Abstract. Background/Aim: Vulva cancer surgery is associated with a high level of morbidity mostly due to wound healing disorders in the inguinal region following lymphadenectomy. Our aim is to evaluate the feasibility of negative pressure wound therapy (NPWT) using the PICO™ device in groin wounds after lymphadenectomy. Patients and Methods: The groins of twenty patients who underwent bilateral lymph node dissection were dressed with the PICO™ device. All patients were followed prospectively with clinical controls up to three months postoperatively using a standardized study protocol. Results: A total of 11 patients (55%) developed a surgical site complication (SSC). One patient suffered from a wound rupture two days after surgery, six a lymphocele and four a surgical site infection. Operation time, blood loss, number of lymph nodes removed, length of hospital-stay and duration of PICO™ treatment did not differ between women with and without SSCs. Conclusion: NPWT using the PICO™ device seems to be a feasible method to reduce the severity of healing disorders in the groin after lymphadenectomy in vulva cancer patients.

Vulva cancer accounts for 1% of all malignancies in women, and for about 5% of all the gynecological cancers. It usually occurs in postmenopausal women but its incidence is raising in younger women (1, 2). The majority of vulva cancer patients have lesions limited to the vulva that are according to the International Federation of Gynaecology and Obstetrics (FIGO) classification, defined as stage I or II disease in case of negative lymph nodes in the groin or as stage III disease if lymph node metastasis is present (3). Most women suffering from early stage squamous vulva cancer can be treated with surgery consisting of either vulvectomy or wide local excision, combined with a uni- or bilateral radical lymphadenectomy or sentinel node extirpation in the groin. Even though the sentinel node concept shows excellent results in terms of overall survival, low complication and recurrence rates, it is only indicated for patients with small uni-focal cancer lesions and clinical negative lymph nodes (4, 5). Approximately 50% of all vulva cancer patients need a radical inguino-femoral lymphadenectomy due to large tumor size, multifocal disease or the presence of confirmed lymph node metastasis and/or suspicious bulky nodes in the groin (3, 6, 7).

According to retrospective studies (8, 9) a radical staging procedure in the groin is associated with a high level of morbidity due to postoperative wound healing complications. About 30% of patients suffer from chronic lymphatic drainage problems, and the risk of developing a surgical site infection (SSIs) or a wound rupture is estimated to about 30-40% (10-13). Furthermore, healing disorders in the groin might jeopardize the initiation of adjuvant radiation or combined chemoradiation therapy in patients with metastasis or insufficient resection margins.

In order to find new strategies for the prevention and treatment of wound healing complications, we investigated prophylactic NPWT in early stage vulva cancer patients. For this purpose we used a single-use, canister-free NPWT device, which operates at a preset level of -80mm Hg and works predominantly by evaporative loss (14). While the majority of the lymphatic wound fluid is still removed by active suction drains, the NPWT dressing is meant to act as a complementary agent, facilitating the wound healing process by i) accelerating internal lymph drainage, ii) evaporating additional wound exudate, and iii) reducing the lateral tension on the closed wound edges (14-16).

As there are no published data regarding the clinical efficacy of NPWT on surgically closed incisions following lymphadenectomy in the groin, we decided to prospectively
evaluate the feasibility of prophylactic NPWT in 20 vulvar cancer patients, prior to the initiation of a prospective randomized controlled trial.

Patients and Methods

In the presented case series, all included patients were followed prospectively after undergoing surgery for vulva cancer over a period of at least three months.

All patients with early stage vulva cancer who were scheduled for vulvectomy and bilateral lymph node dissection in the groin at the gynecological department at the university hospital in Lund between January 2017 and January 2018 were asked to participate in the present pilot study. Each participant was assigned a standardized study protocol following written informed consent. Exclusion criteria were i) an incapability of the patient to understand the study and ii) any condition related to linguistic or cognitive issues.

Study procedures were reviewed and approved by the Regional Ethics Board in Lund (Reference number DNR 2017/10).

Surgical technique. In patients scheduled for complete lymph node dissection access to the groin was gained via an eight- to ten-centimeter long skin incision, which was placed one-to-two centimeters below the inguinal ligament. The dissection of the node-containing fat pad was performed using bipolar scissors (Erbe, Tübingen, Germany) as electrosurgical device. The tissue was reflected medially of the femoral vessels and the saphenous vein. The specimen containing the superficial and deep inguinal nodes was removed in one piece. The saphenous vein could be preserved in all affected groins and detectable lymph vessels were sealed using electrosurgical cautery. After placement of the active suction drains (see below) the wound was closed via adaption of the subcutaneous tissue using 3-0 absorbable suture (Vicryl, Ethicon, Solna, Sweden) and the skin (staples).

