

Successful use of minimal invasive debridement plus negative pressure wound therapy under skin flap and axillary region for refractory postmastectomy seroma

A STROBE-compliant retrospective study

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Abstract

Seroma is the most common wound complication due to dead space remaining after mastectomy and axillary dissection. Seroma formation, which causes pain and tension, together with the limitations of shoulder and arm movements, can cause wound healing problems that can progress to wound dehiscence and flap necrosis. The aim of our study was to investigate the effects of continuous drainage and negative pressure wound therapy (NPWT) in breast cancer patients with refractory postmastectomy seroma. This retrospectively designed study was conducted with 27 patients who were referred to our center between 2018 and 2021 due to refractory seroma after mastectomy. The inclusion criteria of the study were the cases who were planned minimally invasive debridement and NPWT due to having refractory seroma formation with at least 200 cc and having interventions more than 1 month after modified radical mastectomy (MRM), despite conventional treatment methods. All patients' demographics, disease stage, history of possible neoadjuvant therapy, comorbidities, body mass index (BMI), number of wound dressings with NPWT, and total amount of NPWT accumulation were enrolled and compared statistically. Twenty-seven patients included in the study underwent continuous drainage after debridement, and 5 (3–9) dressings were treated with NPWT. None of the patients experienced complications after debridement and NPWT administration. In refractory seroma cases seen after postmastectomy, NPWT especially for the management of debridement and dead space can be evaluated as an appropriate treatment method in patients with high flow rate seroma.

Abbreviations: BMI = body mass index, MRM = modified radical mastectomy, NPWT = negative pressure wound therapy, V.A.C. = vacuum-assisted closure.

Keywords: mastectomy, negative pressure wound therapy, seroma

1. Introduction

Currently, modified radical mastectomy (MRM) is still a crucial choice for the surgical treatment of breast cancer, though breast-conserving and oncoplastic techniques have been increasingly used.^[1] The most common complications in the wound healing process in patients who underwent MRM with especially axillary dissection due to sentinel lymph node positivity or clinical lymph node positivity are seroma, surgical site infections, flap necrosis, and hematoma.^[2] These complications may lead to have more serious ones such as wound dehiscence

and delay adjuvant treatments by prolonging wound healing process.

Seroma is the most common wound complication due to remaining dead space after mastectomy and axillary dissection, and it has been reported to be seen in different ranges up to 10% to 85% according to the literature.^[2,3] Some factors such as obesity, patient age, hypertension, breast volume, presence of metastatic lymph nodes in the axillary region, number of dissected lymph nodes, early shoulder mobilization, and heparin use may also be effective in pathophysiological formation of seroma.^[4-6] Cautery and similar devices used during surgery

The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

Ethics committee approval was not obtained as the study was designed retrospectively.

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increase the pro-inflammatory cytokine response and lead to increased inflammation and tissue damage, affecting the formation of seroma.¹⁷ Prevention methods are primarily evaluated in the development of seroma after breast cancer. After mastectomy, prophylaxis is also recommended in order to prevent seroma formation, with the use of compressive dressings, suction drainage under the vacuum, narrowing the pouch of the dead cavity by suturing the skin flaps and withdrawing drains if the drainage below 30 to 50 mL/day.¹²⁻⁷¹

Seroma is formed in the dead space extending to the subcutaneous and axillary space depending on width of the dissection area. Seroma formation, which causes pain and tension together with the limitations of shoulder and arm movements, may be the cause of wound healing problems that can progress to wound dehiscence and flap necrosis. Infection of the seroma create the catastrophic clinical signs. It also leads to a delay in receiving adjuvant chemotherapy and radiotherapy, and also leads to an increase in the number of hospital admissions after the oncological surgery.

Our aim is to present the intervention options such as debridement at the fibrous capsule, continuous drainage and negative pressure wound therapy (NPWT) on the 27 patients with MRM whom conventional methods could not be treated, and when refractory postmastectomy seroma continued.

2. Methods

This retrospectively designed study was conducted with 27 patients who treated in our center from 2018 to 2021 due to refractory seroma after mastectomy. All patients' demographics, stage of the disease, history of possible neoadjuvant therapy, comorbidities, body mass index (BMI), number of wound dressing with NPWT, and total amount of accumulation of NPWT were recorded.

