

Research Article

Efficacy of Fibrin Glue Versus Mastectomy Flap Fixation in Seroma Reduction After Modified Radical Mastectomy

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Abstract

Background: Since the first mastectomy in 1882, seroma is still a real challenge which faces surgeons postoperatively and may accompany other complications such as skin flaps necrosis, lymphedema, hematoma, infection, wound dehiscence and prolonged hospital stay.

Aim: This study was performed to assess and compare the efficacy of fibrin glue versus flap fixation using sutures in reducing postmastectomy seroma.

Methods: This study was a randomized controlled trial. The included 150 women were divided equally into three groups randomly. Each group included 50 women as following:

- Group I (Fibrin Glue Group): 50 women having axillary and mammary beds sprayed by fibrin glue and conventional drain placement.
- Group II (Quilting Group): 50 women undergone flap fixation with low vacuum drainage
- Group III (Control Group): 50 women undergone conventional closure with low vacuum drainage.

Results: The mean amount of drained fluid in the first day was (160.63+/-52.11) ml, (166.47+/-38.98) ml, (188.37+/-51.30) ml in fibrin glue group, quilting group and control group respectively, making a significant difference ($p=0.011$). The mean hospital stay was (1.41+/-0.38) days in fibrin glue group, (1.67+/-0.51) days in quilting group, and (1.91+/-0.43) days in control group, making a significant difference ($P<0.001$). Detecting seroma made a significant difference among our three study groups. Only 3 women in fibrin glue group developed seroma, 2 of them needed aspiration. Instead, 16 women in quilting group developed seroma, 8 of them needed aspiration, and 28 women in control group developed seroma, 9 of them needed aspiration. However, there was a significant difference in detecting seroma ($P<0.001$), while there was no significant difference in aspiration of seroma ($P=0.074$). There was a significant difference in wound dehiscence. Only one woman was reported with wound dehiscence in fibrin glue glue and 2 in quilting group, while 7 women in control group were reported with wound dehiscence ($P=0.036$).

Conclusion: obliterating dead spaces after modified radical mastectomy and axillary lymphadenectomy by either fibrin glue application or quilting skin flaps can reduce seroma formation, decrease the drained fluid volume and shorten hospital stay. However, fibrin glue application showed a promising higher efficacy in reduction of seroma formation than quilting skin flaps did.

Keywords: Fibrin glue, quilting, flap fixation, mastectomy, seroma.

Introduction

Since the first mastectomy in 1882, seroma is still a real challenge which faces surgeons postoperatively and may accompany other complications such as skin flaps necrosis, wound breakdown, lymphedema, hematoma, wound infection, wound dehiscence and prolonged hospital stay [1]. Seroma is a subcutaneous collection of serous fluid develops under the skin flaps after mastectomy and/or in the axillary dead space after axillary clearance and resolves after few weeks. Although seroma has a variable cited incidence which may be higher than 90%, many surgeons consider it as an inevitable nuisance rather than a serous complication [2,3].

Morbidities such as increasing body weight, obesity, diabetes mellitus and hypertension are risk factors predispose seroma formation. Iatrogenic postmastectomy seroma may occur as result of extensive dissection and axillary lymphadenectomy which damage several blood and lymphatic vessels [4], [5]. Thus, meticulous handling techniques of blood vessels and lymphatics and obliterating dead spaces can guard against seroma formation [6]. In addition, reduction of lymphatic drainage by compression dressings and fibrin glue application in axillary space can reduce the incidence of seroma [7].

Making a short upper flap, suturing it to the fascia below the first rib and skin grafting the remaining part of the defect was first described by Halsted to obliterate dead space [8]. Therefore, diminishing the dead space by fixing the skin flaps to the underlying muscles (quilting) reduces seroma incidence [9].

Human fibrin glue (HFG) is a set of substances having hemostatic and sealing properties. HFG, by its role in hemostasis and healing, can prevent oozing through blood vessels and lymphatics, and so on decreases the incidence of seroma formation [10].

Aim of Work

The present study was performed to assess and compare the efficacy of fibrin glue versus flap fixation using sutures in reducing postmastectomy seroma.

