ahmedarafaa237@gmail.com

Background
Breast-conserving surgery (BCS) is considered the gold standard of early stage invasive breast cancer treatment that achieves adequate surgical margins with an acceptable cosmetic outcome. The margin status is an important prognostic factor for local recurrence after BCS in patients with early breast cancer. The patients receiving BCS have a lifelong risk of local recurrence. To minimize this risk, a technique of margin evaluation, called cavity shaving or cavity margin shaving has been proposed and applied by some surgical teams to reduce the need for re-excisions and to detect multifocality.

Patients and methods
In the present prospective, randomized trial between August 2015 and August 2018, we assigned 40 women with breast cancer of stages 0–III who were undergoing partial mastectomy and divided into two groups; shave group and lumpectomy group. Excision of cavity shave margins consists of resection of breast tissue from four margins; superior, inferior, medial, and lateral after the excision of the primary specimen in the same procedure. We classified the margins as negative (>2 mm), close (<2 mm), or positive based on the distance from the tumor to the margin of resection.

Results
We have 40 patients in the current study. Overall, patients who underwent BCS plus cavity shaving had a higher rate of negative margins (92%) compared with patients who underwent BCS (66.7%). In shaving lumpectomy group (SLG), patients with negative margins before shaving were 15 (60%) versus 23 (92%) after shaving. All patients with positive margins ($n=7$) were offered a re-excision procedure.

Conclusion
Comparing to the lumpectomy alone, cavity margin shaving plus lumpectomy during BCS for early stage invasive breast cancer results in a higher rate of negative microscopic margins for tumor and a lower reoperation rate, although it increases the operation time, the resection volume.

Keywords:
breast carcinoma, breast-conserving surgery, cavity margin, lumpectomy, surgical margins

Introduction

Breast-conserving surgery (BCS) followed by adjuvant radiotherapy is the preferred treatment for localized early breast cancer as it has the same long-term survival and free metastasis survival as the mastectomy [1].

The main purpose of BCS for invasive and in-situ carcinoma is to obtain a complete excision of the tumor with a surrounding margin of normal tissue to prevent local recurrence, while maintaining an acceptable cosmetic breast appearance and this is considered to be obtained for 90% of patients [2].

The recurrence rates after local excision is widely vary among the different studies but there is a good consensus that the pathologic lumpectomy margin status is the most important factor to determine the risk of local recurrence following BCS [3].

Tartter *et al.* [4] clarified that a preoperative diagnosis by fine needle aspiration, a small tumor size and the absence of duct carcinoma *in situ* or the absence of an extensive intraductal carcinoma are all associated with a decreased risk of involved margins on surgical specimen.

In the survey of 702 institutions in North America, Taghian *et al.* [5] showed claimed that the definitions of the negative margins vary from 'no cells on the inked margin' to 'no cells at 5 mm from the inked margin.'

If the final margins are negative, the 5-year risk of local recurrence is 2–7%. While, if the margins are positive, the risk is 0–22% [6].

Unfortunately, up to 40% of patients who undergo BCS require subsequent operations or even a mastectomy to ultimately achieve negative margins [7].

It is absolutely unacceptable to have tumor cells directly at the cut edge of the excised specimen, regardless of the type of postsurgical adjuvant therapy [3].

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) [8].

Studies suggest at least four margins should be sampled [9], although others suggest six, inclusive of an anterior and posterior margin [10]. Samples were sent with the primary tumor for the histopathological examination. The cavity margin shaving (CMS) technique may be especially useful in detecting multifocal disease [10].

Aim of the study

The current investigation was carried out to compare the efficacy and safety between CS plus lumpectomy versus lumpectomy alone with regard to positive margins (tumor margin clearance), operation time, volume of tissue resected, re-excision rate, cosmetic outcome, and hospital stay.

Patients and methods

The present prospective, randomized, controlled trial was carried out between August 2015 and August 2018 in General Surgery Department at Zagazig University Hospitals. This study includes 40 women, 18 years of age or older who underwent BCS for histologically proven primary invasive breast carcinoma of stages 0–III. Randomization was occurred intraoperatively after surgeons had completed standard partial mastectomy. The indication to perform the shaving at the time of lumpectomy solely depending up on the surgeon preference and was not influenced by patient or tumor characteristics. Patients were divided randomly into two groups; group A (shave group) contains 20 patients treated by CMS plus lumpectomy, while group B [lumpectomy group (LG)] contains 20 patients treated by lumpectomy alone. Patients who had undergone an excisional biopsy or attempted partial mastectomy previously were excluded. After written informed consent was obtained, patients were enrolled in the study.