The compressive dressing, repetitive needle aspiration and putting a silicone drain into the dead space including surgical open drainage are applied as the first steps of the treatment of seroma in our clinic. The inclusion criteria of the study were the cases who were planned minimally invasive debridement and NPWT due to remain refractory seroma formation with at least 200 cc and have had interventions more than 1 month, despite conventional treatment methods. Patients with treatment refractory seroma, who were at risk of becoming infected after the drainage, and whose amount of accumulation did not decrease, were also included in the study. Pathologically, all patients who underwent NPWT had negative surgical margins. All patients treated with NPWT continued to receive adjuvant chemotherapy, but radiotherapy was not started until the tissue defects were healed.

Capsule formation was observed in patients physically or radiologically (Fig. 1). Debridement and NPWT sponges were applied to the cavities of the patients under local anesthesia and with the help of ultrasonography (Fig. 2). The capsule area was debrided from the 2 × 2 cm incision made from the drain area or the closest point to the fibrous capsule before the first sponge placement of the patients. The epithelialized area covering the surface of the fibrous capsule was debrided in order to provide healthy granulation tissue (Fig. 3). The debrided fibrous capsule was sent to pathological examination in whole patients. Routine pathological examination of the debrided fibrous capsules revealed no evidence of cancer. After debridement, sponges were applied to fill the whole axillary and skin flap pouch and debridement area and continuous aspiration was provided with negative pressure (Fig. 4). There was no need to place a protective layer between the axillary vein and the sponge in NPWT applications. In USG-guided applications, the sponge was placed at a distance where microdeformation caused by NPWT would not damage the axillary vein. Each time, the amount of sponge was reduced, allowing the pouch to shrink and contract.

The pressure was set to 90 mm Hg at the initial application and kept constant to 120 mm Hg at the subsequent sessions of the NPWT application after debridement. Vacuum-assisted closure (V.A.C.) therapy (KCI, Inc., San Antonio, Texas) was used for NPWT for dressing. Dressing changes were applied every 3 to 5 days. The amount of sponge used in each dressing has been reduced. The dressing was applied to the patients 5 (3–10) times during the NPWT treatment. When the amount of aspirated via NPWT decreased after the rapid reduction of the axillary and skin flap pouch in the patients granulating, the

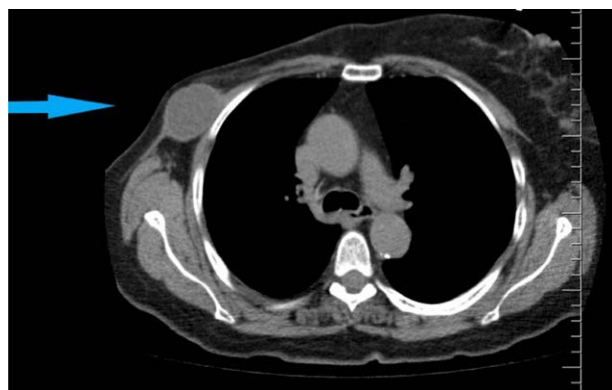


Figure 1. Capsule formation visualized in computerized tomography.



Figure 2. Minimal invasive debridement with the help of ultrasonography.

