

Analysis of Perioperative Risk Factors for Complications Following Modified Radical Mastectomy- A Longitudinal Study

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ABSTRACT

Introduction: Modern therapy for the breast cancer has evolved to include both surgical and systemic therapy. The Modified Radical Mastectomy (MRM) is the standard treatment option for most of the patients with breast cancer. Early complications are defined here as complications occurring within 30 days after surgery. The initial complications following MRM includes wound infections, seromas, chronic pain, flap necrosis and haematomas.

Aim: To study the frequency of occurrence of outcomes such as, seroma, haematoma, flap necrosis, Surgical Site Infection (SSI) following MRM and to associate the outcomes with the clinical, demographic, intraoperative and postoperative factors.

Materials and Methods: The present study was a single centre longitudinal cohort study with sample size of 72. Patients who are admitted for MRM for carcinoma breast between January 2019 to January 2020 in Department of General Surgery, ESIC MC & PGIMSR, Rajajinagar, Bengaluru, Karnataka, India, were taken for study after considering the inclusion and exclusion criteria. The data of risk factors collected were entered into a proforma. After surgery they were observed postoperatively for early complications. They were followed-up for a period

of one month. Information was entered in Statistical Package for the Social Sciences (SPSS) software. Descriptive statistics comprising of mean, average, standard deviation, proportion, and percentage were used. Comparison of continuous data was done by Student's t-test and categorical variables were compared using Chi-square test. Variables with p-value <0.05 were considered as significant risk factor.

Results: Out of the 72 patients, who underwent MRM 27 (37.5%) developed seroma, 6 patients (8.3%) developed SSI and 9 patients (12.5%) developed flap necrosis. There was significant association between Seroma Formation (SF) and higher age (p=0.026), higher BMI (p=0.001), hypertension (p=0.004) and drain volume on day 1 (p<0.001). There was significant association between SSI and Diabetes Mellitus (DM) (p=0.002), prolonged duration of drain (p=0.03). There was significant association between flap necrosis and DM (p=0.003).

Conclusion: The incidence of seroma was higher in older, hypertensive and in more obese patients. It was decreased by flap fixation under muscles. The incidence of SSI and flap necrosis was higher among diabetic patients. Optimisation of glycaemia will help in reducing both.

Keywords: Flap necrosis, Seroma, Surgical site infection

INTRODUCTION

Breast cancer is the second most common malignancy and a major cause of cancer related death with 23% of new cases and 14% of total deaths globally [1]. Modern therapy for the breast cancer has evolved to include both surgical resection for local disease and chemotherapy, hormonal therapy and radiotherapy for the systemic disease [2]. The MRM or wide local excision is the modality of treatment option for patients with breast cancer. Early complications are defined here as complications occurring within 30 days after surgery. It is documented that initial wound complications following MRM are wound infections, seromas, chronic pain, flap necrosis and haematomas [3]. Based on different surveys, a range of 0.8-26% has been reported as the incidence rate of the surgical site complications after the breast surgeries [4,5]. SF is the most common postoperative complication seen following MRM with an incidence of 3-85% [6]. Infection developing within seroma increases morbidity and often increases the financial burden to the patient [7]. Incidence rates for postoperative wound infections are variable and range from 3-19% chronic pain in 20-30% of the cases, flap necrosis is reported between 3-32% [8-10]. The incidence of functionally significant lymphedema after a MRM is <10% [11]. The different factors which causes seroma, flap necrosis and wound infection have been divided into tumour factors (tumour size, lymph node status), patient factors (age, weight, comorbidities) and surgical factors (use of electrocautery/scalpel

for flap dissection, duration of the surgery) [12]. Complications after mastectomy can be minimised with proper preoperative evaluation, meticulous technique, haemostasis and wound closure. In addition to the oncologic evaluation, preoperative evaluation includes assessment of patients overall physiologic condition with emphasis on tolerability of anaesthesia, Body Mass Index (BMI), diabetic status, hypertension, anemia, coagulopathy or steroid therapy, duration of surgery [13].

This study intends to find out the frequency of occurrence of outcomes such as, seroma, haematoma, flap necrosis, Surgical Site Infection (SSI) following MRM and the association between the risk factors and the complications following MRM.

MATERIALS AND METHODS

The present study was a longitudinal study, patients who were admitted in General Surgery Department in ESIC PGIMSR Bengaluru, Karnataka, India, with breast cancer Locally Advanced Breast Cancer (LABC)-Stage 3A from January 2019 to January 2020 were included. It is a single centre longitudinal cohort study with sample size of 72. Considering the incidence of complications 20% [11] with precision of 10% and 95% confidence interval and 80% power sample size obtained was 62. Considering 10% loss to follow-up sample size taken was 72. It was calculated using OpenEpi version 3.03. Ethical clearance was obtained from the institute, with approval number - 532/L/11/12/Ethics/ESICMC&PGIMSR/Estt.Vol..IV.