Our hypothesis is that taking additional tumor cavity margins at the time of the original operation results in lower reoperation rates and does not compromise cosmetic results measured by total volume breast tissue removed.

Surgical procedure

The tumor was widely excised up to the pectoralis fascia with an attempted macroscopic clear margin of at least 1 cm. The lumpectomy always included the overlying skin, if it was macroscopically infiltrated by the tumor. Specimens obtained during the partial mastectomy that were smaller than 5 cm in the greatest dimension were submitted for histologic evaluation in their entirety. A minimum of two sections perpendicular to each margin of the specimen obtained during partial mastectomy were evaluated.

In the shaving lumpectomy group (SLG), additional two to four shaving cavity margins (depending on the shape of the cavity after lumpectomy) of 5–10-mm thickness were taken circumferentially from the wall of the residual cavity of the lumpectomy. In our investigation, neither anterior, nor posterior cavity margins are removed since the initial lumpectomy is supposed to reach superficially the subcutis and deeply pectoral fascia. A complete cavity margins resection consists of removing a rim of breast tissue all around the initial tumor excision site.

Handling the surgical specimen

A single pathologist reviewed all the specimens included in this study. Each shaving was oriented with sutures and sent separately for histological examination after fixing the specimens with buffered neutral formalin 10%, labeled as superior, inferior, medial, or lateral shaving. These specimens are ideally promptly delivered in the fresh state. Importantly, they have been previously orientated with sutures by the surgeon in the operating room to designate a minimum of two orthogonal faces (e.g. superior and medial).

A suture is placed on the side of the new margin and all this side is inked. After formalin fixation, each cavity margin is fully sectioned into 3–5 mm thick slices perpendicularly to the inked surface, and totally transferred into blocks. Slices are placed consecutively but several slices can be put together in the block.

The size will be mentioned in terms of width (the largest after examination of the different slices/blocks

Table 1 Patient baseline characteristics

Patient characteristics	SLG group (*N*=15) [*n* (%)]	LG group (*N*=15) [*n* (%)]	*P* value
Age (years)			
Mean±SD	38.48±5.80	41.26±6.93	0.188[a]
Median (range)	37 (31–49)	39 (32–53)	
Tumor size (cm)			
Mean±SD	1.76±0.87	1.86±0.83	0.570[a]
Median (range)	2 (1–4)	2 (1–4)	
Palpable tumor			
Absent	19 (76)	11 (73.3)	1.000[b]
Present	6 (24)	4 (26.7)	
Tumor stage			
Stage 0	20 (80)	9 (60)	0.273[b]
Stage I	5 (20)	6 (40)	
Tumor type			
Ductal carcinoma *in situ*	19 (76)	13 (86.7)	0.686[b]
Invasive ductal carcinoma	6 (24)	2 (13.3)	
Lymph node			
Negative	22 (88)	12 (80)	0.654[b]
Positive	3 (12)	3 (20)	
Estrogen receptor			
Negative	4 (16)	7 (46.7)	0.065[b]
Positive	21 (84)	8 (53.3)	
Progesterone receptor			
Negative	7 (28)	4 (26.7)	1.000[b]
Positive	18 (72)	11 (73.3)	

N, total number of patients in each group; quantitative data were expressed as mean±SD and median (range); qualitative data were expressed as *n* (%). LG, lumpectomy group. [a]Mann–Whitney *U* test. [b]χ^2 test. *P* value less than 0.05 is significant.

for one margin cavity) or extension along the long axis of the cavity margin (depending on the number of slices involved), and compared to the localization of the tumor on the lumpectomy. Ideally, the distance of the carcinoma to the new margin is simply given in mm when; it is inferior to 1 cm.

To assess the margin status, the cut edges of the resection specimen must be differentially stained so that, they are clearly visible when individual sections are examined. Commonly, India ink has been used to stain the entire cut surface of the specimen, with placement of one or more sutures for directional orientation.

Margins were considered positive if the tumor cells (invasive carcinoma or in-situ carcinoma) were found directly at the cut edge of the surgical specimen, close if the tumor cells were found within 2 mm from the cut edge of the specimen, and negative if no tumor cells was identified more than 2 mm from the cut edge of the specimen.

