

The Effect of Combining Flap Fixation with Gentamicin Lavage of the Surgical Bed for Reducing Postmastectomy Seroma: A Single-Institute Experience

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Abstract

Background: Seroma is the most prevalent complication after mastectomy and can lead to significant morbidity. No single method has been shown to be completely effective in reducing seroma rates. Flap fixation can reduce the dead space after mastectomy, thus decreasing the drainage volume and seroma rates. Gentamicin acts against *Staphylococcus epidermidis* involved in increasing drainage volume, duration, and seroma rates. This study aimed to evaluate the effect of combining flap fixation with gentamicin lavage of the surgical bed for reducing postmastectomy seroma.

Method: This prospective randomized controlled study included 100 women with breast cancer scheduled for modified radical mastectomy (MRM). The patients were allocated into the following four groups of 25: GI: flap fixation; GII: surgical bed lavage with gentamicin-containing solution; GIII: both techniques used in GI and GII; GIV: control group. The patients were followed up for the registration of drainage volume, timing of drain removal, and incidence of seroma.

Results: Total drainage volume was significantly lower; the drain was removed earlier and seroma rates were lower in group III than the other groups ($P = 0.001$, 0.009 , and 0.005 , respectively). Seroma in GIII was mild and managed with aspiration. In the other groups, seroma was more severe and required more aspirations, second tube drainage, or open drainage.

Conclusion: Combining flap fixation and gentamicin lavage of the surgical bed after MRM significantly decreased the amount of drained fluid, allowing an earlier removal of the drain and decreasing the incidence of seroma when compared with using each procedure alone. Moreover, the severity of seroma was significantly lower when both techniques were combined.

Keywords: Flap fixation, Gentamicins, Lavage, Mastectomy, Postmastectomy seroma

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Introduction

Seroma is a collection of acute

inflammatory exudates secondary to surgical trauma and the acute phase

of wound healing. It constitutes the most common complication following mastectomy, with a reported incidence between 15 and 81% secondary to the rich lymphatic drainage of the breast. Moreover, in large-sized breasts, the prolonged excessive drainage of fluids after mastectomy may occur due to large raw areas.¹⁻³ Several factors have been implicated in the formation of seroma, but the true pathophysiology is still poorly understood. Many surgeons regard it as an inevitable nuisance rather than a true complication, while it may lead to significant morbidities, including delayed wound healing, wound infection or dehiscence, flap necrosis, delayed initiation of adjuvant therapy, and the prolongation of hospital stay.^{4, 5} The standard practice of most surgeons is to site one or two suction drains deep to the skin flaps following breast and axillary surgery. These are typically left in situ until fluid drainage is less than 30 to 50 mL/day although this practice varies.⁴ Despite this strategy, seromas requiring aspiration still occur in 10 to 80% of patients following drain removal.^{4, 5} Several techniques have been reported to prevent or reduce seroma formation, ranging from shoulder immobilization, perioperative use of tranexamic acid, prolonged suction drainage, flap fixation, the use of harmonic scalpel or bipolar vessel sealing system, fibrin sealants, and adding hydrocortisone to the anesthetic regimen, with varying degrees of success. However, no single method has consistently proven to be effective.⁶⁻⁹ There is now considerable evidence that skin flap fixation can reduce the dead space after mastectomy, thus decreasing the drainage volume and duration and hence lowering seroma rates.^{10, 11} Halsted first described flap fixation in 1913 and others have since described the techniques of anchoring flaps to close dead space.¹⁰⁻¹² Numerous randomized controlled trials¹⁰⁻¹² have demonstrated that the fixation of the skin flaps via multiple tacking sutures to close the dead space reduces seroma formation in patients undergoing mastectomy. Gentamicin is an antimicrobial agent with an excellent spectrum against *Staphylococcus epidermidis* (*S. epidermidis*), a frequent saprophyte pathogen of

the skin involved in most breast surgical site infections (SSIs) and some authors consider it to be involved in increasing the drainage volume and duration and consequently increasing the risk of postmastectomy seroma formation.¹³⁻¹⁵ The objective of the current work was to evaluate the effect of combining flap fixation with gentamicin lavage of the surgical bed in reducing the incidence of postmastectomy seroma.

