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Original Article

Factors predicting seroma formation after mastectomy for Chinese breast cancer patients

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Abstract

BACKGROUND: Seroma formation after mastectomy typically delays recovery and adds to morbidity. **AIMS:** This retrospective review was undertaken to identify factors which predict development of seroma after mastectomy for breast cancer patients. **SETTING AND DESIGN:** 119 consecutive patients intended for mastectomy for the treatment of primary breast cancer were included. Factors taken into consideration were epidemiological, peri-operative in nature and those related to wound drainage output. **MATERIALS AND METHODS:** Total mastectomy was performed and axillary sampling was taken. All patients were reviewed within two weeks after leaving hospital, unless seroma formation was detected before discharge. The diagnosis of seroma was made clinically when a collection was detected beneath the skin flaps. **STATISTICAL ANALYSIS USED:** Student's t test was used with continuous variables and the X^2 test for categorical situations. Fisher's exact test was applied when small numbers were encountered. A two-tailed test of $P<0.05$ was considered significant. Univariate analyses were performed. **RESULTS:** The incidence of seroma formation was eight per cent. Five factors were identified to be significantly related to seroma formation: i) age over 45 years; ii) hypertension; iii) total drainage output exceeding 500 ml in the first three postoperative days; iv) drainage for more than eight days. Immediate breast reconstruction prevents the formation of seroma. **CONCLUSION:** The presence of hypertension in a patient over 45 years should alert the surgeon to possible seroma formation, particularly when the post-operative drainage exceeded 500 ml in the first three days. Appropriate preventive measures should then be implemented.

Key words: Breast cancer, mastectomy, operation, postoperative drainage, seroma

Introduction

A seroma is a sterile collection of serous fluid at the operative site beneath the skin flaps. Seroma formation is the most common complication following mastectomy.[1] Various methods ranging from shoulder immobilization,[2] peri-operative use of tranexamic acid[3] and prolonged suction drainage[4] have been advocated with varying degrees of success for the prevention of seroma formation after mastectomy. However, peri-operative factors which might identify patients at risk have not been well studied. This study aims to identify factors that predict the development of seroma in patients with breast cancer after mastectomy. Appropriate preventive measures could then be implemented to minimize seroma formation and its unpleasant sequelae.

Materials and Methods

Patients intended for mastectomy for the treatment of primary breast cancer were recruited. The group developing seroma was compared with regard to epidemiological factors, operative factors and drainage output with a group without seroma [Table 1].

Operation

Total mastectomy was performed as described by Forrest.[5] Axillary sampling was taken as a level I dissection and clearance was taken at all three levels.

Table 1: Summary of findings

Variable	Test used	Result
1. Epidemiological factors		
Age (> 45 years)*	Fisher's exact	$P = 0.020$
Menstrual status	Fisher's exact	$P = 0.203$
Staging of disease	X^2	$X^2 = 2.80$, d.f.= 5, $P = 0.731$
Serum albumin (g/l)	t test	t= -1.98, d.f.= 11.12, $P = 0.073$
Preoperative hemoglobin (g/dl)	t test	t= -0.90, d.f.= 4.732, $P = 0.371$
Hypertension*	X^2	$X^2 = 13.86$, d.f.= 1, $P = 0.0013$
Diabetes mellitus	X^2	$X^2 = 0.89$, d.f.= 1, $P = 0.344$
Body weight (kg)	t test	t= 1.49, d.f.= 115, $P = 0.138$
2. Operative factors		
Blood loss (ml)	t test	t= -0.40, d.f.= 6.68, $P = 0.703$
Transfusion requirements (ml)	t test	t= -0.04, d.f.= 11.35, $P = 0.967$
Length of operation (min)	t test	t= 0.97, d.f.= 10.29, $P = 0.354$
Experience of surgeon	X^2	$X^2 = 0.325$, d.f.= 2, $P = 0.850$
Axillary status	X^2	$X^2 = 0.364$, d.f.= 1, $P = 0.849$
Type of axillary surgery	X^2	$X^2 = 2.95$, d.f.= 2, $P = 0.228$
Immediate breast reconstruction*	X^2	$X^2 = 12.29$, d.f.= 3, $P = 0.0065$
3. Drainage outputs		
Duration of drain-in-situ (> 8 days)*	Fisher's exact	$P = 0.005$
Total drain output (ml)*	t test	t= 2.65, d.f.= 89, $P = 0.010$
Early drain output (> 500 ml)	Fisher's exact	$P = 0.049$
Late drain output (ml)	t test	t= 0.32, d.f.= 6.94, $P = 0.759$
Trend of drain output	Fisher's exact	$P = 0.168$

*Indicates statistical significance

Reconstruction was performed using the pedicle Transverse Rectus Abdominis Myocutaneous (TRAM) flap technique. Each patient was managed with Hemovac closed suction drainage with two catheters from one suction device (Hemovac 400 ml Evacuator: Hemovac, Synder laboratories, USA). The catheters were inserted into the chest wound at the end of operation. Drains were retained until the 24h total output was less than or equal to 30 ml.

