Potential risk factors for the development of seroma following mastectomy with axillary dissection

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Abstract. Seroma is a common complication following breast cancer surgery and the controllable predictive factors remain unknown. Patients who underwent mastectomy with axillary dissection between 2008 and 2011 in our hospital were retrospectively investigated. The demographics, clinical characteristics and therapeutic factors of each patient were recorded. The association of seroma incidence with each variable was evaluated by univariate logistic regression analysis. All the variables were considered independent predictors of seroma incidence. The probability of developing seroma following surgery was evaluated by multivariate logistic regression analysis. A total of 102 patients, with a mean age of 54.86±13.02 years (range, 30-89 years), were included in this study and the incidence of seroma was found to be 22.55%. The operative time (P=0.0066, coefficient = 0.0261, OR=1.03) and the use of patient-controlled intravenous analgesia (PCA) (P=0.0002, coefficient = -1.8089, OR=0.03, ref = no) was significantly associated with the incidence of seroma postoperatively. In conclusion, the prediction of the development of seroma following mastectomy with axillary dissection is challenging. However, a longer operative time and the non-use of PCA may represent potential risk factors for this complication.

Introduction

Seroma formation has been troubling patients and surgeons for over a century, since the first mastectomy was performed by Halsted in 1882. Seroma is defined as a subcutaneous collection of serous fluid post-mastectomy under the skin flap, in the dead space of the axilla or the breast following breast-conserving surgery. Seroma is a common complication following breast cancer surgery and several surgeons consider it an 'unavoidable nuisance' (1,2). Seroma may prolong patient recovery and hospital stay, increase health care costs and possibly delay the administration of systemic treatment where required (3). The controllable predictive factors for seroma formation remain unknown. In this study, we aimed to identify the factors that may predict the formation of seroma in patients who underwent mastectomy with axillary dissection (AD) in our hospital.

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Patients and methods

Patients. A total of 102 patients (101 women and 1 man), with a mean age of 54.86±13.02 years (range, 30-89 years) diagnosed with invasive ductal carcinoma by core needle biopsy or incisional biopsy, who underwent mastectomy with AD due to local recurrence following lumpectomy between 2008 and 2011 in our hospital were considered as eligible for inclusion in this study. Patients who received neoadjuvant chemotherapy or breast reconstruction immediately following mastectomy were excluded.

This study was approved by the Institutional Review Board of Shanghai Eighth People's Hospital, Shanghai, China. As the data analyzed in this study were obtained anonymously, written consent from eligible patients was not required; however, written informed consent was obtained from each patient prior to surgery for their information to be stored in our hospital databases and used for research.

Procedures. We performed mastectomy with AD according to the guidelines of the National Comprehensive Cancer Network and the decisions of the patients (some of the patients who fulfilled the criteria for breast-conserving surgery and/or sentinel limph node biopsy decided to undergo mastectomy with AD. At the end of the surgical procedure, two closed suction catheters were placed in the wound (one in the axilla and one in the chest wall). Pressure garments were used in all the patients following surgery. The drainages were removed when the drainage volume decreased to <30 ml per day for 3 consecutive days. All the patients were reviewed within 1 week following discharge from the hospital, unless seroma formation was detected prior to discharge. The patients who developed seroma following surgery were diagnosed by physical examination and treated by aspiration under sterile conditions. The demographic data (age, menopausal status, body weight and body height), clinical characteristics (preoperative serum albumin level, hemoglobin concentration, tumor diameter, axillary lymph node status, history of hypertension

Table I. Univariate logistic regression analysis of characteristics potentially associated with postoperative seroma formation.