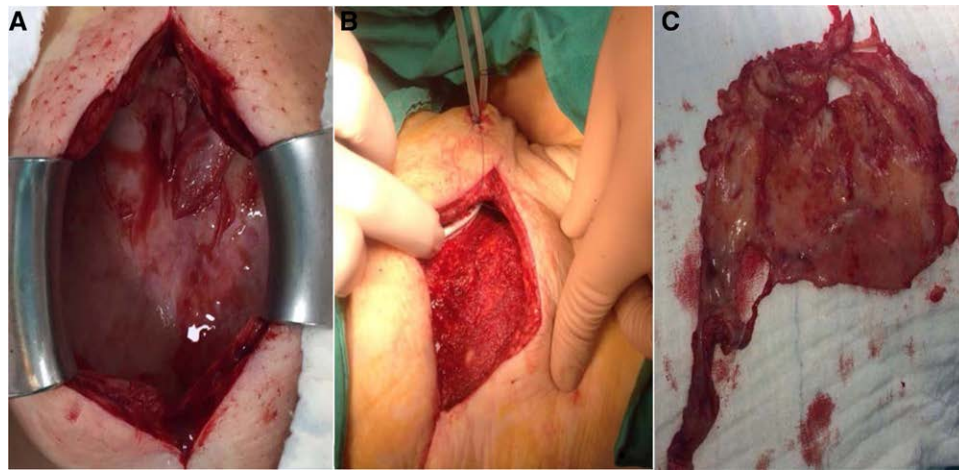


Figure 3. (a) During surgical capsulectomy. (b) Granulated debridement area after capsule excision. (c) Excised fibrous capsule.



Figure 4. Placing the sponges in the pouch.

conventional dressing methods were initiated and the incision area where the sponge was placed left for secondary healing. The incision areas were not sutured to avoid a closed pouch.

Ethics committee approval was not obtained as the study was designed retrospectively.

2.1 Statistical analysis

IBM SPSS Statistics for Windows version 21.0 (IBM Corporation, Armonk, NY) and MS-Excel 2007 (Microsoft Corporation, Redmond, WA) were used for statistical analysis and calculations.

3. Results

The mean age of 27 patients in the study was 58.2 (37–83). BMI of the patients was 26.2 (20–32). Ten patients (37.0%) had

diabetes mellitus, and 11 patients (40.7%) had hypertension as a comorbid disease, and 9 of them (33.3%) received neoadjuvant chemotherapy.

In the postoperative histopathological evaluation, 7 cases (25.9%) were at stage 2A and neither of these patients had lymph node metastasis. Eight (29.6%) patients were at stage 2B, 8 patients (29.6%) were at stage 3A, and 3 (11.1%) patients were at stage 3B and 1 patient was at stage 4. The patient who was at stage 4 had 2 primaries in the lung and breast, and breast and lung surgery were performed in the same session, and breast metastasis was detected in the primary tumor in the lung (tumor to tumor metastasis).^[8]

The mean number of axillary lymph node dissected was 18.1 ± 3.1 , and there were no metastatic lymph nodes in 2 patients in both clinic stage 2A and stage 2B, and in 3 patient in clinic stage 3B. Patients who underwent axillary dissection without metastatic lymph node were those who received a complete pathological response after neoadjuvant therapy. The patients included in the study underwent continuous drainage after debridement and 5 (3–10) dressings in 27 patients treated with NPWT. None of the patients had complications like bleeding or pain after debridement and NPWT administration. No signs of malignancy were detected in debridement materials sent for pathological examination. The median amount of accumulation of NPWT was 1070 cc (540–1280) in 27 patients. The accumulation of NPWT increased with the total number of dressings. All patients who had 5 dressing or lower (10 patients, 37%) had less than 600cc total drainage of NPWT. There were no statistically significant difference between the number of dressings and total amount drainage of NPWT with patients' age, stage of the disease, neoadjuvant therapy, comorbidities and BMI.

Patients were followed for an average of 1 year. There were no local recurrences or seroma recurrences observed during follow-up. Two patients developed lung metastases during follow-up.

4. Discussion

The possible reasons for the fact that the frequency of seroma after postmastectomy have been stated at different rates in the literature may be caused by preferring different such as only physical examination and ultrasonography for the diagnosis, and not including the non-symptomatic cases. Observation is an adequate treatment if seroma is not symptomatic and does not cause complication in an important group of patients and confirmed by physical examination and radiology. Simple aspirations and replacement of the surgical drains are the common and first line treatment modalities in the treatment of seroma.

The subject of this article is the management of complicated cases whose persistent seroma in the axillary region and under the skin flap persists despite aspiration and re-drain placement after MRM. In our study, problems such as bleeding and pain did not develop in any of the patients who underwent NPWT. Therefore, it is concluded that NPWT can be used safely under the skin flap and in the axillary region.

