What really drives seroma formation?
Insights from a retrospective study of 244 patients undergoing mastectomy.

L. Weydandt [1,2], K. Hein* [1,2], M. Lia [1,2], S. Briest [1,2], I. Nel [1,2], B. Aktas[1,2]*

[1] Department of Gynecology, Medical Center, Leipzig University, Leipzig, Germany, [2] Comprehensive Cancer Center Central Germany, Partner Site Leipzig, Germany

Background

A seroma is defined as a collection of watery exudate in unformed tissue cavities [1]. They primarily occur due to the destruction of lymphatic vessels in wounds or surgical procedures and pro-, inflammatory and transudative processes in the surgically damaged soft tissue surrounding the wound, yet their etiology is still not fully understood [2]. While they are considered the most common complication after a mastectomy [3] not all have clinical significance or require an intervention [4]. Still, they can lead to a lot of secondary complications such as impaired wound healing, delayed recovery, worse aesthetic outcome, patient's discomfort, flap necrosis, wound dehiscence, predisposes to sepsis, multiple physician visits, revision in implant surgery and may delay adjuvant therapy [5].

There has been research showing that the chosen surgery procedure i.e. immediate reconstruction, vacutainer suction, shoulder immobilization, the extent of dissection, surgical devices, flap fixation techniques, use of sclerosants, tranexamic acids, fibrin glue and sealants, octreotide, and pressure garments can reduce the post-operative amount of seroma. Though none of these have been consistent [6]. In addition, bigger real life data studies are still quite rare, had low case numbers, few considered or overriding factors or just low incidences of seroma formation [7].

Our study aims to identify clinical factors that predict or influence seroma formation in patients undergoing a skin-sparing or nipple-sparing mastectomy with or without reconstruction and with or without axillary treatment.

Methods

This was a retrospective study of patients undergoing mastectomy for breast cancer at the University Hospital in Leipzig between 2019 and 2023.

All patients received skin- or nipple-sparing modified radical mastectomy (MRM) without or with primary implant reconstruction and/or lymph node resection (sentinel lymph node biopsy or axillary lymph node resection). Each patient was managed with drainages with negative pressure for seroma collection. Negative pressure was removed on the seventh postoperative at the earliest, drains were removed at a flow rate of less than 30 ml in 24 hours. Variable importance was calculated by Random Forests and p-values were calculated by linear regression.

Results

A total of 244 patients (234 women, 7 men) who underwent mastectomy were included in the analysis. 56 patients (all female) received bilateral mastectomy so in total 301 breasts were operated on and each of them viewed individually in the statistical analysis. 215 (71.4%) breasts were operated due to invasive breast cancer and 24 (7.9%) because of carcinoma in situ. While 62 breasts (20.6%) were operated on due to risk-reducing mastectomy or gender reassignment surgery thus did not suffer from breast cancer. 5 patients (2.0%) had advanced breast cancer disease; thus, a palliative mastectomy was performed. The median seroma volume in the axilla was 55 ml (IQR: 0 – 250) and 455 ml (IQR: 295-660) in the mamma.

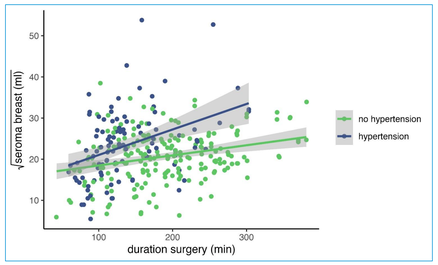


Figure 1. Relationship between surgery duration and seroma volume stratified by hypertension status.

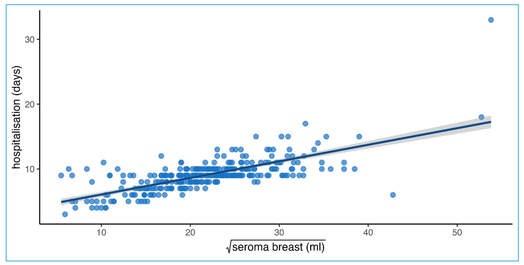


Figure 2. Association between breast seroma volume and length of hospitalisation.

Figure 1 illustrates the relationship between duration of surgery and breast seroma volume, stratified by hypertension status. In both groups, longer operative time was positively associated with greater seroma formation. However, patients with hypertension demonstrated a steeper increase in seroma volume with increasing surgical duration compared with patients without hypertension.

Additionally, a clear positive relationship is observed, with higher seroma volumes corresponding to longer hospital stays (fig. 2).

Results

In univariable linear regression analyses higher BMI ($p < 0.001$), longer duration of surgery ($p < 0.001$), presence of diabetes mellitus type 2 ($p = 0.005$), hypertension ($p = 0.009$), advanced pT-stage ($p = 0.017$) and pN -stage ($p = 0.014$), as well as elevated postoperative CRP levels ($p = 0.021$) were all positively correlated with breast seroma formation.

The five strongest determinants of breast seroma volume according to the random forest analysis were **BMI**, **number of resected lymph nodes**, **duration of surgery**, **hypertension**, and **diabetes** (see fig. 3). These five predictors were subsequently entered into a multivariable linear regression model. All remained independently associated with breast seroma volume (see table 1).