Inclusion criteria: Study included patients with LABC stage 3A and 3B (post-neoadjuvant chemotherapy) and patients who had recurrence after breast conservation surgery.

Exclusion criteria: Study excluded patients undergoing breast conservation surgery, patients with metastatic breast cancer, residual disease, pregnant ladies with carcinoma breast.

A total of 72 cases were selected. A written informed consent was taken from all patient included in the study. A detailed history taking, through clinical examination, baseline investigations including fine needle aspiration cytology, core biopsy were done for these patients. The data of risk factors collected were entered into a proforma. Patients were posted for surgery after preparing the patient and were observed postoperatively for complications and were followed-up for a period of one month. Parameters studied:

1. Factors observed preoperatively: Age of the patient: a) >45 years; b) <45 years, BMI: a) >22.5 kg/m²; b) <22.5 kg/m², preoperative serum proteins, co-morbidities like DM, hypertension.
2. Factors observed intraoperatively: Duration of surgery, modality used for dissection of flap: a) electrocautery; b) scalpel, mechanical closure of dead space done by suture fixation. Technique of skin closure: a) sutures and b) stapler
3. Postoperatively: Duration of drain in-situ: a) >8 days; b) <8 days, drain volume on postoperative day 1, timing of starting of physiotherapy.

STATISTICAL ANALYSIS

The information collected was entered in Microsoft Excel and analysed using SPSS version 23.0 software. Independent variables were usage of electrocautery, mechanical closure of dead space and dependant variables were age, DM, hypertension, BMI, serum protein, skin closure, duration of surgery, timing of removal of drain, drain volume and timing of starting the physiotherapy. Descriptive statistics comprising of mean, average, standard deviation, proportion, and percentage were used. Comparison of continuous data was done by Student's t-test and categorical variables were compared using Chi-square test. Variables with p-value <0.05 were considered as significant risk factor.

RESULTS

Study included 71 female patients and one male patient. Majority (36.1%) of patients were between the age group of 41-50 years, with mean age being 51.25±10.39 years. About 31.9% of the patients had BMI between 25-29.9 kg/m². Almost all of the patients (90.3%) were started with upper limb physiotherapy on postoperative day 1 [Table/Fig-1]. Some of the other risk factors observed were preoperative serum proteins, the mean value of which was 7.4±0.70 gm/dL (Range: 6.729-8.131gm/dL). The mean duration of surgery was 108.61±29.41 minutes, (range: 79.2-138.02 minutes). The mean volume of the drain volume on day 1 was 155.42±84.60 mL. (Range: 70.818- 240.02 mL). Out of the 72 patients, who underwent MRM 27 patients (37.5%) developed seroma, 6 patients (8.3%) developed SSI and 9 patients (12.5%) developed flap necrosis [Table/Fig-1]. There was significant association between SF and with patients >45 years, with BMI >25 kg/m², with hypertension, and with mean drain volume on day 1 [Table/Fig-2]. There was a significant association between SSI and Type 2 DM, and with prolonged drain in-situ [Table/Fig-3]. There was a significant association between flap necrosis and Type 2 DM [Table/Fig-4,5].

Age group (years)	Frequency (n)	Percent (%)
≤30	1	1.4
31-40	9	12.5

41-50	26	36.1	
51-60	22	30.5	
61-70	12	16.7	
>70	2	2.8	
Total	72	100	
BMI (kg/m²)			
Underweight (<18.5)	1	1.4	
Normal (18.5-24.9)	48	66.7	
Preobese (25-29.9)	23	31.9	
Total	72	100	
Co-morbidity			
Type 2 DM	14	19.5	
HTN	22	30.6	
Hypothyroidism	8	11.1	
Modality used for dissection of the flap			
Cautery	71	98.6	
Cautery, Scissors	1	1.4	
Total	72	100	
Mechanical closure of dead space by suture fixation			
Done	7	9.7	
Not done	65	90.3	
Total	72	100	
Timing of starting the physiotherapy			
Day 0	1	1.4	
Day 1	65	90.3	
Day 2	5	6.9	
Day 4	1	1.4	
Total	72	100	
Outcome/Complications			
Seroma	27	37.5	
SSI	6	8.3	
Flap necrosis	9	12.5	
	N	Mean	Std. deviation
Serum protein (gm/dL)	72	7.430556	0.7018364
Duration (min)	72	108.61	29.410
Drain volume (mL)	72	155.42	84.602

[Table/Fig-1]: Risk factors, complications and their percentage.