Patients and Methods

Patient selection

This prospective randomized controlled study included 100 women with primary operable breast cancer who were admitted to the Department of Surgery, Medical Research Institute, University of Alexandria, Egypt, from June 2018 to December 2019 and scheduled for modified radical mastectomy (MRM). Patients with diabetes mellitus (DM), morbid obesity [body mass index (BMI) > 35 kg/m²], distant metastasis, renal impairment, those who smoke, and those receiving neoadjuvant chemotherapy (NAC) were excluded from the current study. The Institutional Research Committee and Ethics Committee in the medical research institute, Alexandria University, Egypt approved the protocol before the study started (ethics code: E/C. S/N. R4). The study was explained to prospective patients and written informed consent was obtained before study entry.

Study protocol

All the patients included in this study underwent complete history taking, full clinical examination, and laboratory and radiological investigations to exclude the presence of distant metastasis. The patients were randomly allocated to one of the four study groups:

Group I (GI) included 25 patients in whom the obliteration of postmastectomy dead space was carried out through simple interrupted sutures 3 cm apart, anchoring the mastectomy skin flaps to the pectoralis major and the lateral chest wall muscles (flap fixation) using 2/0 Vicryl sutures.

Group II (GII) included 25 patients in whom surgical bed lavage was performed immediately before the closure of the wound using an irrigation technique with 500 mL of normal saline followed

Table 1. Distribution of the studied patients according to age, tumor stage, duration of surgery, and BMI

Item	GI (n = 25) %	GII (n = 25) %	GIII (n = 25) %	GIV (Control) (n = 25) %	P
Age	49.1 ± 10.2	48.0 ± 9.1	51.0 ± 11.6	49.0 ± 9.6	0.398
Tumor stage					0.107
IIA	8(32%)	10(40%)	7(28%)	9(36%)	
IIB	9(36%)	8(32%)	10(40%)	11(44%)	
IIIA	5(20%)	4(16%)	6(24%)	4(16%)	
IIIB	3(12%)	3(12%)	2(8%)	1(4%)	
Duration of Surgery (min)	107.0 ± 11.3	104.8 ± 11.7	105.0 ± 9.8	106.0 ± 10.3	0.325
BMI (mean)	29	26	25	27	0.061

χ^2 : Chi-square test for comparing the four groups and each two groups; BMI: Body mass index; GI: Group I, GII: Group II, GIII: Group III, GIV: Group IV; Statistically significant at $P \leq 0.05$

by the aspiration of the saline. Afterwards, a second lavage with a gentamicin-containing solution (240 mg gentamicin in 500 mL normal saline) was done which was left for few minutes and then aspirated.

Group III (GIII) included 25 patients in whom both techniques used in GI and GII (combined gentamicin lavage of the surgical bed with flap fixation) were applied.

Group IV (GIV) or the control group included 25 patients in whom the wound was closed in the conventional method without flap fixation or surgical bed lavage with gentamicin-containing solution.

Surgery was performed for all the patients using the same technique irrespective of their randomization. The dissection of mastectomy flaps was performed with diathermy and sharp dissection was employed for the axillary part. The incidence of intraoperative bleeding and the duration of surgery were recorded. All the patients underwent insertion of a closed suction drain. The drain was maintained on negative suction and removed once the daily drainage volume was below 30 mL for three successive days. Compression dressing was applied for 48 hours and early arm exercises were advised for all the patients. All the patients were followed up post-operatively to record the total drainage volume until drain removal, timing of drain removal, incidence of seroma formation, and for management of the seroma.

Statistical analysis

The data were analyzed using IBM SPSS

software package version 20.0. Qualitative data were described using number and percent. Comparison between different groups regarding categorical variables was tested via chi-square for the Kruskal-Wallis test and the level of significance among the groups was reviewed using the Mann-Whitney test. Once more than 20% of the cells had an expected count of less than 5, correction for chi-square was conducted through the Monte Carlo correction. Correlations between the studied parameters were carried out by use of Spearman coefficient. The significance level was considered to be 0.05 (Kirkpatrick & Feeney, 2013).

Results

The study included 100 women who were randomly allocated into four groups of 25 patients each: GI group patients, in whom flap fixation was performed; GII group patients, in whom surgical bed lavage with gentamicin-containing solution was done; GIII group patients, in whom both techniques used in GI and GII were carried out; and GIV (control group), in whom the wound was closed in the conventional method without flap fixation or surgical bed lavage with gentamicin-containing solution. Considering the distribution of the studied patients based on age, tumor stage, duration of surgery, and BMI, no significant differences were observed between the four groups as shown in table 1.

