The Egyptian Journal of Hospital Medicine (October 2021) Vol. 85 (2), Page 3831-3837

Routine Margin Shaving Of Lumpectomy Cavity During Breast Conserving Surgery Detects Occult Multifocal Cancer, A Prospective Study

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ABSTRACT

Background: Cavity shaving (CS) entails circumferential tissue removal from residual lumpectomy cavity following tumor resection during breast conserving surgery (BCS). It could allow detection of occult multifocal breast cancer (OMFBC).

Objectives: This study aimed to highlight the impact of unidentified OMFBC as essential risk factor for local recurrence after BCS.

Patients and Methods: Eligible breast cancer patients for BCS and CS were prospectively enrolled. Patients with negative margins of "resected tumor specimens" were designated as group A whereas group B comprised those with positive margins. OMFBC, diagnosed in the additionally shaved margins of the "residual lumpectomy cavity" as malignant breast tissues with intervening normal areas, was investigated in both groups. The study was conducted through the period from November, 2017 to March, 2021.

Results: Forty-two patients with median age of 43 years were studied. Group A included 32 patients (76.2%) compared with 10 (23.8%) in group B. Overall, OMFBC was confirmed in the additionally shaved margins in 6 (14.3%) patients. OMFBC rate was less in group A (4/32 patients, 12.5%) compared to B (2/10 patient, 20%), however the difference did not reach statistical significance. In group B, another 1 patient showed persistent positive margins without evidence of OMFBC. All 7 patients with positive CS margins (6 with OMFBC and 1 with persistent positive margin without evidence of OMFBC) had their treatment strategy switched to modified radical mastectomy. Local recurrence occurred in only one among the remaing 35 patients (2.9%) who were treated by BCS with CS.

Conclusions: CS improves outcome of BCS by reducing the rate of positive margins, enabling diagnosis of occult multifocal breast cancer and reducing local recurrence.

Keywords: Breast cancer, Conservative surgery, Cavity shave margin.

INTRODUCTION

Breast conserving surgery (BCS) comprises partial mastectomy (lumpectomy, tumor resection) followed by adjuvant treatment including radiation and possibly systemic therapy [(1)]. Currently, BCS is the standard treatment for early-stage breast cancer. BCS provides not only superior cosmesis, but also equivalent survival benefit compared to the conventional procedures, which involve total mastectomy [(2)]. Safety of BCS relies on achieving negative margins of the resected tumor specimen and avoidance of missing occult multifocal breast cancer (OMFBC) in the walls of the residual lumpectomy cavity. Positive margins and overlooked OMFBC raise the incidence of local recurrence and increase the percentage of reoperations to 20-60% [(3–5)].

Given the unacceptably high re-excision rates, refinements to optimise the outcome of BCS have focused on fulfilment of two objectives including proper description of negative margin and avoidance of missing OMFBC [(6)]. To implement the first, a consensus on precise definition of negative margin based on the types of primary cancer was established [(7)]. In the setting of invasive ductal adenocarcinoma, negative margin was described as absence of malignancy at the border of lumpectomy specimen [(8)]. Nonetheless, ductal carcinoma in situ (DCIS) requires at least 2 mm width of cancer-free breast tissue from the edge of resected lump to conclude a negative margin [(9–11)].

The second objective was accomplished by several techniques, among which cavity shaving (CS), which denotes circumferential resection of additional tissues from the walls of the lumpectomy cavity, has achieved evident attention[(12, 13)]. Multicenter study showed that CS significantly reduced the incidence of positive margins from 36% to less that 10%, which correlated with remarkable decrease of re-operation rates from 24% to 9% [(14)].

However, the efficacy of CS might be challenged by missing OMFBC in the shaved margins of the residual lumpectomy cavity [(12)]. This could occur even in patients who had negative margins of their resected tumor specimens leading to failure of BCS [(15, 16)]. For instance, OMFBC was confirmed in CS margins of 8-23% of patients who initially had negative margins of lumpectomy (resected tumor) specimens [(12, 17, 18)].

In this study, we will highlight the impact of unidentified OMFBC as essential risk factor for local recurrence after BCS.

