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ORIGINAL ARTICLE

Raised Blood Pressure as a Risk Factor of Post-Operative Seroma Formation in Patients of Modified Radical Mastectomy

MUHAMMAD AYYUB ANJUM[1], MUHAMMAD AHMED NASEER[2], AHMAD RAFIQUE[3], BASHIR AHMAD NOOR[4], JAMAL ABDUL NASIR[5], AMINA RASHEED[6]

[1]*Fellowship Trainee FCPS (Breast Surgery) Senior Registrar/ Fellowship Trainee Breast Surgery West surgical ward KEMU/ Mayo Hospital Lahore*
[2]*Senior Registrar Mayo Hospital Lahore, East Surgical Ward.*
[3]*Consultant Surgeon THQ hospital, Jaranwala*
[4]*Consultant Surgeon District Headquarter-DHQ, Jhang*
[5]*Resident Surgeon, Pakistan Institute of Medical Sciences, Islamabad, Pakistan*
[6]*House officer Sir gangaram hospital, Lahore*
Corresponding author: Muhammad Ayyub Anjum, Email: drayyub@yahoo.com

ABSTRACT

Despite seroma is rarely potentially lethal and is typically harmless, it can cause considerable sequelae such as flap necrosis, wound dehiscence, predisposes to infection. The objective of the study was to determine the association of raised blood pressure as a risk factor of development of seroma after MRM in breast cancer patients.

Material Methods: In this case control study, all women of age 30 to 70 years with MRM done for carcinoma of the breast of stage T2 and lymph nodes N2 were enrolled and followed for 3 days after MRM surgery for seroma formation. Out of total 122 patients, 64 patients were cases and 58 controls. Patients with disease upto N2 had level 2 clearances with upfront surgery. Age, history of essential hypertension, compression bandage applied, serum albumin level, seroma formation and volume of seroma on 3rd post-operative day was documented.

Results: Mean age of the patients was 51.2 + 9.5 years and 53.5 + 10.8 years in case and control, respectively. Majority of the patients were of the age group 40 to 50 year's age group. 56.3% (n=36) cases and 43.8% (n= 28) controls had history of essential hypertension. Seroma formation was seen in cases 51% (n=31) as compare to controls 13% (n= 8) with odd ratio OR 1.48. Drainage volume among two groups was analyzed as in case group, the drainage volume was 148.1 + 76.4 ml (range 50 to 290) while in control group the drainage volume was 130 + 56.9 ml (60 to 250) and was statistically significant with p-value <0.001.

Conclusion: Although the pathogenesis of seroma remains controversial, hypertension is the most consistent significant risk factor for seroma formation subsequent to modified radical mastectomy for carcinoma breast. Good pre, peri and post-operative blood pressure control can reduce the risk of seroma formation and the associated morbidity.

Keywords: MRM, Seroma, nodal clearance, breast cancer,

INTRODUCTION

Carcinoma of breast has been one of the most feared of human ailments, despite years of theoretical and academic investigation. It is the most frequent tumor in women in the United States and the second most common disease in India (1). It is also the major cause of cancer-related deaths among females worldwide. Positive family history, early menarche, late first pregnancy, nulliparity, and advance age at menopause all enhance the risk (2).

The illness can remain limited to the breast, disseminate to nearby lymph nodes (most usually axillary), or extend to distant body areas (most commonly bones, lungs, pleura and liver) (3). Breast carcinoma management is determined by the state of the emptying regional lymph nodes, the size of the cancer, whether the cancer contains hormone receptors and/or the protein HER2, the female's age or reproductive status, and the existence of metastases (4). Management options might be localized, such as surgery or radiation (RT), or systemic, such as chemo, hormone treatment, or humanized monoclonal antibodies (5).

Based on the extent of the disease spread and other patient variables, the surgical therapy of choice for these individuals is either modified radical mastectomy (MRM) or breast conservation. ALND is a component of modified radical mastectomy and is the primary therapy for clinically positive or sentinel node biopsy (SNB) positive axillary lymph nodes (6).

Due to late patient diagnosis, surgical methods in popularity, and inconsistent patient check up, MRM is the most often utilized therapy method in Pakistan (7). Seroma development is the most common early consequence of breast carcinoma operations, with estimated rates ranging from 3% to 92 percent (8).