Prolonged, high amounts of fluid, and capsule formation may occur under the flap in these patients with risk factors for the development of seroma. Seroma consists of a fibrous (pseudo) capsule and endothelium lining; single-layered endothelial cells on the surface of the fibrous capsule, as epithelization was considered as a sign of completion of wound healing in such dead places.^[9] Especially in cases where silicone implants or skin expander is used, fibrous capsule formation is frequently observed due to its effect on foreign body reaction.^[10] Pathological findings proved that angiogenesis in the fibrous tissue was inhibited, indicating that the healing process between the flap and wound base was interrupted in the patients with seroma.^[11] NPWT may help control seroma by increasing local blood perfusion and stimulating wound granulation in the skin flap, contributing to the healing process of the skin flap pouch.^[12,13]

On the other hand, sclerotherapy application to dead space in the treatment of chronic seroma is a feasible treatment after mastectomy.^[14] Sclerotherapy applications are based on the closure of the pouch with fibrosis created by filling the dead space with an irritant substance. A wide variety of sclerosant agents including talc, tetracycline antibiotics, ethanol, polidocanol, erythromycin, OK-432, fibrin glue, and povidone-iodine have been used.^[15] Infection risk with a long-term catheter is high, but it may be decreased with prophylactic antibiotics or other strategies to minimize infection risk.^[14] One of the most important handicap is to wait for the decrease of seroma amount after re-draining in sclerotherapy application. Due to the fact that the dead space cannot contract and the surface of the fibrous capsule cannot be debrided, this drained period can be prolonged and cause an increase in the risk of infection as well as impairing patient comfort. It is reported that relapses and re-interventions may be required after sclerotherapy.

To date, there are only limited publications in the literature on surgical treatment for refractory seroma cases after MRM. Debridement and surgical excision of the fibrous capsule in order to treat the seroma has been reported in some stubborn cases.^[16] In addition to surgical excision, it has been reported that closure of supplying regional lymph vessels may be a good treatment option.^[17] Besides the surgical treatment of the fibrous capsule, excision of the fibrous capsule and surgical debridement were also performed in our clinic for a period. An example was demonstrated in Figure 3. The refractory seroma patient has a pouch during surgical capsulectomy, there is an epithelial appearance on the capsule and it was demonstrated in Figure 3a. After resection of the fibrous capsule, a granulated area can be obtained by debridement, so closing the dead space, narrowing with suturing and drain placement can be performed after that (Fig. 3b and c). However, it should be kept in mind that there may be a need for anesthesia, re-placement of the drain in the surgical area and delay at the adjuvant treatments due to surgical problems that may occur. In addition, due to the intervention in the operating room under anesthesia, cancer patients may increase their anxiety levels and decrease their compliance with the adjuvant treatment. Van Bastelaar et al described a case report of removal of encapsulated axillary seroma pocket and closing the dead space with latissimus dorsi flap successfully.^[18] Surgical excision of the fibrous capsule is performed especially in seroma cases in the breast after implant or in fibrous pseudo-capsule cases after abdominoplasty surgery.^[19] Benign fibrous capsule can be resected and closed surgically under anesthesia, and seroma treatment performed by replacing the drain may be considered as overtreatment if alternative non-surgical methods

are available. Risks, complications, and prolonged recovery period of surgery will result in delay in commencing adjuvant therapies and higher surgical expenditures.

Ultrasound-guided scraping of fibrous capsule plus bilayer negative pressure wound therapy techniques is firstly described and used by Bi et al at the 24 patients with the refractory seroma.^[11] In their patient series they used a technique which they developed in their department which includes multiple vaseline gauze pads, 2 drainage tube and a negative pressure source. In our techniques we used a standart NPWT devices V.A.C. Therapy system (KCI USA, San Antonio, TX) which can handle carry on shoulder which not to hinder movement. It also provided outpatient follow-up to prevent some of the patients from causing bed occupation between dressings. The application of NPWT provided rapid closure with the narrowing, contraction and granulation of the axillary and skin flap pouch. UTH et al presents a 74-year-old man with a malignant melanoma suffering from seroma in the axilla after an axillary lymph node dissection and treated with vacuum-assisted closure to the seroma cavity and the researchers also note "it could be interesting to perform a prospective study concerning the use of V.A.C in seromas."^[20] Generating negative pressure is related with excess fluid removal, reduction of edema, increased dermal perfusion, stimulation of granulation tissue formation and reduced bacterial colonization.^[21,22] There was no need to use prophylactic antibiotics in our patients with closed dressing technique that had a negative pressure effect.