Characteristics	Mean ± SD	Patient no. (%) (n=102)	Cases with seroma, no. (%) (n=23)	OR (95% CI)	P-value
Demographics					
Age (years)	54.86±13.02	-	-	1.00 (0.96-1.04)	0.9731
Menstrual status (n=101)[b]					
Postmenopausal	-	57 (56.44)	12 (21.05)	1.25 (0.49-3.18)	0.6394
Premenopausal	-	44 (43.56)	11 (25.00)	-	-
Body weight (kg)	58.45±8.11	-	-	1.00 (0.95-1.06)	0.8919
Body height (cm)	159.33±4.39	-	-	0.92 (0.82-1.02)	0.1242
Clinical characteristics					
Serum albumin (g/l)	70.37±5.44	-	-	0.95 (0.87-1.04)	0.2855
Hemoglobin (g/l)	128.17±11.90	-	-	0.97 (0.93-1.01)	0.1606
Tumor diameter (cm)					
<2	-	47 (46.08)	10 (21.28)	2.70 (0.31-23.68)	0.6116
2-5	-	44 (43.14)	12 (27.27)	3.75	0.2040
>5	-	11 (10.78)	1 (9.09)	-	-
Axillary lymph node status					
Positive	-	34 (33.33)	5 (14.71)	2.09 (0.70-6.22)	0.1861
Negative	-	68 (66.67)	18 (26.47	-	-
Hypertension					
Yes	-	15 (14.71)	6 (40.00)	0.36 (0.114-1.163)	0.0882
No	-	87 (85.29)	17 (19.54)	-	-
Diabetes mellitus					
Yes	-	4 (3.92)	1 (25.00)	0.87 (0.09-8.77)	0.9048
No		98 (96.08)	22 (22.45)	-	-
Therapeutic factors					
Operative time (min)	128.01±43.40	-	-	1.01 (1.00-1.03)	0.0137[a]
Initial 48-h drain output (ml)	273.85±128.30	-	-	1.00 (1.00-1.01)	0.1150
Duration of drain *in situ* (days)	12.12±6.36	-	-	1.04 (0.97-1.12)	0.2217
Intravenous analgesia					
Yes	-	57 (55.88)	3 (5.26)	14.40 (3.91-52.98)	<.0001[a]
No	-	45 (44.12)	20 (44.44)	-	-

[a]Statistically significant. [b]One of the patients was male. OR, odds ratio; CI, confidence interval.

and diabetes) and therapeutic factors [operative time, volume of initial 48-h drain output, duration of drain *in situ* and use of patient-controlled intravenous analgesia (PCA)] of each patient were recorded and retrospectively collected.

Statistical analysis. The association of seroma incidence and each variable of the demographic, clinical characteristics and postoperative factors (operative time, volume of initial 48-h drain output, duration of drainage and use of PCA) were evaluated by univariate logistic regression analysis. All the variables were considered as independent predictors of seroma incidence. The probability of developing seroma following surgery was assessed by multivariate logistic regression analysis. All the statistical tests were performed using SAS software, version 9.1 (SAS Institute Inc., Cary, NC, USA) and the two-sided significance level was set at P<0.05.

Results

Patients. A total of 102 patients with a mean age of 54.86±13.02 years (range, 30-89 years) were included in this study. Of the 102 patients, 101 were female and 1 was male. The mean body weight of the patients was 58.45±8.11 kg (range, 43-82 kg) and their mean body height was 159.33±4.39 cm (range, 148-171 cm). A total of 23 patients (22.55%) developed seroma postoperatively and they were all treated with aspiration.

Seroma incidence and patient characteristics. The mean preoperative serum albumin level was 70.37±5.44 g/l (range, 60-86 g/l) and the mean preoperative hemoglobin concentration was 128.17±11.90 g/l (range, 98-160 g/l). Twelve of the 57 postmenopausal and 11 of the 44 premenopausal

Table II. Multivariate logistic regression analysis of characteristics potentially associated with postoperative seroma formation.

Characteristics	Coefficient	Standard error	OR (95% CI)	P-value
Demographics				
Age	0.00	0.05	1.00 (0.90-1.10)	0.9277
Menstrual status				
Postmenopausal	-0.07	0.63	0.87 (0.08-10.15)	0.9116
Premenopausal	-	-	-	-
Body weight	0.03	0.06	1.03 (0.92-1.15)	0.6150
Body height	-0.20	0.09	0.82 (0.68-0.98)	0.0272[a]
Clinical characteristics				
Serum albumin	-0.08	0.08	0.92 (0.79-1.07)	0.2951
Hemoglobin	0.00	0.04	1.00 (0.92-1.07)	0.9054
Tumor diameter				
<2 cm	-0.10	0.80	1.91 (0.08-46.56)	0.3700
2-5 cm	0.84	0.59	4.86 (0.35-67.87)	-
>5 cm	-	-	-	-
Axillary lymph node status				
Positive	0.11	0.51	0.80 (0.11-5.86)	0.8260
Negative	-	-	-	-
Hypertension				
Yes	0.34	0.61	1.99 (0.18-22.12)	0.5747
No	-	-	-	-
Diabetes mellitus				
Yes	0.63	0.96	3.53 (0.08-149.35)	0.5095
No	-	-	-	-
Therapeutic factors				
Operative time	0.03	0.01	1.03 (1.01-1.05)	0.0066[a]
Initial 48 h-drain output	0.00	0.00	1.01 (1.00-1.01)	0.1630
Duration of drain *in situ*	0.06	0.07	1.06 (0.93-1.20)	0.3948
Intravenous analgesia				
Yes	-1.81	0.49	0.03 (0.00-0.18)	0.0002[a]
No	-	-	-	-