In the presence of positive lumpectomy margins in the LG or positive shaving margins in the SLG, reoperation was undertaken in order to ensure a negative margin: re-excision or mastectomy depending on margin status,

multifocality, breast volume, and patient's preference. Adjuvant chemotherapy, radiation therapy, and hormonal therapy were given according to the standard regimen and protocol prevailing at the time. Completeness of excision was confirmed with intraoperative specimen radiographs for nonpalpable tumors that required wire localization and by gross inspection and palpation for other tumors.

The volume of excised breast tissue (after formalin fixation) was obtained from the pathology report by multiplying the three main diameters of the specimen. In the SLG, the volume of separately excised shavings was added to that of the lumpectomy specimen.

Study end points
The primary end point was the rate of positive margins on final pathological testing. Positive margins were defined as the tumor touching the specimen edge that was removed in patients with invasive cancer and tumor that was within 1 mm of the edge of the specimen removed in those with ductal carcinoma *in situ*.

The secondary end points included the volume of tissue excised, defined as cubic measurements (length×width×height) of all pieces of tissue

Table 2 Operative data and outcome

Operative data and outcome	SLG group (N=15) [n (%)]	LG group (N=15) [n (%)]	P value
Operation time (min)			
Mean±SD	84.92±14.14	71±17.84	0.007[a]
Median (range)	90 (50–100)	75 (35–100)	
Blood loss (ml)			
Mean±SD	163.20±32.46	179.33±27.37	0.109[a]
Median (range)	170 (100–200)	190 (100–200)	
Volume of lumpectomy (ml)			
Mean±SD	133.34±36.66	152.01±50.85	0.193[a]
Median (range)	140 (73–180)	160 (70.20–220)	
Volume of cavity shaving (ml)			
Mean±SD	14.24±4.11	0±0	<0.001[a]
Median (range)	15 (6.80–20.40)	0 (0–0)	
Total volume of excised breast tissue (ml)			
Mean±SD	143.40±39	154.88±49.01	0.379[a]
Median (range)	145 (84.90–198.30)	160 (70.20–220)	
Reoperation			
Absent	23 (92)	10 (66.7)	
Present	2 (8)	5 (33.3)	
Tumor margin Before shaving			
Negative	15 (60)	10 (66.7)	0.673[b]
Positive	10 (40)	5 (33.3)	
After shaving			
Negative	23 (92)	10 (66.7)	0.081[b]
Positive	2 (8)	5 (33.3)	
P valuec	0.013		
Hematoma			
Absent	25 (100)	14 (93.3)	0.375[b]
Present	0 (0)	1 (6.7)	
Cosmetic outcome*			
Poor	1 (4)	1 (6.7)	0.956[b]
Fair	3 (12)	2 (13.3)	
Good	12 (48)	6 (40)	
Excellent	9 (36)	6 (40)	
Hospital stay (h)			
Mean±SD	34.72±7.70	38.40±7.98	0.184[a]
Median (range)	33 (24–48)	40 (24–48)	

N, total number of patients in each group; quantitative data were expressed as mean±SD and median (range); qualitative data were expressed as n (%). LG, lumpectomy group. [a]Mann–Whitney U test. [b]χ^2 test. [c]McNemar's test. *Correspondence to Cosmesis was graded by the patients on a 4-point Likert scale (with 1 indicating poor, 2 fair, 3 good, and 4 excellent). P-value < 0.05 is significant.

removed, reoperation rates, and patient-reported cosmesis on a four-point Likert scale (with 1 indicating poor, 2 fair, 3 good, and 4 excellent). Reoperation rates, defined as the proportion of patients who were returned to the operating room for further surgery for margin clearance, were also recorded.

Postoperative follow-up
All patients had follow-up that consisted of annual breast radiography, ultrasound, and clinical examination.

Statistical analysis
Continuous variables were expressed as the mean±SD and median (range) and the categorical variables were expressed as a number (percentage). Continuous variables were checked for normality by using Shapiro–Wilk test. Mann–Whitney U test was used to compare between two groups of non-normally distributed data. Percent of categorical variables were compared using χ^2 test or Fisher's exact test when appropriate. Mc-Nemar's test was used for paired categorical data. All tests were two sided. P value less than 0.05 was considered statistically significant. All data were analyzed using Statistical Package for Social Science for Windows, version 20.0 (SPSS Inc., Chicago, Illinois, USA).
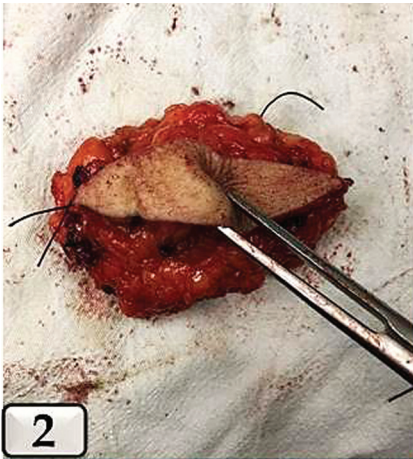
Results
Between August 2015 and August 2018, a total of 40 patients were enrolled in the trial. Patients of the two study