Characteristic	Beta (95% CI)	p-value
BMI (kg/m2)	16 (7.8 to 24)	<0.001
number of resected lymphnodes (n)	15 (7.6 to 23)	<0.001
duration of surgery (min)	1.6 (0.90 to 2.4)	<0.001
hypertension		
No	—	
Yes	151 (41 to 260)	0.007
diabetes mellitus		
No	—	
Yes	184 (39 to 328)	0.013

Table 1. Multivariate analysis of the five most influential factors for seroma formation in the breast, CI = confidence interval

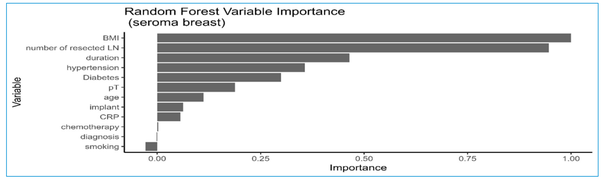


Figure 3. Results of random forest analysis for predicting factors of seroma formation in breast.

In univariable linear regression analyses, **higher BMI** ($p < 0.001$), **advanced pN-stage** (all $p < 0.001$ for stages 1–2), **advanced pT-stage** ($p = 0.010$ for stage 3) and a **greater number of resected lymph nodes** ($p < 0.001$) were significantly associated with increased seroma volume in the axilla. While having a carcinoma in situ was significantly linked to lower amounts of seroma (p=0.019).

Characteristic	Beta (95% CI)	p-value
number of resected lymphnodes (n)	20 (12 to 27)	<0.001
BMI (kg/m2)	10 (3.5 to 16)	0.003

Table 2. Multivariate analysis of the two most influential factors for seroma formation in the axilla, CI = confidence interval.

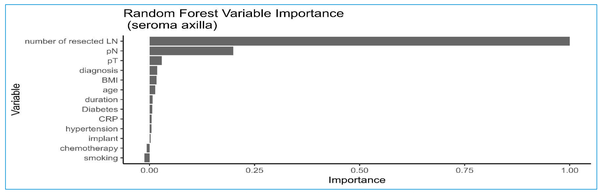


Figure 4. Results of random forest analysis for predicting factors of seroma formation in axilla.

The variable importance plot derived from random forest analysis indicated that the number of resected lymph nodes and pN-stage were by far the strongest determinants of axillary seroma volume, followed by pT-stage, diagnosis and BMI (see fig. 4). These five predictors were subsequently entered into a multivariable linear regression model. The **number of resected lymph nodes** and **BMI** remained independently associated with higher seroma volume (see table 2). Diagnosis, pN- and pT-stage were not significantly associated with axillary seroma volume in the multivariable model.

Conclusion

- We were able to show that the most important factors leading to more seroma in the **breast** are **higher BMI**, **more removed lymph nodes**, **longer surgery duration** and the **presence** of **hypertension** and **diabetes**.
- Respectively in the **axilla** those are **more removed lymph nodes** and **higher BMI**.

1. McCaul JA, Aslaam A, Spooner RJ, Loudon I, Cavanagh T, Purushotham AD. Aetiology of seroma formation in patients undergoing surgery for breast cancer. The Breast. 2000 June;9(3):144–8.
2. Kuroi K, Shimozuma K, Taguchi T, Imai H, Yamashiro H, Ohsumi S, et al. Evidence-Based Risk Factors for Seroma Formation in Breast Surgery. Jpn J Clin Oncol. 2006 Apr 1;36(4):197–206.
3. Anand R, Skinner R, Dennison G, Pain JA. A prospective randomised trial of two treatments for wound seroma after breast surgery. Eur J Surg Oncol EJSO. 2002 Sept;28(6):620–2.
4. Bootsma SY, Throckmorton AD, Boughey JC, Holtfield AC, Zakaria S, Hoskin TL, et al. Incidence of Clinically Significant Seroma after Breast and Axillary Surgery. J Am Coll Surg. 2009 Jan;208(1):148–56.
5. Lista F, Tutino R, Khan A, Ahmad J. Subjacobian Breast Augmentation with Textured, Anatomic, Cohesive Silicone Implants: A Review of 440 Consecutive Patients. Plast Reconstr Surg. 2013 Aug;132(2):295–303.
6. Srivastava V, Basu S, Shukla VK. Seroma Formation after Breast Cancer Surgery: What We Have Learned in the Last Two Decades. J Breast Cancer. 2012;15(4):373.
7. Unger I, Rutkowski R, Kohlmann T, Fwzyko S, Zygmunt M, Ohlinger R. Potential Risk Factors Influencing the Formation of Postoperative Seroma After Breast Surgery – A Prospective Study. Anticancer Res. 2021 Feb;41(2):859–67.

Corresponding author: laura.weydandt@medizin.uni-leipzig.de

This presentation is the intellectual property of the author/presenter. Contact them at laura.weydandt@medizin.uni-leipzig.de for permission to reprint and/or distribute.