[a]Statistically significant. OR, odds ratio; CI, confidence interval.

female patients developed seroma. Seromas were detected in 6 of the 15 patients with hypertension and in 17 of the 87 patients without hypertension. Of the 4 patients with diabetes mellitus, 1 developed seroma. Seromas were diagnosed in 10 of 47, 12 of 44 and 1 of 11 patients with a tumor diameter of <2 cm, 2-5 cm and >5 cm, respectively. Of the 34 patients with positive axillary lymph nodes, 5 developed seroma.

The mean operative time was 128.01±43.40 min (range, 45-240 min) and the mean drain output volume during the initial 48 h postoperatively was 273.85±128.30 ml (range, 49-705 ml). The mean duration of drainage was 12.12±6.36 days (range, 3-40 days). Of the 57 patients receiving PCA and the 45 patients without PCA, 3 and 20 developed seroma, respectively.

The multivariate logistic regression analysis indicated that operative time was significantly associated with the incidence of seroma postoperatively (P=0.0066, coefficient = 0.03, OR=1.03), with an increase in operative time by 10 min being associated with a 30% higher risk of seroma formation. The use of PCA was a significant protective factor against seroma formation (P=0.0002, coefficient = -1.81, OR=0.03, ref = no). The odds of seroma formation among intravenous analgesia users were 97% lower compared to among non-users and PCA significantly lowered the incidence of seroma.

The factors affecting seroma formation according to the univariate and multivariate logistic regression analyses are presented in Tables I and II, respectively.

Discussion

Seroma is one of the most common complications following breast cancer surgery. The precise etiology of seroma formation remains unknown and it may delay the initiation of

adjuvant chemotherapy and radiotherapy, predispose to wound infection, delay wound healing and may also be associated with arm lymphoedema (2,4-7), which may be the cause of unnecessary tribulation and worse patient outcome. Although seroma is considered to consist of lymphatic fluid due to lymphatic vessel damage, its pathophysiology remains poorly understood and controversial (3,5,7). The reported incidence of seroma varies widely between 8 and 81% (8-13). In our study, we observed a seroma incidence of 22.55% following modified radical mastectomy.

Several studies were focused on patient characteristics associated with the development of seroma following breast surgery. Burak *et al* (14) reported a positive association between body weight and seroma formation, whereas Kumar *et al* (15) demonstrated that hypertension was associated with an increase in the incidence of seroma. By contrast, other studies consistently reported no association between the presence of anemia (16) or diabetes mellitus (16) and seroma formation, whereas existing evidence were inconclusive regarding age (13-15,17). In our study, no patient characteristic was found to be associated with postoperative seroma formation.

As regards tumor characteristics, the data on the association between axillary lymph node status, tumor size and seroma formation were inconclusive (13,15,17-22). No such association was identified by the present study.

In addition, the available evidence have been inconclusive regarding the association of the surgeon's skill or experience with seroma formation (23-25). Previous studies demonstrated that a longer operative time increases the risk of seroma formation (16,24), which was consistent with our observations.

Burak *et al* (14) and Kopelman *et al* (26) reported a positive association between drain output volume during the initial 72 h and seroma formation. However, in our study, there was no significant association between drain output volume or duration of drain *in situ* and seroma formation.

Various approaches have been used to prevent seroma formation, including closing the dead space under the mastectomy skin flap by suturing (27), delaying shoulder exercises during the recovery phase (4), using external compression dressings (28), ultrasound cutting devices (29), or suction drainage systems (30), applying bovine thrombin during surgery (15), tetracycline sclerotherapy (31,32), talc poudrage (33) and using fibrin sealant (34). In our institution, certain patients requested PCA for the first 24 h following surgery, even if not suggested by the anaesthesiologist. In our study, we observed that the use of PCA may significantly reduce the incidence of seroma formation following mastectomy with AD. However, this finding requires confirmation by further cohort studies and the underlying mechanism has not yet been elucidated.

In conclusion, the prediction of seroma formation following mastectomy with AD remains challenging. We identified no potential risk factors other than the longer operative time and the non-use of PCA, which are both controllable factors. In addition, the latter may represent a novel approach to the prevention of seroma following breast cancer surgery.

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