Patients and Methods

This study was performed over 150 women with breast cancer, during the period from December 2015 to November 2017. It was carried out in Surgical Oncology Department, Al-Ahrar Zgazig Teaching Hospital, Egypt, in General Surgery Department, El-Sahel Teaching Hospital and Banha Teaching Hospital Egypt (on 150 women). Modified Radical Mastectomy (MRM) with axillary clearance surgery under general anesthesia was performed to all the included 150 women after taking their consent.

Inclusion Criteria

- Only female patients
- Age > 20 years
- Breast Cancer stage I and II

- Scheduled to modified radical mastectomy with axillary clearance surgery
- No history of previous breast and/or axillary surgeries
- No history of previous chest radiotherapy
- No history of previous chemotherapy
- No uncompensated morbidities; no uncontrolled diabetes mellitus, no uncontrolled hypertension, no advanced cardiac or hepatic disorders
- Normal coagulation profile; platelets count > 100,000/mL, no bleeding dyscrasia/coagulopathy, no history of anticoagulant therapy
- No extreme of body weight; not severely obese or severely slim
- No history of steroid using

Exclusion Criteria

- History of previous chest radiotherapy
- History of previous chemotherapy
- Scheduled to immediate breast reconstruction
- Scheduled to sentinel lymph node biopsy
- History of previous breast and/or axillary surgeries
- Uncompensated morbidities; uncontrolled diabetes mellitus, uncontrolled hypertension, advanced cardiac or hepatic disorders
- Abnormal coagulation profile; platelets count < 99,000/mL, bleeding dyscrasia/coagulopathy, history of anticoagulant therapy
- Extreme of body weight; severely obese or severely slim
- History of steroid using
- Pregnant or lactating women

Study Design

This study was a randomized controlled trial. The included 150 women were divided equally into three groups randomly using a computer-generated random number. Each group included 50 women as following:

- Group I (Fibrin Glue Group): 50 women having axillary and mammary beds sprayed by fibrin glue and conventional drain placement.
- Group II (Quilting Group): 50 women undergone flap fixation with low vacuum drainage
- Group III (Control Group): 50 women undergone conventional closure with low vacuum drainage.

Techniques

All the 150 women included in our study undergone surgeries (modified radical mastectomy and axillary lymph nodes dissection) by the same surgical staff using standard electrocautery-based dissection technique. Skin flaps were kept cranially and caudally. After mastectomy, axillary lymph nodes dissection was done through the same incision, with preserving other axillary structures (Brachial plexus and major nerves, axillary vesicles and cephalic vein). Only levels I and II axillary clearance were done (lateral to and behind pectoralis minor muscle) in our study. Level III axillary clearance was not done to avoid

injuring lymphatic which causes more seroma, in addition to brawny edema of upper limb.

In Group I (Fibrin Glue Group), axillary and mammary beds were sprayed by fibrin glue and conventional drain was placed in every woman after mastectomy. We used only one pack of (FIBROGLOO) of Cairo Medical Centre Blood Bank for each woman to spray the dead space under skin flaps and axillary bed.

In Group II (Quilting Group), after mastectomy, we took multiple interrupted sutures starting in the lower flap from medial to lateral between mastectomy flap. We took pectoralis muscle between flaps to obliterate dead space by 2/0 Vicryl sutures. Distance between all sutures was about 5 cm. We always tried to avoid skin dimpling. We handled the upper flap with the same technique. We did not approximate axillary area by sutures.

In Group III (Control Group), we closed the wound traditionally without quilting. We closed the skin in two layers manner without using flap fixation.

In the three groups, we closed skin incisions in a double-layer fashion. We used inverted 2/0 Vicryl stitches on the subcutaneous to approximate the wound margins, and we closed the wound by skin stapler. We used a redivac drain which has two limbs, one limb inserted in the axilla, and the other one inserted anterior to pectoralis muscle.

Patients 'follow-up

All patients were followed up routinely for

- immediate complications
- Late complications: hemorrhage, flap necrosis, wound sepsis
- Seroma: diagnosed clinically and/r sonographically
- If seroma developed: total number of aspirations
- Pathological data.