After a breast cancer mastectomy or axillary lymph node removal, a seroma can grow between the chest wall and skin. Unknown is seroma's pathogenesis. Seroma can be caused by a large surgical field, lymphoid channel separation, a loose axillary skin hollow, and the region's manoeuvrability and reliance. Seroma often occurs without explanation or paroxysmal indication. Some writers consider seroma as a "necessary evil" that affects a predicted percentage of people. (9).

The presence of malignant nodes in the axilla, past surgical biopsy, and usage of heparin has all been linked to an increased risk of seroma (10). Surgery can cause seroma. It's more common if the folds are raised with diathermy rather than a surgical blade, and it's more common in modified radical mastectomy than breast-sparing surgery, axillary lymph node dissection than sentinel lymph node dissection, and modified radical mastectomy without instantaneous reconstruction than with instantaneous reconstruction. (11).

Seroma is seldom dangerous and usually innocuous, but it can cause flap necrosis, wound dehiscence, infection, a long healing time, lymphedema, and repeated health checks. It can also postpone adjuvant treatment. (12). Seromas cause psychological pain in addition to financial costs and delayed healing. This can embarrass the surgeon, whose experience has little bearing on seroma after mastectomy. (13).

Several techniques have been used to reduce seroma. Most aim to reduce dead space behind skin flaps and drain collections. These include using bovine thrombin, fibrin glue, and sealant, suturing flaps to deeper tissues or fascia, and using tubes to remove buildup. (14).

MATERIAL AND METHODS

This case control study was conducted, after approval from ethical and research committee of hospital from 25/04/2020 to 24/10/20. All women of age 30 to 70 years with MRM done for carcinoma of the breast of stage T2 and lymph nodes N2 were enrolled and followed for 3 days after surgery for seroma formation.

Out of total 120 patients, 64 patients were enrolled in the case group and 58 patients in the control group. Cases were those women who had underwent MRM for carcinoma breast and had raised blood pressure in the post-operative period while controls were those women who underwent MRM for carcinoma breast with no documented raised blood pressure in post-operative period.

Seroma formation was noted in the post-operative period (initial 72 hours).

Any patient with drainage volume of more than 150 ml on 3rd post-operative day was labeled as having seroma formation. All the patients underwent level II axillary clearance. Patients with disease upto N2 were taken and only those with upfront surgery were included.

The purpose and goals of this research were given to all participants, and signed consent permission was acquired after stressing the use of the research and the importance of anonymity. Among both cases and controls, detailed history was taken along with careful scrutiny of past medical and surgical records. This was done to avoid confounders and possible bias in the study results.

All the observations, diagnosis of seroma and clinical assessments were conducted under supervision of a team of expert general surgeons. Patients having history of bleeding disorder, fungating carcinoma, intake of antithrombotic or antiplatelet drugs and Body Mass Index of > 25 were excluded because they act as confounders and will make the study results biased. Extreme care was exercised in the selection of cases and controls to avoid selection bias. Age, history of essential hypertension, compression bandage applied, serum albumin level, seroma formation and volume of seroma on 3rd post-operative day was demented.

Data was analyzed using SPSS and chi square test was applied to compare the categorical variables to determine the statistical significance of difference between the two groups. Similarly, t-test was applied to compare continuous variables like age and seroma volume. p value calculated using these tests was taken significant below 0.05.

RESULTS

This study was conducted at Surgical Unit Mayo Hospital Lahore in which 120 cases were observed to determine the association of raised blood pressure with seroma formation in post-operative patients of modified radical mastectomy for carcinoma breast.

Mean age of the patients was 51.2 + 9.5 years and 53.5 + 10.8 years in case and control, respectively. Majority of the patients were of the age group 40 to 50 year's age group. 56.3% (n=36) cases and 43.8% (n= 28) controls had history of essential hypertension. In our study, seroma formation was seen in cases 51% (n=31) patients as compare to controls 13% (n= 8) with odd ratio OR 1.488. Drainage volume among two groups was analyzed as in case group, the drainage volume was 148.1 + 76.4 ml (range 50 to 290) while in control group the drainage volume was 130 + 56.9 ml (60 to 250) and was statistically significant with p-value <0.001.

Data of incidence of seroma formation was stratified for the data of history of essential hypertension, compression bandage done after surgery, and low level of serum albumin in all the patients was compared between the two groups, and post-stratification chi square was applied. Analysis showed that p value was significant for history of essential hypertension, and low serum albumin level.