Received: 12/7/2021
Accepted: 8/9/2021

PATIENTS AND METHODS

This prospective comparative study was carried out at the Surgical Oncology Unit, Department of Surgery, Sohag University Hospitals, Sohag, Egypt. The study was conducted through the period from November, 2017 to March, 2021. Eligible patients were females ≥ 30 years with unilateral early breast cancer (stages I and II). Patients underwent breast conserving surgery (BCS) including partial mastectomy (lumpectomy) followed by cavity shaving (CS) of the residual lumpectomy margins. All patients had preoperatively biopsy-proven invasive or in situ ductal carcinoma.

Exclusion criteria:

Advanced and/or bilateral breast cancer, large tumor size (> 5 cm), neoadjuvant systemic therapy and inflammatory breast cancer.

Patients were then classified according to the histopathological status of lumpectomy (resected tumor) margin into group A with negative margins and group B with positive margins. Likewise, CS margins from both groups were histopathologically assessed.

Primary outcome was the rate of OMFBC in specimens of shaved margins of the residual lumpectomy cavity in both groups. Secondary outcomes included blood loss, operative time, postoperative complications and length of hospital stay.

Ethical approval:

Every patient provided a written informed consent on all surgical and non-surgical related procedures. The study was approved by Medical Research Ethics Committee, Sohag Faculty of Medicine. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Preoperative workup:

Thorough reviewing of the medical history, results of clinical examination, medical imaging and laboratory investigations was consistently undertaken in all patients. Medical imaging comprised bilateral breast and axillary ultrasonography with core needle biopsy from the identified breast mass, bilateral mammogram, contrast-enhanced computed tomography of the chest. Magnetic resonance was carried out in selected cases.

Surgical pocedures and histopathological evaluation:

Breast conserving surgery (BCS) was conducted by 2 surgeons. Initially, the first surgeon performed partial mastectomy (lumpectomy) by tumor resection with adequate (≥ 1cm) safety margin. The extent of this margin was decided during intraoperative assessment of the tumor. Furthermore, patients with stage II invasive disease underwent axillary dissection (levels I and II) through separate axillary incision. Then, another surgeon carried out cavity shaving (CS) by further circumferential tissue removal from the entire lumpecomy cavity without cosmetic compromise. Of note, frozen tissue examination was not done neither for lumpectomy specimen nor shaved cavity margins.

The resected lumpectomy specimens were marked with sutures to define at least two perpendicular aspects (e.g., superior and lateral). Furthermore, shaved margins were marked in accordance with their location and adjusted to indicate their sites in relation to the lumpectomy margin. The excised tissues (lumpectomy specimens and additionally shaved margins) were properly preserved and subsequently sent for histopathological assessment. Patients were regularly followed-up by multidisciplinary team in the Breast Surgery Ourpatient Clinic.

Statistical analysis

Statistical analysis was performed by Graphpad Prism 7. Number and percentages were utilized to express qualitative data, whereas median and standrad deviation were used to express quantitative data. Comparison between quantitative variables was undertaken using Student t-test. Difference were considered statistically significant if $p \leq 0.05$.

RESULTS

Forty-two patients were enrolled, including 32 (76.2%) in group A and 10 (23.8%) in group B. Overall, age ranged from 31-62 (median: 43) years without statistically significant difference between group A (median: 41& range: 31-58) and group B (median:43 & range: 30-62) years. Prior to the current study, patients gave no history of any surgical or radiological therapeutic breast procedure. All patients had no associated ovarian or other cancers and denied any history of smoking of any form. Surgical procedures and histopathological assessment are outlined in figure (1).