In women planned for sentinel node extirpation, 99mTc radiocolloid (Ultradechnekow FM, St. Louis, MO, USA) was injected intradermally around the vulva lesion one day before operation. Intraoperatively, sentinel node detection was performed with a hand-held gamma detection device. Once the sentinel nodes were identified, they were extirpated via a minor skin incision. No external drains were placed in women undergoing the sentinel procedure. Wound closure was performed in the same manner as described for patients undergoing complete lymphadenectomy.

All women received prophylactic administration of oral antibiotics consisting of a combination of metronidazol and sulfamethoxazole/trimethoprim or doxycycline in the morning at the day of the operation.

For the prevention of thromboembolic events patients were treated with a low weight molecular heparin (Innohep 4500 I.E., LEO Pharma, Ballerup, Danmark) for at least seven days after the operation.

Wound care. The first PICO™ dressings were applied on the groin wounds in the operation room under sterile conditions. All groin incisions were closed with staples and suction drains were placed in the wound beds, according to our study protocol. NPWT was applied with a single-use, canister-free instrument, the PICO™ device (Smith & Nephew AB, Möln达尔, Sweden). This device operates at a preset level of -80 mmHg and is equipped with a small portable battery-operated vacuum unit. The PICO™ device consists of a four-layer absorbent dressing, which has a total fluid management capacity of up to 200 ml (20 × 15 cm dressing pad) and works predominantly by evaporative loss (14).

In order to facilitate a tension-free application of the PICO™ device, we chose to locate the exit hole of the suction drain approximately 10 cm away from the lateral edge of the groin incision. When deciding on the size of the PICO™ dressing, we tried to cover the incision and the adjacent area in order to reduce the amount of interstitial fluid in the uncompromised surrounding tissue (17, 18) (Figure 1). We used a volume-controlled active drain management and indication for removal was given when drain production was less than 50 ml within 24 h. Independently of the output, suction drains were left in place for at least three days. In case of clinical infection signs, a wound culture was obtained in order to verify the presence of a pathogen microbial agent. An additional ultrasound examination of the groin area was performed if clinical signs of deep infection and/or impaired lymphatic drainage were present.

Follow-up. All included patients were followed-up for three months postoperatively. All patients received their first postoperative control before discharge. The first four follow-up examinations after discharge were scheduled at seven-day intervals in order to perform the clinical assessment and the change of the PICO™ dressing simultaneously.

PICO treatment was discontinued after the removal of all suction drains in the presence of satisfying healing conditions in the groin area. All patients received at least one postoperative change of the PICO dressing. If there were clinical signs of an upcoming severe healing disorder, such as wound rupture, the NPWT was interrupted earlier.

After removal of the PICO™ dressings, the follow-up intervals were extended to 10 to 14 days. Healing disorders in the groin that became apparent within the first four weeks after the operation were classified as short-term complications and those who developed after four weeks as long-term complications. Pre- and postoperative surveillance data were assessed with the help of a standardized follow-up protocol containing information on i) SSC, ii) SSI, iii) operation related data, iv) patient characteristics and v) laboratory chemical results.

Regarding the latter, the highest postoperative values of C-reactive protein (CRP) and white blood cell count (WBCC) were used for statistical analysis. Other patient related data, including i) histological findings, ii) cancer stage, iii) wound culture results and iv) type of antibiotic treatment were obtained from patients’ files and added to the study protocol.

Independent of the need for adjuvant radiation or combined chemo-radiation therapy, all patients were scheduled for a further clinical control three months postoperatively. If necessary, those follow-up data were completed via phone interview or with the help of patient oncological charts.

Definitions. A wound healing complication was classified as a SSI if typical clinical infection signs and a positive wound culture were present. In order to improve the objectivity and standardization of the clinical observation, we also used both the Center for Disease Control and Prevention (CDC) classification and the ASEPIS scoring system as additional assessment tools.