Statistical Analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges while qualitative variables were presented as number and percentages. The comparison between groups regarding qualitative data was done by using Chi-square test while the comparison between groups regarding quantitative data with parametric distribution was done by using One Way ANOVA test. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant at the level of < 0.05.

Results

This study included 150 women with breast cancer who were scheduled to modified radical mastectomy with axillary clearance surgery. The women were randomized into three equal groups; 50 in fibrin glue group, 50 in quilting group, and 50 in control group.

Regarding patients epidemiological characteristics as shown in **Table-1**, there was no significant difference in the mean age of women; (42.25+/-7.55), (43.82+/-6.42), (44.62+/-4.24) years in fibrin glue group, quilting group and control group respectively (P=0.157, t=1.877). The mean BMI of women in fibrin glue group was (28.35+/-4.06) kg/m², in quilting group was (27.09+/-4.86) kg/m², and in control group was (28.01+/-5.12)kg/m², making a nonsignificant difference (P=0.385, t=0.961). Concerning menstrual status of women in this study, premenopausal/menstruating women were 37 in fibrin glue group, 40 in quilting group, and 30 in control group. Thus, menstrual status of women among the three groups of this study made no significant difference (P=0.076, t=5.151).

Smoker women in this study were 28 in fibrin glue group, 34 in quilting group and 30 in control group, which made no significant difference (P=0.455, t=1.574).

Table-2 shows the morbidities in women included in our study. Regarding diabetes mellitus, there was no significant difference as diabetic women were 11, 10, 9 in fibrin glue group, quilting group and control group respectively (P=0.882, t=0.250). Hypertension also made no significant difference; 13 women in fibrin glue group, 15 in quilting group, and 12 in control group (P=0.787, t=0.477). Family history of breast cancer made a nonsignificant difference; 11, 9, 13 women in fibrin glue group, quilting group and control group respectively had positive family history of breast cancer (P=0.627, t=0.932).

Tumors characteristics of the studied women is plotted in **Table-3**. Women with tumor stage T1 were 22 in fibrin glue group, 13 in quilting group, and 10 in control group. Tumor stage T2 were diagnosed in 22, 25, 27 women in fibrin glue group, quilting group, and control group respectively. Tumor stage T3 were diagnosed in 8,12, 13 women in fibrin glue group, quilting group, and control group respectively. Thus, there was no significant difference in tumor characteristics in our study (p=0.143, t=6.857).

Postoperative collected data are listed in **Table-4** and illustrated in **Figure-1**. The mean amount of drained fluid in the first day was (160.63+/-52.11) ml, (166.47+/-38.98) ml, (188.37+/-51.30) ml in fibrin glue group, quilting group and control group respectively, making a significant difference (p=0.011, t=4.672). The mean time to remove the drain was (11.26+/-0.73) days in fibrin glue group, (12.57+/-1.01) days in quilting group, and (13.17+/-1.18) days in control group, having a significant difference (P<0.001, t=48.586). The mean hospital stay was (1.41+/-0.38) days in fibrin glue group, (1.67+/-0.51) days in quilting group, and (1.91+/-0.43) days in control group, making a significant difference (P<0.001, t=15.914).

Detecting seroma made a significant difference among our three study groups. Only 3 women in fibrin glue group developed seroma, 2 of them needed aspiration. Instead, 16 women in quilting group developed seroma, 8 of them needed aspiration, and 28 women in control group developed seroma, 9 of them needed aspiration. However, there was a significant difference in detecting seroma

($P < 0.001$, $t = 29.064$), while there was no significant difference in aspiration of seroma ($P = 0.074$, $t = 5.183$).

There was a significant difference in hematoma formation; hematoma developed in only one woman in fibrin glue group, 9 women in quilting group, and 12 women in control group ($P = 0.006$, $t = 10.334$). There was no significant difference in wound infection among the three groups. 3 women in fibrin glue group suffered of wound infection, 2 in quilting group, and 2 in control group ($P = 0.860$, $t = 0.300$).

Flap necrosis was detected in 1 woman in fibrin glue group, 4 in quilting group, and 8 in control group, making a significant difference ($P = 0.044$, $t = 6.232$). There was a significant difference in wound dehiscence. Only one woman was reported with wound dehiscence in fibrin glue glue and 2 in quilting group, while 7 women in control group were reported with wound dehiscence ($P = 0.036$, $t = 6.643$).