After the debridement applied through a small incision allowing sponge placement, it is possible to debride the remaining fibrous capsule and close the gap by granulation with the effect of negative pressure provided by the macro deformation and micro deformation. The effect of negative pressure devices on the wound surface under pressure with a sponge provides cellular proliferation with the effect of mechanotherapy and stimulates the increase of granulation.^[12,13,23] This compressive pressure created by negative pressure with the contraction of the wound edges with the effect of macro deformation helps the shrinkage of the wound and contraction of the pouch with a contractile force. It is beneficial that during the whole dressing like exudate control in chronic wounds, the seroma has disappeared and contraction is provided, thereby narrowing the pouch accompanied by a sponge. Reducing the amount of sponge needed in recurrent dressings enables the dead space to close rapidly. The phase of preparing the patient with seroma for NPWT application by placing a sponge in the axillary and skin flap pouch after debridement was demonstrated in Figure 4. The biological interaction between the foam and the wound surface is an aberrant foreign body-like reaction or results from unknown specific pathways.

NPWT is effective, which likely because of improvement in bacterial clearance from the wounds, increase of local blood perfusion, and stimulation of wound granulation.^[12,13] Understanding the role of the wound/foam interface is crucial, as in clinical practice different interfaces are often placed between the wound and the foam (such as gauze) and may radically change the effects on blood vessel formation. Micro deformation at a microscopic level, the application of suction results in wound bed tissue being drawn up into the pores of the filler, causing mechanical force/strain that modulates cellular behavior, such as proliferation, through a process referred to as mechanic transduction.^[13] The relation of the fibrous capsule in the axillary region with the axillary vein and other vascular structures can be a problem for NPWT. Surgical capsulectomy or sclerotherapy may likewise create axillary vein neighborhood problems, but the fibrous capsule does not contain these anatomical structures with its structure consisting of usually endothelium. NPWT can be applied to these regions via the use of special protective layers.

The refractory seroma is frequently encountered entity in clinical practice, and especially in centers where intensive breast surgery is applied. The technical microinvasive method that we apply to our patients under local anesthesia is a simple method

with debridement and NPWT, as well as the possibility of outpatient follow-up. The frequency of hospital admission of patients is decreasing and delay in adjuvant treatments can be prevented with the introduction of this method in question worldwide.

5. Conclusion

In refractory seroma cases seen after postmastectomy, NPWT especially for management of axillary and skin flap pouch debridement can be evaluated as an appropriate treatment method in patients with high flow rate seroma.

Author contributions

Ebru Esen, Kerim Bora Yilmaz and Mehmet Ali Gulcelik contributed to conceptualization and methodology. Ebru Esen, Ibrahim Burak Bahcecioglu, Melih Akinci contributed to the data curation and formal analysis. Ebru Esen, Kerim Bora Yilmaz and Melih Akinci contributed to the investigation, software and visualization. Kerim Bora Yilmaz and Mehmet Ali Gulcelik contributed to supervision. All authors contributed to the writing of the original draft and review and editing the paper.