Seroma formation was stratified among various age groups in both case and controls, but was not significant. Similarly, application of compression bandage for seroma formation was also not significant. t-test was applied for mean volume of seroma between the two groups, difference was statistically significant, p value <0.0001.

Tables 1: showing the details of seroma formation with respect to age, essential hypertension, low serum albumin and compression bandage application. (n=120)

Crosstabs					
Groups	Prev. H/o Essential Hypertension	Seroma formation		Total	P value
		Yes	No		
Case	Yes	30	5	35	0.0001
	No	0	28	28	
Controls	Yes	8	29	37	0.026
	No	0	20	20	
Groups	Compression Bandage done	Seroma formation		Total	P value
		Yes	No		
Case	Yes	19	17	36	0.385
	No	12	15	27	
Controls	Yes	4	27	31	0.522
	No	4	22	26	
Groups	Low Sr. Albumin	Seroma formation		Total	P value
		Yes	No		
Case	Yes	4	23	27	0.0001
	No	27	9	36	
Controls	Yes	0	21	21	0.016
	No	8	28	36	
Groups	Age Groups	Seroma formation		Total	P value
		Yes	No		
Case	30-40	2	9	11	0.058
	41-50	15	14	29	
	51 -60	5	6	11	
	61-70	9	3	12	
Control	30-40	0	11	11	0.026
	41-50	0	16	16	
	51 -60	3	11	14	
	61-70	5	11	16	

Table 2:

One-Sample Statistics: Seroma Quantity						
Group	N	Min	Max	Mean	Std. Deviation	Std. Error Mean
Case	64	50	290	148.1	76.4	9.6
Control	58	60	250	130.0	56.9	7.5

One-Sample Test						
Group	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					lower	Upper
Case	15.505	63	0.000	148.12500	129.0345	167.2155
Control	17.388	57	0.000	130.00000	115.0285	144.9715

DISCUSSION

Similar results were also observed in another study done by Akinci M et al 106 in which hypertension were found to be more likely to develop, 50% among the cases while 11% in controls. In another study done by Soomro SA et al 107 an incidence of seroma in 61% in hypertensive patients as compare to 5% in normotensive patients with relative risk of 12.72% (16) Given that age is generally associated with high blood pressure due to vascular sclerosis and nephropathy, our finding that hypertension was related to seroma production in the univariate rather than multivariate analysis is not surprising and is backed up by numerous other studies. (17, 18). Seromas can be created by inflammatory exudation or lymphogenous effusion, hence it is thought that increased blood pressure leads to seroma formation, most likely through extended contact area secretion. (19, 20).

There are disagreements on the effect of neoadjuvant chemotherapy on seroma development (21). We found no significant difference in seroma production among patients who had induction chemotherapy and those who did not (22). As a result, more research with a bigger sample size is needed to explain this issue. We found that low levels of total protein and albumin in serum were linked to a higher likelihood of seroma development, even when both median levels were all within normal limits. Seroma is a component of acute healing process that is dependent on proper feeding (23). According to this concept, assessing overall nutritional status, particularly total protein and albumin levels in serum, may be critical in predicting the incidence of postoperative seroma development (24,25). The daily drainage volume was substantially prognostic of eventual seroma development. (26).

Around four investigations on axillary lymph node dissection have uniformly found that the amount of LNs excised has no effect

on seroma development (9, 10, 27, 28). Likewise, one research found that the degree of axillary lymph node dissection had no effect on seroma production (10). In Purushotham et al RCT in contrast, found that sentinel LN biopsy (SLNB) is linked with much less seroma development than standard axillary lymph node dissection (29).

In terms of chemo radiation, Say et al. found that pre- or postoperative radiation therapy had no effect on seroma production in individuals who underwent modified radical mastectomy (30). Additionally, in an RCT comparing neoadjuvant chemotherapy to upfront MRM, preoperative chemotherapy had no effect on seroma development (30).

Compression bandage of wound is a typical treatment used by many clinicians to limit seroma incidence (31). A research found that wearing a pressure clothing to minimise postoperative discharge after the axillary clearance for breast cancer is unnecessary (32). Nevertheless, we believe that wearing a compression garment and restricting arm movement for an extended period of time not only minimises seroma formation but also increases the likelihood of seroma formation following drain retrieval and may potentially induce shoulder pain.