Regarding the total drainage volume, it was significantly lower in group III compared with the other three groups ($P = 0.001$) and as

Table 2. Distribution of the studied patients according to total drainage volume

Item	GI (n = 25) %	GII (n = 25) %	GIII (n = 25) %	GIV (Control) (n = 25) %	MCp
Total drainage volume	595.0 ± 107.5	671.4 ± 82.7	465.0 ± 107.5	871.4 ± 82.7	0.001*
pControl	FE <i>P</i> = 0.002*	MC <i>P</i> = 0.004*	MC <i>P</i> < 0.001*		
Significance among groups	MC <i>P</i> 1 = 0.006*, MC <i>P</i> 2 < 0.009*, MC <i>P</i> 3 = 0.001*				

MCp: for comparing GIII with the other three groups. pControl: *P* value for comparing group IV (control) and each of the other groups. *P*1: *P* value for the comparison between groups I and II, *P*2: *P* value for the comparison between groups I and III, *P*3: *P* value for the comparison between groups II and III; *: Statistically significant at ≤ 0.05

compared with each group separately (with GI, GII, and GIV; *P* values were < 0.009, 0.001, and < 0.001, respectively). However, it was still significantly lower in GI and GII compared with GIV (*P* = 0.002 and 0.004, respectively) as shown in table 2.

The drain was removed earlier in GIII than in the other three groups, with a significant difference of *P* = 0.009, and compared with each group separately (with GI, II and IV; *P* values were < 0.008, 0.002, and 0.002, respectively). It was removed earlier in GI and GII compared with GIV (*P* = 0.004 and 0.006, respectively), as shown in table 3.

The incidence of seroma formation was the least in GIII {two patients (8%)} and the highest rate was in GIV {nine cases (36%)} with a significant difference between GIII and the other three groups (*P* = 0.005) and with each group separately (with GI, GII and GIV; *P* values were < 0.006, 0.001, and 0.001, respectively). The incidence was significantly different between GI and GII compared with GIV (*P* = 0.003 and 0.006, respectively) as shown in table 4.

The two cases with seroma in GIII were mild and managed conservatively with two and three aspirations. In the other three groups, seroma was more severe. In GI, four patients had seroma, three of which required multiple aspirations (> 3 times) and one needed a second tube drainage. In GII, six patients developed seroma, four of which needed a second tube drainage whereas the other two resolved with multiple aspirations (> 5 times). In GIV, nine cases developed seroma; only one was mild and it resolved after multiple aspirations (four times), four cases needed a second tube drainage, and the remaining four cases needed open drainage and reinsertion of the Redivac after the failure of multiple aspirations

and a second tube drainage.

Discussion

Flap fixation and gentamicin lavage of the surgical bed after MRM are effective methods for decreasing seroma formation rates. In regard to decreasing the total drainage volume and the incidence of seroma formation along with allowing an earlier removal of the drain, a combination of both procedures is more effective than a single one. Moreover, the degree of severity of seroma was reduced. Although the exact mechanism behind postmastectomy seroma formation is not fully known,⁴ it may form in response to surgical trauma.^{1, 2} MRM, when compared with CBS, causes damage to several blood and lymphatic vessels due to extensive dissection with subsequent oozing of blood and lymphatic fluid from a larger raw surface area leading to a higher incidence of seroma formation rates.¹⁶ Fluid accumulation elevates the flaps from the chest wall and axilla, thereby preventing their adherence to the chest wall bed and delaying their healing.¹⁶ Gonzalez et al.¹⁷ and Hashemi et al.¹⁸ reported higher seroma rates in MRM than following wide local excision and axillary dissection due to larger dead space found after mastectomy. Although seroma formation has a multifactorial background, there was no strong evidence supporting any risk factors. However, there was moderate evidence (grade B) to support the increased risk of seroma formation in individuals with heavier body weight, MRM as compared with simple mastectomy, a greater initial three-day drainage volume, and axillary dissection when compared with sentinel lymph node biopsy (SLNB).¹⁶ In the current study, we only included the cases that were planned for

Table 3. Distribution of the studied patients according to the timing of drain removal