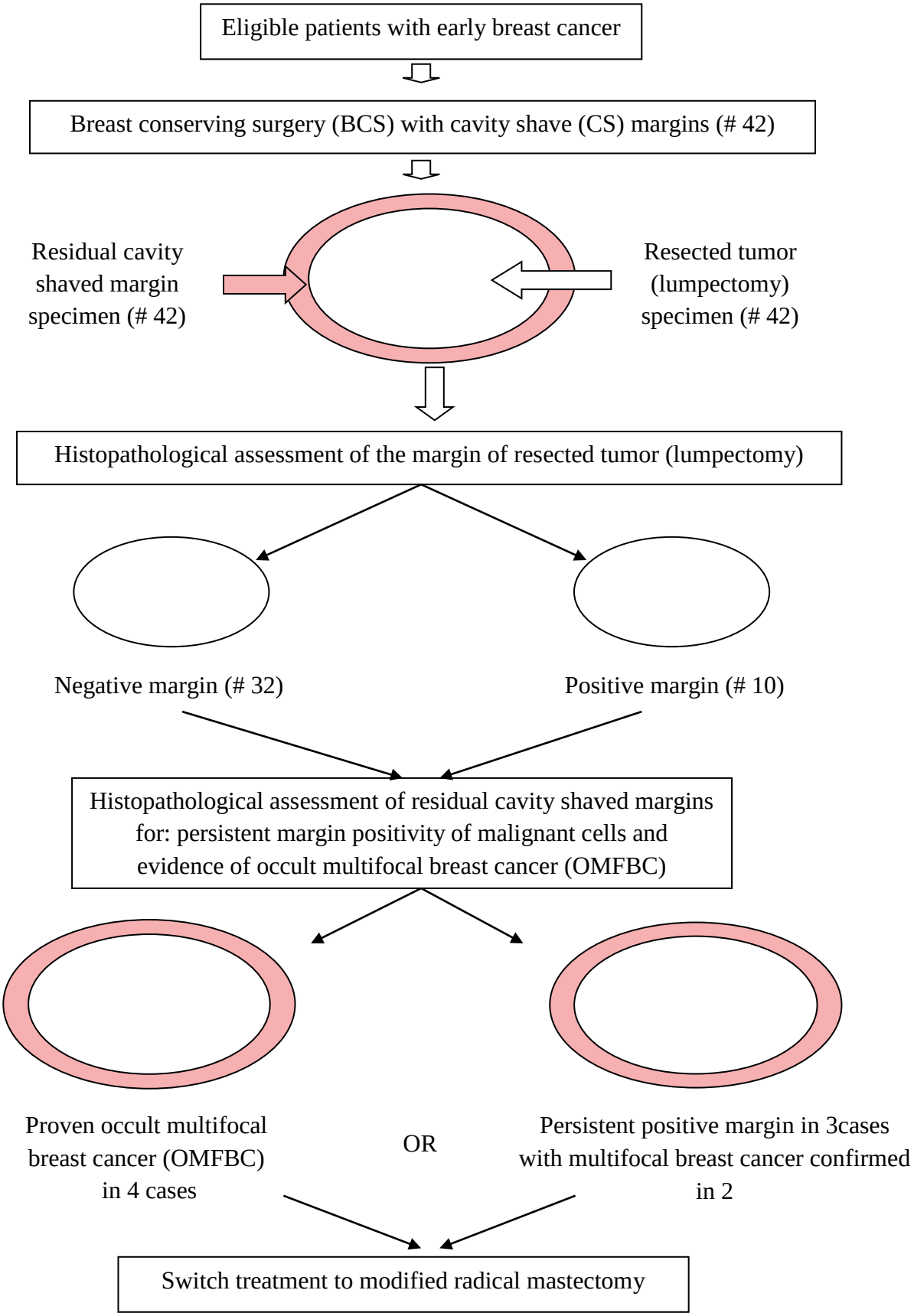

Figure (1): Summary of surgical procedures, histopathological assessment and results

Histopathological status of "resected tumor specimens" and tumor characteristics:

Histopathological assessment of the margins of the resected "tumor specimens" showed negative margins in 32 patients (76.2%) who constituted group A. In contrast, the margins of lumpectomy specimens were positive in 10 patients (23.8%) who comprised group B. All patients had ductal adenocarcinoma including invasive and in situ variants. Invasive ductal carcinoma occured in 23 patients (55%) compared to 19 patients (45%) who suffered from ductal carcinoma in situ (DCIS). The majoritiy of patients had stage I disease (30 patients, 71%) followed by stage II (12 patients, 29%). Tumor diameter ranged from 2 to 5 centimeters with no significant difference between both groups. As shown in table (1).