		Fibrin glue group No. = 50	Quilting group No. = 50	Control group No. = 50	Test value	P value
Age (years)	Mean ±SD	42.25±7.55	43.82±6.42	44.62±4.24	1.877•	0.157
	Median (Range)	41 (35 - 56)	42 (37 - 62)	42.5 (35 - 58)		
BMI (kg/m ²)	Mean ±SD	28.35±4.06	27.09±4.86	28.01±5.12	0.961•	0.385
	Median (Range)	28 (18-35)	27 (19-33)	28 (19-36)		
	Average	15 (30.0%)	11 (22.0%)	19 (38.0%)	6.389*	0.171
	Overweight	31 (62.0%)	28 (56.0%)	24 (48.0%)		
Obese	4 (8.0%)	11 (22.0%)	7 (14.0%)			
Smoking	Nonsmoker	22 (24.0%)	16 (32.0%)	20 (40.0%)	1.574*	0.455
	Smoker	28 (56.0%)	34 (68.0%)	30 (60.0%)		
Menstrual state	Premenopausal	37 (74.0%)	40 (80.0%)	30 (60.0%)	5.151*	0.076
	Postmenopausal	13 (26.0%)	10 (20.0%)	20 (40.0%)		

BMI: Body mass index

•: One Way ANOVA; *: Chi-square test

Table 1: Clinical Characteristics of the studied groups.

		Fibrin glue group No. = 50	Quilting group No. = 50	Control group No. = 50	Test value*	P value
Diabetes mellitus	Absent	39 (78.0%)	40 (80.0%)	41 (82.0%)	0.250	0.882
	Present	11 (22.0%)	10 (20.0%)	9 (18.0%)		
Hypertension	Absent	37 (74.0%)	35 (70.0%)	38 (76.0%)	0.477	0.787
	Present	13 (26.0%)	15 (30.0%)	12 (24.0%)		
Family history	Negative	39 (78.0%)	41 (82.0%)	37 (74.0%)	0.932	0.627
	Positive	11 (22.0%)	9 (18.0%)	13 (26.0%)		

*: Chi-square test

Table 2: Morbidities in the studied groups.

Tumor Sage (T)	Fibrin glue group No. = 50	Quilting group No. = 50	Control group No. = 50	Test value*	P value
T1	22 (44.0%)	13 (26.0%)	10 (20.0%)	6.857	0.143
T2	22 (44.0%)	25 (50.0%)	27 (54.0%)		
T3	8 (16.0%)	12 (24.0%)	13 (26.0%)		