Figure 1
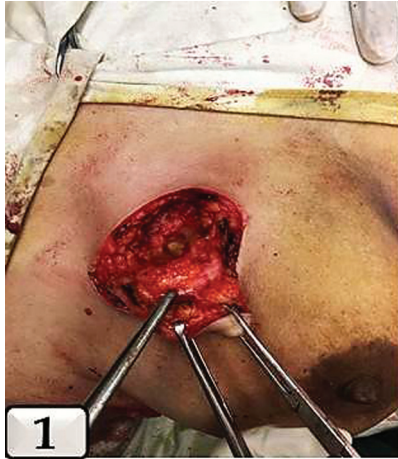
Excision of the breast lump.

Figure 3

Cavity shaved margins taken with scissors.

Figure 2

Lumpectomy specimen removed from cavity and orientated by silk sutures (two sutures superiorly and one suture medially).

Figure 4

Breast lump with four shaved cavity margins orientated by silk sutures (three sutures superiorly and two sutures medially and one suture inferiorly).

groups (SLG vs. LG) were well-matched with regard to baseline characteristics, tumor stage, and biology (Table 1).

The operation time was longer in SLG; where median and mean±SD were 90 and 84.92±14.14 in SLG and 75 and 71±17.84 in LG, respectively, with *P* value=0.007. The median lumpectomy volume was 140 ml in the SLG versus 160 ml in the LG (*P*=0.193). After additional shaving (median=15 ml), the total volume of removed breast tissue in the SLG rose to 145 ml, still not significantly different from the volume removed in the LG (160 ml) (*P*=0.379).
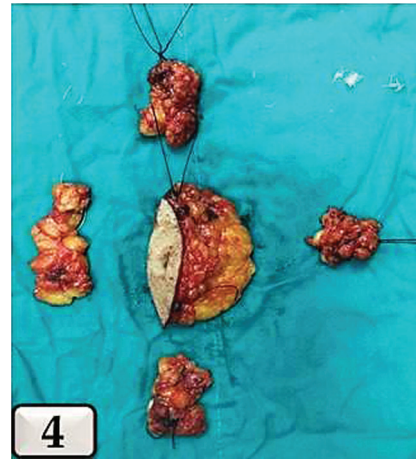
Overall, the patients who underwent BCS plus CS had a higher rate of negative margins (92%) compared with the patients who underwent BCS (66.7%) (*P*=0.081). In SLG, the patients with negative margins before shaving were 15 (60%) versus 23 (92%) after shaving

(*P*=0.013). All patients with positive margins (*n*=7) were offered a re-excision procedure. No significant difference in postoperative hematoma was observed between the two groups; being one in LG versus zero in SLG (*P*=0.375).

No significant difference in the cosmetic outcome was observed between the two groups (Table 2). No significant difference in the hospital stay was observed between the two groups; with mean±SD 34.72±7.70 in SLG versus 38.40±7.98 in LG with *P* value=0.184 (Figs 1–5).

Discussion

BCS includes wide local excision of the primary breast tumor followed by adjuvant radiation therapy, has

become the standard therapy for early breast cancer, with long-term survival that is comparable to mastectomy [11].

Successful BCS means complete tumor excision with adequate margins and when the margins are involved with tumor, reoperation for re-excision is recommended [10].

Local recurrence following BCS has been shown to be impacted by a number of patient and tumor characteristics, including patient age, tumor size, tumor grade, and presence of multifocal or multicentric disease [12]. However, the strongest predictor of the presence of

residual disease and local recurrence remains that of the surgical margin status [12].

Options for the intraoperative evaluation for margins status include gross examination of the specimen, frozen section, and touch preparation cytology of the margins [13].

Due to a high false-negative rate, technical complexity, and duration of such intraoperative procedures, none of these methods have been accepted as standard procedures for the margin assessment [14].

In early years, cavity shave sampling was utilized as a pathological procedure to examine residual disease in the remnant cavity or tumor bed [8].

Many trials have evaluated the impact of positive margins on local and distant recurrence and on survival [15].

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 [16].