Table (1): Preoperative pathological data

Preoperative pathological data		
	Group A negative lumpectomy Margins (n, 32)	**Group B positive lumpectomy margins (n, 10)**
Pathological type:		
- Invasive ductal carcinoma	18/23 (78.3%)	5/23 (21.7%)
- Carcinoma in-situ	14/19 (73.7)	5/19 (26.3)
Clinical TNM staging:		
- I	24/30 (80%)	6/30 (20%)
- II	8/12 (66.7%)	4/12 (33.3%)
Tumor diameter *	2.5 (1-5)	3 (2-5)

CS; cavity shaving, TNM: T, tumor status, N; lymph node metastasis, M; distant metastasis.
* median (range) measured in centimeters

Operative parameters, complications and hospital stay:

There was no statistically significant difference between both groups in regard to blood loss, operative time and positive axillary lymph nodes. Only minor complications occurred postoperatively and required medical therapy or intervention under local anesthesia. The severity of complications was almost similar in both groups, no statistically significant difference could be confirmed. Postoperative complications entailed wound seroma and infection, mild arm edema, pain during arm movements and chest infection. In the same line, the length of hospital stay was not significantly different between both groups (Table 2).

Table (2): Operative data and hospital stay.

Operative complication score and hospital stays*			
	Group A (n, 32)	**Group B (n, 10)**	**p-value**
Operative time (minutes)	80 (65-110)	75 (60-115)	ns
Blood loss (milliliter)	150 (30-200)	150 (50-250)	ns
Resected volume (cubic centimeter)			
- Before CS	70 (55-90)	65 (50-90)	ns
- After CS	120 (100-135)	125 (105-140)	ns
Hospital stay (hours)	32 (28-40)	36 (30-42)	ns

* Results shown as median (range), ns; non-significant difference.

Evaluation of the additionally shaved margins from "residual lumpectomy cavity":

Firstly, we looked into the influence of CS on the positive margins of resected tumors from patients constituting group B. CS reduced the number of patients with positive margins from ten to three (70% reduction compared to the resected tumor margin status prior to CS). To explore the likelihood of OMFBC, the additionally shaved margins from "residual lumpectomy cavity" was histopathologically evaluated in all patients, including those with their "tumor specimens" showing negative (group A) or positive (group B) margins. Overall, OMFBC was confirmed in 6 patients (14.3%). Interestingly, OMFBC was found in 4 (12.5%) from group (A) while free margins were documented in the remaining 28 (87.5%) patients. In group B, OMFBC was confirmed in the shaved margins of residual lumpectomy cavities in 2 patients (20%), meanwhile a third patient had persistent positive margins with no evidence of OMFBC. Despite the higher percentage of cases with OMFBC in group B, it was not statistically different compared to group A. The influence of CS on margin status was summarized in table (3). Similarly, the number of positive lymph nodes in patients who had axillary lymph node dissection was not statistically significant between both groups.

Table (3): Tumor characteristics

	Margin status prior to and after cavity shaving	
	Before cavity shaving	**After cavity shaving**
Group A:		
- Negative margin	32	28
- Positive margin	0	4*
Group B:		
- Negative margin	0	7
- Positive margin	10	3**

*All contained occult multifocal breast cancer (OMFBR)
**Two out of 3 showed occult multifocal breast cancer (OMFBR)

Postoperative follow-up

All 35 patients who were successfully treated with BCS and CS were advised to continue regular follow-up postoperatively. During the follow-up (median: 19, range: 6 – 46) months, local recurrence was documented in only one patient (2.9%).

Figure (2): Conservative breast surgery (lumpectomy) before cavity shaving: lumpectomy and axillary evacuation were carried out and suction drains were inserted.

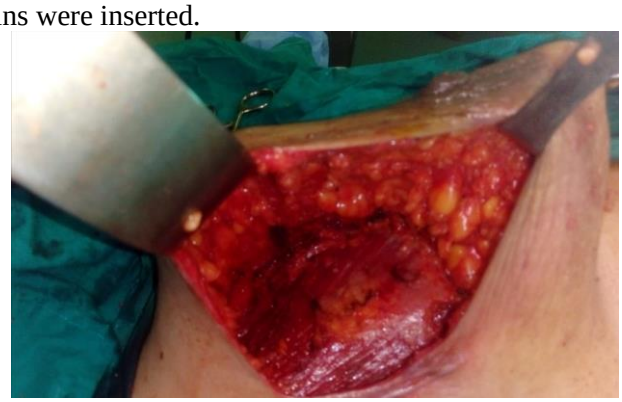

Figure (3): Breast surgery (lumpectomy) after cavity shaving: lumpectomy cavity after additional tissues were circumferentially removed fromm its walls.