Item	GI (n = 25) %	GII (n = 25) %	GIII (n = 25) %	GIV (Control) (n = 25) %	MC _p
Timing of drain removal	10.5 ± 1.6	12.0 ± 1.2	8.5 ± 1.0	15.5 ± 1.8	0.009*
pControl	FE P = 0.004*	MC P = 0.006*	MC P = 0.002*		
Significance among groups	MC P1 = 0.003*, MC P2 < 0.008*, MC P3 = 0.002*				

MCP: for comparing GIII with the other three groups. PControl: P value for the comparison between group IV (control) and each of the other groups. P1: P value for the comparison between groups I and II, P2: P value for the comparison between groups I and III, P3: P value for the comparison between groups II and III; *: Statistically significant at $P \leq 0.05$.

MRM and excluded patients with DM, morbid obesity (BMI > 35 kg/m²), smokers, and those who received NAC to omit any confounding factor and to avoid any selection bias by unifying the selection criteria. The increased incidence of postoperative seroma has been correlated with using electrocautery in dissection because of the increased thermal trauma as documented by the present evidence.¹⁹ The influence of this factor was abolished in our study as all the mastectomies in all the groups were performed employing the same technique irrespective of their randomization to unify our steps to avoid any confounding factor that may affect the accuracy of our results. The dissection of mastectomy flaps was performed with diathermy and the dissection of the axillary part was carried out with sharp dissection. Considering the methods used for reducing seroma magnitude, conflicting results were noted in the literature regarding the use of external compression dressing, immobilization of the arm, the use of fibrin glue, use of the electric scalpel, use of ligature, and insertion of multiple drains.²⁰ Herein, as no single method has consistently been shown to be completely effective in preventing postmastectomy seroma, we aimed to evaluate the effect of combining two methods in reducing postmastectomy seroma formation and assessing how different and more effective it is than applying a single method alone. Several studies have found that it is useful to close the dead space by securing the flaps to the chest wall with sutures.^{11, 12} This allowed a better and smoother recovery after mastectomy with less disability as reported by Larsen et al.²¹ Similarly, this technique reduced the incidence of seroma formation significantly, decreased the breakdown of wound edges, reduced serous discharge, and did not lead to a reduced

functional range of shoulder motion among patients undergoing mastectomy. It is interesting to note that in the randomized controlled trial by Purushotham et al.,²² flap fixation without drainage did not increase surgical morbidities, including seroma formation with early discharge with an overall cost reduction. Gentamicin is a bactericide antimicrobial agent with an excellent spectrum against gram-negative bacteria, but also against Staphylococcus species, a frequent saprophyte pathogen of the skin.¹⁵ *S. epidermidis* has been present in 25% of the positive cultures in many series, yet this micro-organism has been reported to be responsible for up to 60% of axillary SSIs in the literature.^{23, 24} Therefore, *S. epidermidis* seems to be the more aggressive pathogen of the saprophyte flora of the skin when contaminating other tissues. Moreover, because it is possibly the pathogen triggering greater inflammatory cascade, its eradication is probably responsible for lowering the immune response, resulting in a reduction in the drainage volume and consequently reducing the incidence of postmastectomy seroma.¹⁵ Local gentamicin application has been studied in various trials particularly in abdominal surgery and bone and soft-tissue surgeries,^{15, 25} as it has the capacity to kill bacteria by inhibiting protein synthesis and destabilizing the lipid bilayer membranes of bacteria.²⁶ The advantages of locally applied gentamicin are that it does not impair renal function and the risk of developing resistant pathogens is small.²⁶ Local gentamicin application can be applied as a solution to irrigate a cavity or a wound, as we have performed in the current work, or be used in collagen sponges.²⁷ An increase of the infection rates was reported with the use of impregnated collagen sponges, which

Table 4. Distribution of the studied patients according to the incidence of seroma formation

Item	GI (n = 25) %	GII (n = 25) %	GIII (n = 25) %	GIV (Control) (n = 25) %	MCp
Incidence of seroma formation	4(16%)	6(24%)	2(8%)	9(36%)	0.005*
pControl	FE $P = 0.003^*$	MC $p = 0.006^*$	MC $p = 0.001^*$		
Significance among groups	MC $p1 = 0.004^*$	MC $p2 < 0.006^*$	MC $p3 < 0.001^*$		