According to the CDC classification system, SSIs were classified as either superficial incisional, deep incisional or organ related (19).
The ASEPSIS classification was implied as a further objective categorization method to measure the severity of the documented SSI (20). This scoring system differentiates between: i) wound healing disorders (0-20 points), ii) minor wound infections (20-31 points), iii) moderate wound infections (31-40 points), and iv) severe wound infections (>40 points). This numerical score represents the sum of several factors, including i) the administration of antibiotics, ii) the drainage of pus under local anesthesia, iii) the debridement of the wound under general anesthesia, iv) the presence of serous discharge, v) erythema, vi) purulent exudate and/or vii) the separation of deep tissue. In case of wound rupture, open vacuum-assisted wound closure (KCI Medical AB, Solna, Sweden) was used for treatment followed by operative wound revision.

The primary endpoint was the occurrence of SSC and especially of SSI during follow-up. Secondary endpoints included i) the measurement of re-admissions and re-operations due to SSCs, ii) the length of hospital stay and iii) the duration of PICO™ treatment.

Statistical analysis. All statistical comparisons were two-sided and \( p \)-Values less than 0.05 were considered statistically significant. Statistical analysis was performed using SPSS (PASW) version 22.0.0 (SPSS Inc., Chicago, IL, USA). The independent t-test was used to compare the means between two unrelated groups. In case the dependent variable was continuous but not normally distributed, the Mann-Whitney U-test was used to compare the differences in medians between the two groups. The observed frequencies of categorical variables were compared using the chi-squared test. In cases of a small sample size the Fisher Exact Test was used for statistical comparison.

Results

Surgical management. Thirteen women underwent a complete, radical lymphadenectomy. The mean number of retrieved lymph nodes did not differ between the right (6.0) and the left groin (6.1). Seven women had a sentinel procedure with a mean number of 4 nodes harvested from the right and three from the left side (\( p = 0.43 \)). Radical lymphadenectomy was performed in a total of 26 groins and the sentinel procedure in a total of 14 groins. None of the patients in the sentinel group were in need of further lymph node dissection as no metastatic cells were found on histopathological evaluation.

Except for one woman who was operated with the sentinel technique all patients received bilateral active suction drains, which were in place for at least three days. The mean time of drain treatment was 12 days on the right and 14 days on the left side (\( p = 0.44 \)). The mean time of hospital stay was nine days (SD +/- 4.0 days).

Wound outcomes. In 20 patients the PICO™ dressing was applied to the groin wounds on both sides. The mean time of treatment was 15.7 days (SD +/- 4.9 days). Patients who suffered from SSCs did not differ from patients without SSCs in terms of i) age (\( p = 0.061 \)), ii) BMI (\( p = 0.57 \), iii)
hypertension (p=0.50), iv) atrial fibrillation (p=0.50), v) diabetes (p=0.24) or vi) smoking (p=0.50).

A total of 11 patients (55%) developed an SSC during our follow-up period and a total of 13 groins were affected. Most healing disorders became apparent during the first two weeks after the operation (n=10; 50%). Readmission became necessary in three patients. While one woman was in need of operative revision due to a unilateral wound rupture, the other two patients were readmitted for clinical observation and prophylactic administration of oral antibiotics.

**Surgical site complications.** The occurrence of a lymphocoele formation was the most common complication during the early postoperative period diagnosed in a total of six patients (30%, see Table I). At the time of diagnosis, ultrasound examination revealed that the accumulation of lymphatic fluid was about 2 cm in diameter in all affected groins (n=7). After continued PICO™ treatment for another 7 to 10 days with the suction drains in place there were no longer signs of impaired lymphatic drainage neither on clinical examination nor on ultrasound control.

SSIs were observed in four women, including three cases of an isolated, unilateral infection and one case of local infection adjacent to a unilateral wound rupture. In all four patients the SSI was characterized as superficial (Table I) as only a mild redness of the skin could be observed. A bacterial colonization could be identified in all affected groins and patients received oral antibiotics adapted to the sensitivity profile of the corresponding pathogen microorganism (Table I). In all four women, the infection resolved after a mean antibiotic treatment time of 11.2 (SD+/– 5.4 days) days.

One patient developed a wound rupture two days after surgery. The other wound rupture occurred 14 days after completed PICO™ treatment and secondary to a spontaneous hemorrhage probably caused by therapy with a Factor Xa inhibitor.

**Comparison of patient characteristics and surgical outcome between patients with and without SSCs.** Patients with an SSC did not differ from patients without SSCs in terms of perioperative findings or operation related data (Table II). Length of stay was similar in both groups. Women who had a longer wound treatment with suction drains due to higher production of wound fluid were more likely to develop an SSC (Table II). Women who underwent a complete lymphadenectomy were more likely to develop an SSC (n=10; 50%) compared to those who were operated using the sentinel technique (n=1, 5%, p=0.012).