Routine CMS have been suggested as a means to potentially reduce the frequency of positive margins and subsequent need for reoperation [17].

Approximately 20–40% of patients have positive margins (margins positive for tumor) after partial mastectomy and require a second operation for margin clearance [18].

A strong correlation between the local recurrence rate (LRR) and the margins status has been demonstrated in a large number of other studies based on the follow-up after BCS plus local radiotherapy, but the adequacy of microscopic margins width remains controversial [19].

However an evident association between the odds of LRR and the decreasing of threshold

Figure 5

Closure of the wound in layers.

Table 3 Comparison of recent literature evaluating cavity margin shaving

References	Preoperative diagnosis of carcinoma	SLG group	LG group	Routine CSM of margin	Definition of CMS (number of additional margins)	Definition of negative margin	Reduction in re-excision	P value
Cao et al. [25]	Unknown	126	NA	Yes	4–6	2 mm	61/103	
Jacobson et al. [26]	Unknown	125	NA	Yes	Most had all 6 margins	2 mm	61/83	
Marudanayagam et al. [27]	Yes	394	392	Yes	4	No tumor at inked margin	6.92%[a]	< 0.01
Rizzo et al. [28]	Yes	121	199	Yes	4–5	1 mm	27.9%[b]	< 0.05
Tengher-Barna et al. [29]	Yes	107	NA	Yes	4	3 mm	27/47	

CMS, cavity margin shaving; LG, lumpectomy group; NA, not applicable. [a]49/392 (12.5%) versus 22/394 (5.58%) requiring reoperation. [b]183/320 (57.2%) versus 272/320 (85.1%) with negative margins.

distances for negative margins was observed, confirming the influence of surgical margin status on LRR [20].

Gage and colleagues have described in 1996 four types of margins status: negative if more than 1 mm between tumor cells and the inked surface; close if less than or equal to 1 mm; positive if presence of tumor cells at the inked margin; and focally positive if tumor cells are present at the margin in three or fewer low-power fields. The 5-year LRR were 3, 2, 28, and 9%, respectively [21].

Patients with extensively positive margins had LRR of 27%, while patients with focally positive margins had an LRR of 14% [22].

A single study that examined age, tumor size, lymph node status, and clinical stage found that none of these were significantly associated with the presence of positive margins [23].

Tartter *et al.* [24] examined 674 excision biopsy specimens from patients who were candidates for BCS. By univariate analysis, they found that positive biopsy margins were associated with younger patient age, family history of breast cancer, larger tumor size, presence of ductal carcinoma *in situ*. Table 3 shows the comparison of recent literature evaluating CMS.

Peterson *et al.* [30] showed LRRs of 8, 10, and 17%, respectively, for negative, focally positive, and focally close (≤ 2 mm) margins from a series of consecutive 1021 stage I or II breast cancers.

Bolger and colleagues have recently reported with CMS, a re-excision rate of 25%, compared with 34%, if no margins assessment is carried out. Thus, cavity shave margins reduced significantly the likelihood of having residual disease ($P=0.02$). Of note, close margins (<2 mm) are correlated with the presence of residual disease ($P=0.01$) [31]. In our study, all patients with positive margins ($n=7$) (17.5%), two in SLG and five in LG, were offered a re-excision procedure.

Marudanayagam *et al.* [27] showed negative margins in 94.4% of 394 patients who underwent lumpectomy plus CMS, compared to 87.5% of 392 patients with lumpectomy only. In our study, the patients who underwent BCS plus CS had a higher rate of negative margins (92%) compared with patients who underwent BCS (66.7%) ($P=0.081$). In SLG,

the patients with negative margins before shaving were 15 (60%) versus 23 (92%) after shaving ($P=0.013$).

Although lumpectomy plus CMS is cost effective and it significantly reduces the rate of positive margins, it may lengthen the operating time, but it is not correlated with a worse cosmetic outcome due to larger final volumes of resection [32]. In our study, no significant difference in cosmetic outcome was observed between the two groups (Table 2). Operation time was longer in SLG; where median and mean±SD were 90 and 84.92±14.14 in SLG and 75 and 71±17.84 in LG, respectively, with *P* value=0.007.

Conclusion

From our results, we can concluded that additional CS after lumpectomy was effective in achieving appropriate tumor margin clearance, local disease control, reducing reoperation rate while ensuring good cosmetic results when compared with partial mastectomy alone. It is worth noting that these advantages can be achieved without any increase in the total volume of breast tissue removed.

Conflicts of interest
There are no conflicts of interest.

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