Seroma formation after breast cancer surgery persists despite surgical improvements. Due to the controversial process of seroma production, it is unknown how successful it is to filter out persons who will get seroma, restricting prophylactic and therapeutic efforts. This study and others have looked for seroma risk factors as a strategy to compensate for the lack. To reduce seroma risk, limit discharge quantity and duration with local pressure, injections of exudate reduction and healing medicines, and increased blood total albumin levels.

CONCLUSION

Although the pathogenesis of seroma remains controversial, hypertension is the most consistent significant risk factor for seroma formation subsequent to modified radical mastectomy for carcinoma breast. Good pre, peri and post-operative blood pressure control can reduce the risk of seroma formation and the morbidity that is caused by this. However small sample size is the limiting factor to this study. More research must be undertaken to confirm this association.

REFERENCES

1. Akram M, Iqbal M, Daniyal M, Khan AU. Awareness and current knowledge of breast cancer. Biological Research. 2017;50(1):33.
2. Khalis M, Charbotel B, Chajès V, Rinaldi S, Moskal A, Biessy C, et al. Menstrual and reproductive factors and risk of breast cancer: A case-control study in the Fez region, Morocco. PLoS One. 2018;13(1):e0191333.
3. Welch DR, Hurst DR. Defining the Hallmarks of Metastasis. 2019;79(12):3011-27.
4. Sohail SK, Sarfraz R, Imran M, Kamran M, Qamar S. Estrogen and Progesterone Receptor Expression in Breast Carcinoma and Its Association With Clinicopathological Variables Among the Pakistani Population. Cureus. 2020;12(8):e9751.
5. Ho AY, Wright JL, Blitzblau RC, Mutter RW, Duda DG, Norton L, et al. Optimizing Radiation Therapy to Boost Systemic Immune Responses in Breast Cancer: A Critical Review for Breast Radiation Oncologists. International journal of radiation oncology, biology, physics. 2020;108(1):227-41.
6. Wang L, Ouyang T, Wang T, Xie Y, Fan Z, Lin B, et al. Breast-conserving therapy and modified radical mastectomy for primary breast carcinoma: a matched comparative study. Chinese journal of cancer research = Chung-kuo yen cheng yen chiu. 2015;27(6):545-52.
7. Gulzar F, Akhtar MS, Sadiq R, Bashir S, Jamil S, Baig SM. Identifying the reasons for delayed presentation of Pakistani breast cancer patients at a tertiary care hospital. Cancer Manag Res. 2019;11:1087-96.
8. Pochert N, Schneider M, Ansorge N, Strieder A, Sagasser J, Reiger M, et al. Seroma after Simple Mastectomy in Breast Cancer-The Role of CD4+ T Helper Cells and the Evidence as a Possible Specific Immune Process. 2022;23(9).
9. Faisal M, Abu-Elela ST, Mostafa W, Antar O. Efficacy of axillary exclusion on seroma formation after modified radical mastectomy. World journal of surgical oncology. 2016;14(1):39.
10. Gambardella C, Clarizia G, Patrone R, Offi C, Mauriello C, Romano R, et al. Advanced hemostasis in axillary lymph node dissection for locally advanced breast cancer: new technology devices compared in the prevention of seroma formation. BMC Surg. 2019;18(Suppl 1):125.
11. Faisal M, Abu-Elela ST, Mostafa W, Antar O. Efficacy of axillary exclusion on seroma formation after modified radical mastectomy. World journal of surgical oncology. 2016;14(1):39.
12. Jørgensen MG, Toyserkani NM, Hyldig N, Chakera AH, Hölmich LR, Thomsen JB, et al. Prevention of seroma following inguinal lymph node dissection with prophylactic, incisional, negative-pressure wound therapy (SEROMA trial): study protocol for a randomized controlled trial. Trials. 2018;19(1):441.
13. Pan XF, Huan JL, Qin XJ. Potential risk factors for the development of seroma following mastectomy with axillary dissection. Molecular and clinical oncology. 2015;3(1):222-6.
14. Lese I, Tsai C, Matter M, Wüthrich T, Scheer HS, Taddeo A, et al. Mixed Metal Oxide Nanoparticle Formulations for the Treatment of Seroma. ACS Biomaterials Science & Engineering. 2021;7(6):2676-86.