**Discussion**

In the presented series eleven out of 20 patients (55%) who received bilateral NWPT in the groin following lymphadenectomy or sentinel extirpation for early stage
vulva cancer, developed at least one type of SSC within the first three months after the operation.

Even though the complication frequency of 55% appears to be relatively high, it has to be noticed that nine out of those eleven women (82%) had an SSC of mild character. In all women with an isolated SSI (n=3), the complication was classified as superficial, according to the CDC classification, and could be treated conservatively with administration of oral antibiotics. Also, when applying the ASEPSIS score, isolated SSIs were either classified as minor or moderate. The same observed length of hospital-stay in patients with and without SSCs supports the view that the SSCs were indeed predominantly minor.

Furthermore, one case of postoperative wound rupture became apparent several weeks after the completed PICO™ treatment in connection with an anticoagulation induced hemorrhage. Even though this patient did not show the picture of a typical primary healing complication, the case was classified as SSC, as clinical signs of a concomitant SSI were present.

The overall frequency of major (n=2; 10%) or combined (n=1; 5%) SSCs was relatively low when compared to the literature. Three retrospective studies evaluating the incidence of healing disorders in the groin after vulva cancer surgery report overall complication frequencies varying between 40-75%, measured among patient cohorts of about 100-200 women. Severe healing complications, such as wound rupture, were reported in about 20-30% (9-12). Furthermore, we have reviewed our own experience, evaluating 121 women operated with lymphadenectomy between 2013 and 2015 for early stage vulva cancer. The overall wound complication rate was 45% and wound ruptures occurred in more than 40% of the investigated women (Maddalena Falagario, Department of Gynecology, Lund University Hospital).

During the actual follow-up period three patients were re-admitted, however, surgical intervention was needed in one woman only. It seems that a combined wound management consisting of suction drain and NPWT using the PICO™ device reduces the severity of wound complications in the groin area after lymph node dissection. Even though most of the lymphatic fluid is still removed via the suction drains, the PICO™ dressing seems to help remove the remaining wound exudate via internal absorption and/or evaporation through its semipermeable layer.

The fact that the PICO™ dressing helps minimize the accumulation of fluid in the wound area is of clinical importance, as the development of early postoperative lymphocele formation is associated with a higher risk for long-term complications in the groin area (6). Both in vitro and in vivo experiments have demonstrated that the PICO™ dressing is able to handle clinically relevant production of wound fluid at both high and low exudate conditions (14).

Based on our clinical observations, we would recommend to not discontinue the PICO™ treatment during the first two weeks after the operation, as it seems that most SSCs following lymphadenectomy develop during the early postoperative period. This also accounts for women operated using the sentinel procedure. Furthermore, there is no evidence in the literature that the risk of developing a SSC increases proportionally with the amount of dissected lymph nodes (6).

As the PICO™ dressing complements the action of the suction drain, we assume that the NPWT treatment should be continued as long as the suction drains remain in place. The clinical significance of suction drains in the management of groin wounds following lymph node dissection is a controversy in the literature. While some studies report a protective effect of volume-controlled drainage (21), other authors state that drainage time has no influence on the onset of short- or long-term complications (9, 10). In our case, series
In our series, the assessment of an SSI was based on clinical findings as well as the presence of a pathogenic microorganism on wound swab culture. A drawback of the objective CDC and ASEPSIS classification systems is the less critical evaluation of wound swab cultures in relation to clinical findings, and the risk of interpreting microbiological findings indicative of bacterial contamination as SSI. This misclassification can lead to a higher proportion of false positive SSIs resulting in unnecessary antibiotic treatment.

According to our data, it seems that NPWT administered using the PICO™ device can reduce the severity of SSCs in the groin after lymphadenectomy in vulva cancer patients. We assume that the PICO™ dressing complements the action of the suction drain, and suggest that the NPWT treatment should be continued as long as the suction drains remain in place.

As most of the complications appear within the early postoperative period, the PICO™ treatment should be considered for at least 14 days postoperatively. A larger randomized trial is warranted.

Conflicts of Interest

All Authors declare no conflicts of interest.

Authors’ Contributions

KCA: Study design, acquisition and interpretation of data, manuscript drafting. SA: Study design and revision of the manuscript. CB: Study design and manuscript revision.

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