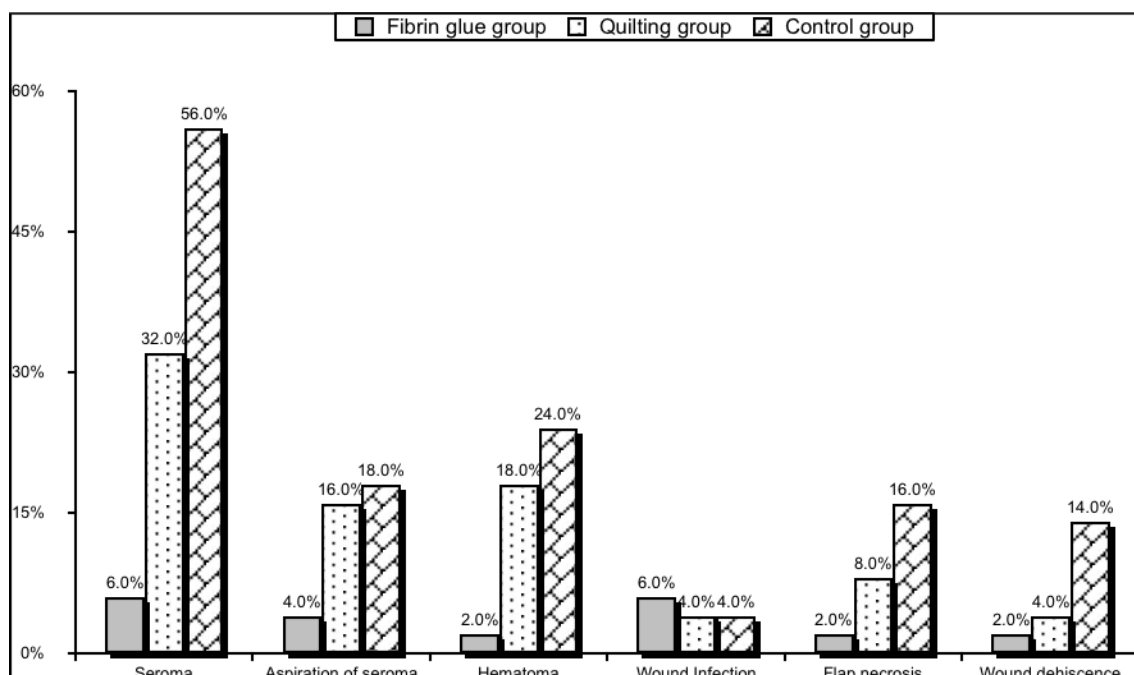
*: Chi-square test

Table 3: Tumor characteristics of the studied groups.

	Fibrin glue group No. = 50	Quilting group No. = 50	Control group No. = 50	Test value	P vaue
Amount of drained fluid in the first postoperative day (CC) Mean+/-SD	160.63±52.11	166.47±38.98	188.37±51.30	4.672•	0.011
Time to remove drain (days) Mean+/-SD	11.26±0.73	12.57±1.01	13.17±1.18	48.586•	<0.001
Hospital Stay (days) Mean+/-SD	1.41±0.38	1.67±0.51	1.91±0.43	15.914•	<0.001
Seroma	3 (6.0%)	16 (32.0%)	28 (56.0%)	29.064*	<0.001
Aspiration of seroma	2 (4.0%)	8 (16.0%)	9 (18.0%)	5.183*	0.074
Hematoma	1 (2.0%)	9 (18.0%)	12 (24.0%)	10.334*	0.006
Wound Infection	3 (6.0%)	2 (4.0%)	2 (4.0%)	0.300*	0.860
Flap necrosis	1 (2.0%)	4 (8.0%)	8 (16.0%)	6.232*	0.044
Wound dehiscence	1 (2.0%)	2 (4.0%)	7 (14.0%)	6.643*	0.036

•: One Way ANOVA; *: Chi-square test

Table-4: outcome of the studied groups.



Discussion

Although many surgeons believe that seroma is not a serous postmastectomy complication, seroma still a major indication of prolonged hospital stay. Seroma carries the risk of wound infection, wound dehiscence, flap necrosis and lymphedema [1].

Therefore, many studies performed to assess the different measures taken to reduce axillary lymphatic drainage and diminishing the dead space to reduce the incidence of seroma formation. Using fibrin glue to stabilize small vessels and lymphatics to reduce oozing in prevention of postmastectomy seroma formation is debatable, although it has promising effect in general surgery [3,11]. However, fibrin glue is effective whenever wound closure is done rapidly after sealant application to take the advantages of sealant polymerization which strength its adhesive effect and enhance bonding of wound surfaces. On the other hand, delaying wound closure after fibrin glue application may cause an anti-adhesive effect as the process of polymerization of sealant make it acting as a barrier interferes with wound surfaces [12].

In addition, surgical obliteration of dead spaced after mastectomy by flap fixation is another well-known surgical technique to reduce formation of seroma [13]. However, studies and researches describing the sequelae in patients undergone this surgical technique are not many [14].

Thus, in our study we demonstrated that obliteration of dead apace after mastectomy by either fibrin glue application or flap fixation (quilting) reduces seroma formation in comparison with conventional closure without fibrin glue application and without flap fixation (non quilting) techniques.

Present study was designed to include 150 women with breast cancer undergone modified radical mastectomy (MRM) and axillary clearance. Theses 150 women were randomly divided equally into three groups, each group included 50 women. In group I (Fibrin Glue Group), axillary and mammary beds were sprayed by fibrin glue (only one pack of FIBROGLOO) and conventional drain was placed after mastectomy. In Group II (Quilting Group) multiple interrupted sutures were taken after mastectomy starting in the lower flap from medial to lateral between mastectomy flap. In Group III (non quilting - control group), the wounds were closed traditionally without quilting, and the the skin was closed in two layers manner without using flap fixation.