MCp: for comparing GIII with the other three groups. P Control: P value for the comparison between group IV (control group) and each other group, P1: P value for comparing groups I and II, P2: P value for the comparison between groups I and III, P3: P value for the comparison between group II and III. *: Statistically significant at $P \leq 0.05$

we justified as the accumulation of bacteria in the collagen network once the antibiotic was diluted.²⁵⁻²⁷ In the current work, we decided to combine gentamicin lavage of the surgical bed with flap fixation as these two methods target two important risk factors for seroma formation: the large dead space found after MRM and the great inflammatory response triggered by *S. epidermidis*. Literature focuses on the effect of flap fixation on the magnitude of seroma formation rates, yet its effect on the drainage volume and drainage period has not been widely discussed. Herein, we not only focused on the incidence of seroma formation but also studied the amount of drained fluid and the drainage time (timing of drain removal) as seroma may not occur, but the drainage time may be extended, delaying the adjuvant treatment or causing secondary complications, such as wound infection, cellulitis, and wound breakdown. In our research, the total drainage volume was significantly lower in GIII (combined gentamicin lavage of the surgical bed and flap fixation) compared with each method alone and of course with the control group. However, it was still significantly lower than that in GI (flap fixation group) and GII (gentamicin lavage group) compared with GIV (control group). Each method is effective alone to a certain extent, but when we combine the two methods together, the effect becomes better with significant differences. The same findings were observed regarding the timing of drain removal (average 8.5 days versus 10.5-15.5 days in the other groups; $P = 0.009$) and the incidence of seroma (8% versus 16%-36%; $P = 0.005$). Not only the rate but also the severity of seroma were lower in GIII; thus, the maneuver employed to manage seroma was simpler in the combination group compared with the other groups (just aspirations

versus second tube drainage and/or open drainage). Our results were in accordance with those of many studies;^{3, 12, 14, 15} however, all of these studies evaluated only one technique, either flap fixation or gentamicin lavage. According to these studies, although any of the two techniques is effective when compared with a control group, the combination of both techniques is still more effective. Sakkary et al.³ concluded that the average total drainage volume in the flap fixation group was 524 mL. In our study, the combination group yielded 465 mL. The same findings resulted in the incidence of seroma (15% versus 8%, respectively). The only difference was in the timing of drain removal (5 versus 8.5 days). In the present paper, we believe that the delay of removal of the drain resulted from maintaining the drain on negative suction and removing it when the daily drainage volume was less than 30 mL for three successive days. Conversely, Sakkary et al.³ removed the drain when yielding 50 mL for only one day. Jaime Ruiz-Tovar et al.¹⁵ concluded that the axillary drainage volume is significantly lower in the patients undergoing surgical bed lavage with a gentamicin-containing-solution than in the patients undergoing a lavage with normal saline, as the surgical bed of ALND presents a contamination with the saprophyte flora of the skin in up to 60% of the cases. A reduction in the contamination was not obtained after lavages with normal saline, yet after a lavage with gentamicin solution, a significant reduction could be observed (5%). In addition, Ruiz-Tovar et al.¹⁵ concluded that no seromas occurred in the lavage group with the only difference being only the inclusion of ALND and not MRMs. Thus, the raw area in our patients was wider. What they added to our study is the support of the rationale of the ability of locally applied

gentamicin to prevent and treat the subclinical infection caused by *S. epidermidis* which seems to be the more aggressive pathogen of the saprophyte flora of the skin when contaminating other tissues and is possibly the one triggering greater inflammatory cascade. Thus, its eradication can lower the magnitude of the immune response, consequently reducing drainage volume and decreasing the incidence of seroma. The main limitations of this study were the low number of included patients and the short period of the study. Moreover, the combining technique should be compared to the other techniques applied for the reduction of seroma formation rates to assess its effectiveness.

We recommend to carry out this study on a wider scale to prove its validity in decreasing the incidence of seroma formation and its subsequent complications, therefore introducing the combination of both procedures as a part of mastectomy operation.

Conclusion

Flap fixation and gentamicin lavage of the surgical bed after MRM are valuable procedures that decrease the total amount of drained fluid significantly, allowing an earlier removal of the drain along with decreasing the incidence of seroma formation. The results of the both procedures combined are better than that of each procedure alone. Moreover, the need for frequent visits for seroma fluid aspiration and the rate of complications are decreased by combining both techniques. In combination, the degree of severity of seroma was reduced.

Conflict of Interest

None declared.

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