Factors	Variables	Seroma present (n=27)	Seroma absent (n=45)	p-value
Age (years)		54.74 (±8.90)	49.16 (±10.7)	0.026* (Student's t-test)
BMI (kg/m ²)	<18.5	0	1	0.001* (Chi-square)
	Normal (18.5-24.9)	11	37	
	Preobese (25-29.9)	16	7	
Type 2 DM		5	9	0.87 (Chi-square)
HTN		10	12	0.004* (Chi-square)
Hypothyroidism		1	7	0.12 (Chi-square)
Post neoadjuvant chemotherapy		5	8	0.93 (Chi-square)
Serum protein		7.38±0.6	7.46±0.75	0.64 (Student's t-test)
Modality used for dissection of the flap	Cautery	27	44	0.43 (Chi-square)
	Cautery, scissors	0	1	
Mechanical closure of dead space by suture fixation	Done	1	6	0.18 (Chi-square)
	Not done	26	39	

Skin closure	Staplers	25	39	0.43 (Chi-square)
	Sutures	2	6	
Timing of removal of drain	>8 days	27	28	0.35 (Chi-square)
	5 th day	0	8	
	6 th day	0	8	
	7 th day	0	1	
Duration of surgery (min)		110±28.3	107±30.3	0.75 (Student's t-test)
Drain volume (mL)		209.63±73	122±74.2	<0.001* (Student's t-test)
Timing of starting the physiotherapy	Day 0	1	0	0.165 (Chi-square)
	Day 1	25	40	
	Day 2	1	4	
	Day 3	0	0	
	Day 4	0	1	

[Table/Fig-2]: Association between the seroma and the risk factors. *p<0.05 is significant (Chi-square test and Student's t-test were used)

Factors	Variables	SSI Present (n=6)	SSI Absent (n=66)	p-value
Age (years)		52.83±15.2	51.1±9.93	0.71 (Student's t-test)
BMI (kg/m ²)	<18.5	0	1	0.59 (Chi-square)
	Normal (18.5-24.9)	3	45	
	Preobese (25-29.9)	3	20	
Type 2 DM		4	10	0.002* (Chi-square)
HTN		3	19	0.28 (Chi-square)
Hypothyroidism		1	7	0.65 (Chi-square)
Post Neoadjuvant chemotherapy		0	13	0.23 (Chi-square)
Serum Protein		7.11±0.77	7.45±0.69	0.25 (Student's t-test)
Modality used for dissection of the flap	Cautery	6	65	0.76 (Chi-square)
	Cautery, scissors	0	1	
Mechanical closure of dead space by suture fixation	Done	0	7	0.49 (Chi-square)
	Not done	6	59	
Skin closure	Staplers	5	59	0.65 (Chi-square)
	Sutures	1	7	
Timing of removal of drain	>8 days	5	50	0.03* (Chi-square)
	5 th day	0	8	
	6 th day	1	7	
	7 th day	0	1	
Duration of surgery (min)		113.33±39.2	108.18±28.69	0.68 (Student's t-test)
Drain volume (mL)		203.3±79.1	151.06±84.29	0.14 (Student's t-test)
Timing of starting the physiotherapy	Day 0	0	1	0.76 (Chi-square)
	Day 1	6	59	
	Day 2	0	5	
	Day 3	0	0	
	Day 4	0	1	

[Table/Fig-3]: Association between the Surgical Site Infection (SSI) and risk factors. *p<0.05 is significant (Chi-square test and Student's t-test used)

DISCUSSION

The complications noted in present study were, seroma, SSI and flap necrosis. SF collection under skin flaps or in the axillary dead space

Factors	Variables	Flap necrosis present (n=9)	Flap necrosis absent (n=63)	p-value
Age (years)		48.80±11.6	51.5±10.2	0.47 (Student's t-test)
BMI (kg/m ²)	<18.5	0	1	0.65 (Chi-square)
	Normal (18.5-24.9)	5	43	
	Preobese (25-29.9)	4	19	
Type 2 DM		5	9	0.003* (Chi-square)
HTN		5	17	0.08 (Chi-square)
Hypothyroidism		2	6	0.25 (Chi-square)
Post Neoadjuvant chemotherapy		0	13	0.13 (Chi-square)
Serum protein		7.27±0.59	7.45±0.7	0.48 (Student's t-test)
Modality used for dissection of the flap	Cautery	9	62	0.73 (Chi-square)
	Cautery, scissors	0	1	
Mechanical closure of dead space by suture fixation	Done	0	7	0.29 (Chi-square)
	Not done	9	56	
Skin closure	Staplers	8	56	0.9 (Chi-square)
	Sutures	1	7	
Timing of removal of drain	>8 days	8	47	0.68 (Chi-square)
	5 th day	1	7	
	6 th day	0	8	
	7 th day	0	1	
Duration of surgery (min)		112.78±11.4	108.02±31.1	0.65 (Student's t-test)
Drain volume (mL)		196.6±99.2	149.52±81.0	0.11 (Student's t-test)
Timing of starting the physiotherapy	Day 0	0	1	0.88 (Chi-square)
	Day 1	9	56	
	Day 2	0	5	
	Day 3	0	0	
	Day 4	0	1	