15. Jones NR, McCormack T, Constanti M, McManus RJ. Diagnosis and management of hypertension in adults: NICE guideline update 2019. The British journal of general practice : the journal of the Royal College of General Practitioners. 2020;70(691):90-1.
16. Vettuparambil A, Subramanya C. Flap Fixation as a Technique for Reducing Seroma Formation in Patients Undergoing Modified Radical Mastectomy: an Institutional Experience. Indian journal of surgical oncology. 2021;12(1):48-53.
17. Wang-Evers M, Casper MJ, Glahn J, Luo T, Doyle AE, Karasik D, et al. Assessing the impact of aging and blood pressure on dermal microvasculature by reactive hyperemia optical coherence tomography angiography. Scientific reports. 2021;11(1):13411.
18. Chowdhury EK, Nelson MR, Ernst ME, Margolis KL, Beilin LJ, Johnston CI, et al. Factors Associated With Treatment and Control of Hypertension in a Healthy Elderly Population Free of Cardiovascular Disease: A Cross-sectional Study. American journal of hypertension. 2020;33(4):350-61.
19. Sampathraju S, Rodrigues G. Seroma formation after mastectomy: pathogenesis and prevention. Indian journal of surgical oncology. 2010;1(4):328-33.
20. Srivastava V, Basu S, Shukla VK. Seroma Formation after Breast Cancer Surgery: What We Have Learned in the Last Two Decades. jbc. 2012;15(4):373-80.
21. Axelsson CK, Qvamme GM, Okholm M, Lanng C, Arpi M, Mortensen MB, et al. Bacterial colonization of seromas after breast cancer surgery with and without local steroid prophylaxis. World journal of surgical oncology. 2019;17(1):120.
22. Zieliński J, Jaworski R, Irga N, Kruszewski JW, Jaskiewicz J. Analysis of selected factors influencing seroma formation in breast cancer patients undergoing mastectomy. Archives of medical science : AMS. 2013;9(1):86-92.
23. Keller U. Nutritional Laboratory Markers in Malnutrition. J Clin Med. 2019;8(6).
24. Garrett MP, Kakarla UK, Porter RW, Sonntag VK. Formation of painful seroma and edema after the use of recombinant human bone morphogenetic protein-2 in posterolateral lumbar spine fusions. Neurosurgery. 2010;66(6):1044-9; discussion 9.
25. Utariani A, Rahardjo E, Perdanakusuma DS. Effects of Albumin Infusion on Serum Levels of Albumin, Proinflammatory Cytokines (TNF-α, IL-1, and IL-6), CRP, and MMP-8; Tissue Expression of EGRF, ERK1, ERK2, TGF-β, Collagen, and MMP-8; and Wound Healing in Sprague Dawley Rats. International journal of inflammation. 2020;2020:3254017.
26. Prevention of seroma formation after mastectomy and axillary dissection by lymph vessel ligation and dead space closure: a randomized trial. Am J Surg. 2010;200(3):352-6.
27. Abass MO, Gismalla MDA, Alsheikh AA, Elhassan MMA. Axillary Lymph Node Dissection for Breast Cancer: Efficacy and Complication in Developing Countries. Journal of global oncology. 2018;4:1-8.
28. Isozaki H, Yamamoto Y, Murakami S, Matsumoto S, Takama T. Impact of the surgical modality for axillary lymph node dissection on postoperative drainage and seroma formation after total mastectomy. Patient Safety in Surgery. 2019;13(1):20.
29. Gherghe M, Bordea C, Blidaru A. Sentinel lymph node biopsy (SLNB) vs. axillary lymph node dissection (ALND) in the current surgical treatment of early stage breast cancer. Journal of medicine and life. 2015;8(2):176-80.
30. Bawoke G, Kejela S, Alemayehu A, Bogale GT. Experience with modified radical mastectomy in a low-income country: a multi-center prospective observational study. BMC Surgery. 2021;21(1):371.
31. Moncrieff MD, Sharma RA, Gathura E, Heaton MJ. Improved Perioperative Seroma and Complication Rates Following the Application of a 2-Layer Negative Pressure Wound Therapy System After Inguinal Lymphadenectomy for Metastatic Cutaneous Melanoma. Ann Surg Oncol. 2020;27(10):3692-701.
32. Ochalek K, Gradalski T, Partsch H. Preventing Early Postoperative Arm Swelling and Lymphedema Manifestation by Compression Sleeves After Axillary Lymph Node Interventions in Breast Cancer Patients: A Randomized Controlled Trial. Journal of pain and symptom management. 2017;54.