Our study showed that both clinical characteristics of patients (including age, BMI, smoking and menstrual status) and presence of morbidities (diabetes mellitus, hypertension and family history of breast cancer) have no significance on seroma formation. In addition, there was no significant difference with tumor characteristics (tumor staging) on formation of seroma.

This study demonstrated a significant reduction of seroma formation in both fibrin glue group (6%) and quilting group (32%) versus control group (56%), with favor to fibrin glue

group ($p<0.001$). The amount of drained fluid from the wound in the first day was decreased significantly in fibrin glue group and in quilting group with comparison to control group, and fibrin glue group reported for the least amount ($p=0.011$). Therefore, there was a significant shortening in time taken to remove drains and in hospital stay in fibrin glue group and in quilting group against control group, with favor to fibrin group ($p<0.001$).

On the light of previous results, fibrin sealant application had the best outcome considering reduction of seroma and drained fluid, and had the shortest hospital stay among other groups. More et al reported similar findings, as their study showed a significant reduction of both seroma formation and quantity of drained serosanguinous fluid with fibrin sealants application [15]. In addition, Jain et al studied 116 women undergone mastectomy for breast cancer and they reported a significant reduction of seroma formation in their study which included 116 women undergone mastectomy for breast cancer [16]. Another prospective randomized trial, done by Ko et al, over 100 women undergone breast lumpectomy and axillary clearance concluded that fibrin sealant application reduced drainage duration and overall drain output [17]. Moreover, many studies reported significant reduction in both times passed to remove drain and hospital stay with using fibrin glue [15, 17-20].

On the other hand, some studies concluded that application of fibrin sealants after mastectomy had no significant effect on reduction of seroma formation, but it only reduced postoperative serous fluid amount. Ruggiero et al investigated the role of fibrin glue over 90 women undergone quadrantectomy or mastectomy with level I/II axillary lymphadenectomy. They reported that compared with the conventional treatment, fibrin sealant application had reduced significantly seroma volume ($p=0.004$) and duration ($p=0.02$), although fibrin sealant application does not always prevent seroma formation [20]. Another study by Bonjar et al over 60 women reported that fibrin sealant application had nonsignificant decrease in seroma formation rate versus drain placement. They also noted that the higher cost and burdensome technique make fibrin sealant application had no advantage over drain placement [21]. Gilly et al found mentioned that although fibrin sealant application did not reduce seroma formation, it had significantly reduced both of postoperative drained fluid quantity and hospital stay [22].

Our study also reported a significant beneficial effect of quilting the skin flaps to reduce seroma formation, drained fluid volume and short hospital stay, compared to conventional surgical technique. Khater et al performed a randomized controlled study to assess quilting flaps in reducing seroma formation among 120 women who were candidates for mastectomy and axillary clearance. The 120 women were randomly equally divided into two group; intervention group included 60 women had quilting flaps after mastectomy, and control group included 60 women had no quilting. A significant reduction of seroma formation in intervention group (20%) versus control group (78.3%) was reported ($p<0.001$). In addition, intervention group

showed significant shorter duration (9 days versus 11 days, $P < 0.001$) and smaller drainage volume (710 mL versus 1160 mL, $P < 0.001$) compared with control group [23]. Similar study by Van Basteelaar et al over 180 women undergone mastectomy; 92 in quilting flaps group and 88 in control group. They reported a significant reduction of seroma formation in quilting flap group (35.9%) versus (59.1%) in control group ($p=0.002$). They also noted that only (15.2%) of quilting flap group needed aspiration of seroma, while (43.2%) of control group did ($p<0.001$) [13].

Conclusion

According to our findings, we can conclude that obliterating the dead spaces after modified radical mastectomy and axillary lymphadenectomy by either fibrin glue application or quilting skin flaps can reduce seroma formation, decrease the drained fluid volume and shorten hospital stay. However, fibrin glue application showed a promising higher efficacy in reduction of seroma formation than quilting skin flaps did.

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