[Table/Fig-4]: Association between flap necrosis and risk factors. *p<0.05 is significant (Chi-square test and Student's t-test used)



[Table/Fig-5]: Flap necrosis.

following mastectomy with axillary dissection detected clinically or by imaging [14]. It is the most common early complication [10]. It can lead to morbidity as delayed wound healing, wound infection, wound dehiscence, prolonged hospital stays, financial constraint to the patient [15]. In this study, 37.5% of patients developed seroma which was more, compared to 27% in a study by Suresh BP et al.,

and 28% in a study by Chaudhary A and Gautam S, [16,17]. As age increases, risk of SF increases as most of the patients developing the complications were >45 years in this study. In a study by Suresh BP et al., age >40 years developed seroma and Chaudhary A and Gautam S, age >62 years developed seroma [17]. Increase in BMI was found to be a significant risk factor for seroma. Overweight patients developed seroma the most in this study, which was in accordance with Suresh BP et al., (27%) and Chaudhary A and Gautam S (28%) studies [16,17]. Hypertension was significantly associated with seroma in this study. Similarly, in the Loo WT and Chow LW study, 8% of patients had seroma [18]. Increased drain output on the first day of surgery is a predictive factor for SF which was also mentioned in a study by Anjani J et al., [19].

Surgical Site Infection (SSI): The National Healthcare Safety Network classifies breast operations as clean procedures with an expected 1-2% SSI incidence [20]. SSI defined by the Centers for Disease Control and Prevention (CDC) as infection related to an operative procedure that occurs at or near the surgical incision within 30 days of the procedure, or within 90 days, if prosthetic material is implanted at surgery- is among the most common preventable complication after surgery. It increases the morbidity, psychological trauma, additional cost and delay in postoperative adjuvant therapy [21]. In this study, there was significant association between diabetes and SSI (66% of SSI was seen in diabetic patients) which was also true according to Nyaoncha A et al., and Olsen MA et al., [22,23]. Prolonged duration of drains in-situ has an increased probability of SSI, also mentioned in the Nyaoncha A et al., study [22]. Hence, drain removal is recommended as early as possible, preferably within one week. Other factors like, age, BMI, HTN, hypothyroidism, serum proteins, usage of cautery, duration of surgery, drain volume and timing of starting physiotherapy did not have any association with the formation of SSI.

Flap necrosis: It occurs when the blood supply to the skin flaps is insufficient to meet their metabolic needs. It may present as partial or full-thickness necrosis. It is a major debilitating factor as it hinders adjuvant therapy leading to morbidity among other constraints like anxiety, distress, aesthetic, and financial implications [24]. In this study, 12.5% of the patients developed flap necrosis. Flap necrosis has a significant association with T2DM as evidenced in other studies like Hultman CS and Daiza S, and Matsen CB et al., [25,26]. Therefore, care should be taken while rising flap in diabetic patient and glycaemic control is necessary. The other factors like age, BMI, HTN, hypothyroidism, usage of cautery, duration of surgery, prolonged drain in-situ timing of starting the physiotherapy did not have any association with formation of flap necrosis. As treatment of obesity takes long duration, surgery for carcinoma breast can not be postponed. Hence, expectant management of seroma in such cases is necessary and techniques like, mechanical closure of dead space should be employed in all cases of BMI >25.01 kg/m² along with strict control of hypertension postoperatively. In diabetics, flap thickness may be maintained at the higher value (7-8mm) [11] to prevent flap necrosis and adequately followed-up for the need of radiotherapy in case of recurrence. Adequate antibiotics are to be given postoperatively in patients with diabetes and consider higher antibiotics in patients with prolonged drain in-situ.

Limitation(s)

A single institute study with a small sample size of 72 was studied. If the outcomes of this study must be extended to all patients, a multicenter study with a larger sample size may be required. Also, diathermy usage was the only dissection method studied. Hence, it's causative role in complications cannot be commented upon.

CONCLUSION(S)

Seroma, SSI and flap necrosis are some of the most common complications after MRM. Important preoperative risk factors for seroma, were to age >45 years, HTN, overweight category and postoperatively, higher drain volume on first day increased the risk significantly. T2DM was significantly associated with SSI and flap necrosis following MRM, optimal glycaemic control, whenever feasible, should be considered before surgery. Prolonged drain in-situ may be a significant risk factor for SSI and hence, early removal may be recommended.

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