DISCUSSION

This study underlines the influence of cavity shaving (CS) during breast conserving surgery (BCS) not only on reduction of the rates of positive margins but also detection of occult multifocal breast cancer (OMFBC) with subsequent elimination of key players in tumor recurrence.

In the setting of negative lumpectomy margin (group A), diagnosis of OMFBC in 4 patients in the additionally shaved margins of the lumpectomy cavity significantly shifted the treatment plan from BCS to modified radical mastectomy. The same strategy was applied in 3 patients in group B due to persistence of positive margins (2 with OMFBC and 1 without evidence of OMFBC). Likewise, detection of OMFBC prompts rigorous follow up, even after total mastectomy.

Worldwide, breast cancer is among the foremost disorders implicated in cancer-related mortality in females[19]. Surgery, in combination with other systemic therapies, remains the gold standard management of in situ and early invasive breast

cancer[20]. Compared with radical procedures, patients with early breast cancer who were properly selected for BCS had the benefit of similar long-term survival and lower surgery-related complication rates [21]. However, failure to achieve negative margins is a major shortcoming that leads to high re-operation rates (up to 60%) [22].

In the current study, 10 out of 42 patients (23.8%) had positive margins of the resected tumor. This figure conforms with previous studies, which reported variable rates of positive margins after BCS[23]. For instance, a multicenter prospective randomized-controlled trial was conducted on 396 breast cancer patients who underwent partial mastectomy with or without cavity shaving. Histopathological evaluation confirmed that rate of positive margins was significantly reduced in the "shave" group to 9.7% compared with 36% in the "no shave" group [14] In the same line, recent Egyptian study on 40 patients with early breast cancer who were randomized to BCS with or without cavity shaving, patients who underwent cavity shaving had significantly lower rates of positive margins (8%) compared to those who had lumpectomy (tumor resection) alone (33.3%) [24].

On the other hand, failure of BCS could occur in relation to lack of diagnosis of OMFBC after partial mastectomy, even in patients with negative margins of resected lumpectomy specimens. In this context, previous reports indicated that cavity shaved margins could contain malignant cells in 3-10% of patients despite the negative margins obtained from the resected lumpectomy specimen [18,25]. In our study, where intraoperative frozen section evaluation was not available, all patients underwent partial mastectomy followed by cavity shaving. The resection margins of the resected tumor (lumpectomy specimen) and corresponding locations in the residual lumpectomy cavity were negative in 32 patients (76.2%) while 10 patients had positive margins. Nonetheless, histopathological assessment of the additional tissues obtained by cavity shaving yielded different results. Among the 32 patients with initially negative margin, cavity shaving resulted in confirming OMFBC in 4 cases (12.5%). Furthermore, among the 10 patients with originally positive margins, cavity shaving achieved negative margins in 7 patients, contrary to the remaining 3 patients who had persistent positive margins where OMFBC was diagnosed in 2 cases. Thus, the total number of cases with OMFBC uncovered after cavity shaving was 6 (14.3%). Our data agree with previous study, which demonstrated that cavity shaving reduces the rate of positive margins by more than 50% compared to standard partial mastectomy, with all positive margins in the cavity shave group showing criteria of multifocal cancer [16]. Another comparative study was carried out on 139 breast cancer patients who were treated with partial mastectomy and additional cavity shaving. The authors reported that OMFBC was confirmed in 23% of cases who were initially reported to have negative margins of their resected tumor (lumpectomy specimen) [12].

In agreement with the reported worse prognosis of multifocal breast cancer [17], we shifted our treatment to modified radical mastectomy in all patients with confirmed multifocal disease.

During a follow-up period ranging from 6 to 46 months (median > one and half year), local recurrence was discovered in one patient (2.9%). This result accords with recent meta-analysis, which showed a rate of locoregional recurrence of 3% after cavity shaving [26].

CONCLUSION

This study highlighted the advantages of cavity shaving following partial mastectomy in the setting of breast conserving surgery. Cavity shaving remarkably reduced the rates of positive margins, uncovered occult multifocal breast cancer and optimized the surgical treatment strategy.

DECLARATIONS

Funding: No funding was received in this series.

Conflict of interest: All authors declare that there is no conflict of interest.

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