Seroma formation and its management

All patients were reviewed within two weeks after leaving hospital, unless seroma formation was detected before discharge. The diagnosis of seroma was made clinically when a collection was detected beneath the skin flaps. Aspiration under sterile condition was performed for both diagnostic confirmation and management. The aspirate was sent for bacterial culture and aspiration repeated weekly until no collection could be detected.

Statistical analysis

Student's t test was used with continuous variables and the X^2 test for categorical situations. Fisher's exact test was applied when small numbers were encountered. A two-tailed test of $P<0.05$ was considered significant. Univariate analyses were performed. The number of patients with seroma formation did not enable meaningful multivariate analysis to be carried out.

Results

A total of 119 patients with a mean age of 56.2 years (range: 26-92 years) were included in this study. Ten patients (8%) developed seroma after mastectomy, eight of whom required repeated aspirations [Table 2]. 'Recovery', defined as the day of drain removal in the control group and the day when the last aspiration was performed in those with seroma formation, was 4.5 (s.d.= 1.7) and 32.7 (s.d.= 20.7) days, from the day of operation, for the respective groups. The patients without seroma recovered significantly earlier than those with seroma (Wilcoxon rank sum W test, $P=0.000$).

Epidemiological factors

Patients older than 45 years old had a statistically significant higher chance of developing seroma than younger patients (Fisher's exact test, $P=0.02$). However, no significant correlation was found between menstrual

Table 2: Duration of seroma formation

Patient referral number	Number of aspirations	Last aspiration day
8	2	12
9	1	14
21	2	31
37	2	78
38	3	15
64	2	23
67	6	28
77	1	53
105	3	28
107	2	45

status and seroma formation.

Patients with hypertension were also more likely to develop seroma after mastectomy (X^2= 13.86, P= 0.001), but no such difference was found in patients with diabetes mellitus. Furthermore, statistical correlation was not found between the preoperative serum albumin concentration, hemoglobin concentration, disease stage, body weight and the development of seroma.

Operative factors

Of the four types of operation performed [Table 3], the at-risk group for seroma were patients who had undergone axillary dissection and immediate reconstruction with the TRAM flap obviated this tendency reconstruction (X^2= 12.29, P= 0.007). Neither axillary status nor the type of axillary disturbance (no axillary dissection, axillary sampling or axillary clearance) were demonstrable as significant variables. Other operative factors such as intraoperative blood loss, transfusion requirements and operation time did not correlate with seroma formation. The relative experience of surgeons in terms of their grades was also not a significant variable.

Drainage output

Drains were kept for significantly longer in the seroma forming group, 6.6 days (range: 3-12 days), than in the control group, 4.5 days (range: 1-8 days) (t test, P= 0.008). When a drain was required for more than eight days, a significantly higher chance of seroma formation was found (Fisher's exact test, P= 0.005). Drain output of more than 500 ml total for the first three days was associated with seroma formation (Fisher's exact test, P= 0.049). Although the total drain output showed a strong linear relationship with the duration of drainage (Linear regression: B_0= -150.73, sigT= 0.000; B_1= 98.53, sigT= 0.000. R^2=0.69), neither the total drain output nor the late drain output, i.e., the drain output for the last three days revealed any correlation with seroma formation. Two kinds of drain output trends were identified: continuously decreasing and undulating. No statistically significant difference was observed between these two types of drainage output and seroma formation.

Table 4 lists the identified significant factors affecting seroma formation and their relative risk estimates.

Discussion

Although seroma formation may be considered as a trivial complication after mastectomy, it is the commonest complication and may be a nuisance. The incidence of seroma formation varies quite remarkably from 8-85% [Table 5], a median rate of 20% often being quoted. Seroma may lead to delayed wound healing and infection.[6] Besides the economic loss due to prolonged hospital stay and delay in rehabilitation,

Table 3: Seroma formation and type of operative procedure

	Total mastectomy	Total mastectomy + axillary sampling	Total mastectomy + axillary clearance	Patey + immediate breast reconstruction (TRAM)
Seroma group	1	4	5	0
Non-seroma group	21	18	55	14

Table 4: Risk estimates for the identified factors

Factor	Seroma formation (total no of patients in brackets)	Odds ratio
Age > 45; Age </= 45	10 (76); 0 (34)	10.89
Hypertension; No hypertension	5 (15); 5 (99)	9.4
Immediate breast reconstruction; No immediate breast reconstruction	0 (14); 9 (103)	3.73
Drain required more than 8 days; Drain required less than 8 days	2 (2); 5 (89)	76.82
Early output > 500 ml; Early output </= 500 ml	2 (5); 6 (95)	9.89