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References

- [1] Tokgöz S, Karaca Umay E, Yilmaz KB, et al. Role of intraoperative nerve monitoring in postoperative muscle and nerve function of patients undergoing modified radical mastectomy. *J Invest Surg.* 2019;12:1–8.
- [2] Ozaslan C, Yilmaz KB, Dogan L, et al. Effect of mechanical closure of dead space on seroma formation in modified radical mastectomy. *Turk J Med Sci.* 2010;40:751–5.
- [3] Kuroi K, Shimoizuma K, Tagushi T, et al. Evidence-based risk factors for seroma formation in breast surgery. *Jpn J Clin Oncol.* 2006;36:197–206.
- [4] Unalp HR, Onal MA. Analysis of risk factors affecting the development of seromas following breast cancer surgeries: seromas following breast cancer surgeries. *Breast J.* 2007;13:588–92.
- [5] Kumar S, Lal B, Misra MC. Post-mastectomy seroma: a new look into the aetiology of an age old problem. *J R Coll Surg Edinb.* 1995;40:292–4.
- [6] Ozdogan M, Yilmaz KB, Ozaslan C, et al. Scalpel versus electrocautery dissections: the effect on wound complications and pro-inflammatory cytokine levels in wound fluid. *Turk J Med Sci.* 2008;38:111–6.
- [7] Yilmaz KB, Dogan L, Nalbant H, et al. Comparing scalpel, electrocautery and ultrasonic dissector effects: the impact on wound complications and pro-inflammatory cytokine levels in wound fluid from mastectomy patients. *J Breast Cancer.* 2011;14:58–63.
- [8] Turker S, Çilbir E, Yilmaz KB, et al. Tumor-to-tumor metastasis: breast cancer metastasis to lung cancer. *Breast J.* 2020;26:534–5.
- [9] Baltzer A, Brehmer F, Forkel S, et al. Percutaneous ultrasound-guided drainage of needle aspiration-refractory seromas following lymph node excision. *J Dtsch Dermatol Ges.* 2016;14:850–2.
- [10] Spear SL, Rottman SJ, Glicksman C, et al. Late seromas after breast implants: theory and practice. *Plast Reconstr Surg.* 2012;130:423–35.
- [11] Bi H, Fang S, Jiang D, et al. Ultrasound-guided scraping of fibrous capsule plus bilayered negative pressure wound therapy for treatment of refractory postmastectomy seroma. *J Plast Reconstr Aesthet Surg.* 2015;68:403–9.
- [12] Yang SL, Han R, Liu Y, et al. Negative pressure wound therapy is associated with up-regulation of bFGF and ERK1/2 in human diabetic foot wounds. *Wound Repair Regen.* 2014; 22: 548–54.
- [13] Lalezari S, Lee CJ, Borovikova AA, et al. Deconstructing negative pressure wound therapy. *Int Wound J.* 2017;14:649–57.
- [14] Throckmorton AD, Askegard-Giesmann J, Hoskin TL, et al. Sclerotherapy for the treatment of postmastectomy seroma. *Am J Surg.* 2008;196:541–4.
- [15] Sood A, Kotamarti VS, Therattil PJ, et al. Sclerotherapy for the management of seromas: a systematic review. *Eplasty.* 2017;17:e25. eCollection 2017.
- [16] Matsui Y, Yanagida H, Yoshida H, et al. Seroma with fibrous capsule formation requiring a surgical resection after a modified radical mastectomy: report of a case. *Surg Today.* 1998;28:669–72.
- [17] Stanczyk M, Grala B, Zwierowicz T, et al. Surgical resection for persistent seroma, following modified radical mastectomy. *World J Surg Oncol.* 2007;5:104.
- [18] van Bastelaar J, van Roozendaal LM, Meesters-Caberg M. Surgical removal of fibrous axillary seroma pocket and closing of dead space using a latissimus dorsi flap. *J Surg Case Rep.* 2018;2018:rjy032.
- [19] Goldman A, Wollina U, França K, et al. Chronic encapsulated seroma persisting for three years after abdominoplasty and a successful surgical solution. *Open Access Maced J Med Sci.* 2018;6:82–4.
- [20] Caspara Uth C, Bentzen VE, Hölmich LR. Vacuum-assisted closure in the treatment of seroma after axillary lymph node dissection. *Eur J Plast Surg.* 2016;39:217–20.
- [21] Matusiak D, Wichtowski M, Pieszko K, et al. Is negative-pressure wound therapy beneficial in modern-day breast surgery? *Contemp Oncol (Pozn).* 2019;20:69–73.
- [22] Orgill DP, Bayer LR. Update on negative-pressure wound therapy. *Plast Reconstr Surg.* 2011;127(Suppl 1):105–15.
- [23] Scherer SS, Pietramaggiore G, Mathews JC, et al. The mechanism of action of the vacuum-assisted closure device. *Plast Reconstr Surg.* 2008;122:786–97.