Table 5: Incidence of seroma formation after total mastectomy

	Sample size	Incidence (%)
Knight *et al.*[2]	38	72
Oertli *et al.*[3]	160	37
O'Brien *et al.*[14]	289	19
Coveney *et al.*[10]	40	85
Wedgwood and Benson[15]	148	15
Funnell *et al.*[7]	164	16
O'Dwyer *et al.*[11]	37	8
Hoefer *et al.*[8]	101	11
Cohen *et al.*[16]	99	21

seroma formation also adds to psychological trauma. This is, in addition, often to the embarrassment of the operating surgeon, whose experience in surgery does not influence the incidence of seroma after mastectomy.[7] Reasons that may account for the occurrence of seroma include a large operative field, division of lymphatic channels, the loose axillary skin hollow that follows surgical resection and the highly mobile, dependent nature of the area.[8] Seroma is often encountered for no obvious reason and without prodromal warning.

Several prophylactic measures have been proven to be effective in decreasing the incidence of seroma formation. Tranexamic acid was employed by Oertli *et al*,[3] peri- and postoperatively in a dose of 1g three times daily in a randomized double-blind trial. A significant reduction in the mean postoperative drainage volume as well as the incidence of seroma formation was observed in the treatment group.

The efficacy of shoulder immobilization has been investigated by Knight *et al*.[2] Although seroma resulted in delay in return to normal shoulder mobility, no patient sustained long-term musculoskeletal dysfunction.

Retention of the drain in-situ for a longer period seems to be a logical measure as formed seroma usually subsides with aspiration.[9] Estes and Glover[4] described the use of a vacutainer suction device as a convenient method of resolving seroma. This is no different in principle to re-establishment of the operative drain, a suction drain left in-situ for a prolonged period maintains physical contact between contiguous surfaces so as to facilitate adhesion. Conveney *et al.*[10] and O'Dwyer *et al.*,[11] demonstrated that both drainage and seroma formation were significantly less when dead space was obliterated by suturing the skin flaps to muscle. A similar flap tacking procedure was advocated by Chilson *et al.*,[1] as of proven value in seroma prevention. Lindsey *et al.*,[12] applied topical fibrin glue in the operative site in a Sprague-Dawley rat model and similarly decreased the incidence of seroma following mastectomy.

We have identified both age and hypertension to be risk factors for seroma formation. Patients older than 45 with hypertension are at a greater risk of developing seroma than their younger counterparts without hypertension. From the age correlation noted it has been speculated that the menstrual status might be relevant in seroma formation. No significant conclusion could, however, be drawn from our data. Alternatively, a decrease in elastic properties of the overlying skin flaps and less rapidity in re-draping to fill up the resultant space from surgical extirpation may be another possible factor. Similar findings have also been reported by Kumar *et al.*,[13] who postulated that a higher tendency to continuous exudation at the operative site is responsible for the association between hypertension and seroma formation.

Operative blood loss, transfusion requirements and operation time are parameters which may reflect technical difficulties. Their relationship to seroma formation is of interest but no statistically significant relationship was found. Similarly, the experience of surgeons was not a significant factor. The same observation has also been reported by Funnell *et al.*,[7] who found that seroma formation was not totally avoidable with good technique.

It is logical to suspect that the larger the magnitude of the surgery, particularly when axillary lymphatics are disturbed, the greater the likelihood of seroma formation. This hypothesis is, however, not supported by the present set of data. The tendency towards seroma formation, though, was obviated by the addition of foreign well-vascularised tissue. The TRAM flap presumably provided an additional site for fluid resorption and represents an additional benefit for immediate breast reconstruction with living tissues. Another inference is that seroma formation is a manifestation of an imbalance between fluid resorption and excessive production. In the presence of a good fluid resorption mechanism, excessive fluid production is overshadowed and no clinical seroma formation occurs. A similar reduction in postoperative seroma was observed by O'Brien *et al.*,[14] employing immediate breast reconstruction with prostheses. A possible explanation here might be a reduction in the tendency to excessive exudation as a result of tension in the breast pocket.

A drain retained in-situ for longer than eight days

due to a persistently high output is probably a direct reflection of an underlying tendency to excessive fluid production. Early drainage output in excess of 500 ml should alert the clinician as early as the fourth post-operative day.

In conclusion, there are identifiable peri-operative risk factors which may help to avoid prolonged hospital stay and morbidity. The presence of the factors identified should alert the clinician to possible seroma formation following mastectomy. Preventive measures may be warranted so as to reduce the risk of developing this not uncommon complication.

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