

Vulvar carcinoma electroresection with inguinal lymphadenectomy. A preliminary evaluation of treatment outcomes

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SUMMARY

The aim of this study was to assess the efficacy of electroresection and inguinal lymphadenectomy in the surgical treatment of early stages of vulvar carcinoma (FIGO IB–II). From May 2016 to February 2017, vulvar electroresection with inguinal lymphadenectomy was performed in 16 patients aged 47–81 in the Center of Woman's and Child's Health in Zabrze, Poland. There were no intraoperative complications. In 14 cases, the postoperative period raised no concerns. The patients were discharged on the 7th or 8th day after the operation. Massive lymph accumulation in the inguinal region was noted in 2 patients, but it subsided up to 12 days after surgery. In one case, the right medial margin was positive. A radical procedure was therefore applied. Two patients were ordered postoperative radiotherapy due to narrow surgical tissue margins. One patient needed treatment for lymph node metastases found in a postoperative examination. Electroresection with inguinal lymphadenectomy is an effective treatment method in vulvar carcinoma. No tension of sutured skin results in better wound healing. Hospital stay is reduced to 7–8 days, and treatment costs are lower. The number of needed analgesics is significantly lower as well. After 10 weeks, the wound is healed completely, allowing a return to normal life. There is no feeling of mutilation. The results presented here are preliminary due to a small group of operated women and short postoperative follow-up.

Key words: vulvar carcinoma; vulvar electroresection; inguinal lymphadenectomy

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INTRODUCTION

Vulvar carcinoma is a rare gynecological cancer. It accounts for 3–5% of all female genital cancers. Each year, 300–400 new cases are diagnosed in Poland. Vulvar carcinoma is the fourth most common genital malignancy after endometrial, cervical and ovarian cancers. According to the data of the Polish National Cancer Registry from 2014, 200 women die each year due to this disease [1]. The raw incidence ratio is 1.4/100,000. The risk of vulvar carcinoma in Poland is estimated as average.

Vulvar carcinoma is usually diagnosed in women after 65 years of age, but it can also develop in younger women. The most common predisposing factors include: diabetes, autoimmune diseases, renal transplant (immunosuppressive factors), infectious diseases of the genitals, such as *chlamydia trachomatis*, herpes virus or HPV (type 16, 18), sociodemographic conditions (the risk is inversely proportional to the level of education), smoking (the risk is 4 times higher in smokers) and lichen sclerosus [2]. A 10–100-fold increase in the risk of vulvar carcinoma is observed in women with lichen sclerosus [3].

The most common are two histological types of vulvar carcinoma: keratinizing squamous cell carcinoma that develops within a background of VIN (vulvar intraepithelial neoplasia) or lichen sclerosus, and non-keratinizing squamous cell carcinoma. The keratinizing type is more common in older women. It exhibits p53 mutation and/or p53 overexpression and TGF 2-alpha expression. The non-keratinizing type is more common in younger women and is related with HPV infection (type 16, 18). It results from undifferentiated VIN progression (VIN3 according to the WHO). It presents as clearly demarcated nodules and macules that

protrude over the level of healthy skin. There is no p53 overexpression [4].

Vulvar carcinoma may assume either an exo- or endophytic form. Endophytic tumors produce metastases to lymph nodes faster and are characterized by worse prognosis [2]. The disease spreads through extension, and metastases usually occur in the superficial inguinal lymph nodes, and next in the deep and pelvic lymph nodes [5]. Itching, burning and pain are the most common symptoms of vulvar carcinoma. They are, however, poorly specific. Pain and discomfort in the vulva, bleeding and micturition disorders occur in more advanced cases.

Surgery is of primary significance in the treatment of vulvar carcinoma. The type of surgery and the level of its radicality depend on cancer stage, tumor location and general state of the patient [6]. Surgeries by Taussig and Way, which improved survival of women with vulvar cancer from 8% to 60–70% and decreased mortality to 2%, were a breakthrough in the surgical treatment of this cancer. These procedures involved radical en block tumor resection along with the inguinal lymph nodes. However, they were accompanied by a vast number of complications, starting from surgical wound dehiscence to infections and pathological lower limb swelling. The procedures were frequently unacceptable by patients due to

deteriorated sexual life. Hacker's surgery, also referred to as the *three cuts technique*, occurred to be a significant progress. This method reduced the extensiveness of a surgical wound and decreased the complication rate significantly. The three cuts technique consists in broad excision of the vulva and inguinal lymphadenectomy, conducted through a separate incision. This reduces the extensiveness of the surgical wound and speeds up the healing process [7]. The most significant prognostic factors include the regional lymph node status and the size of a vulvar tumor. This is reflected in the FIGO classification, published in 2009 (Tab. 1).

Adjuvant treatment includes radiotherapy [8] when the surgical margins are narrow or positive and/or when there are metastases to the inguinal, iliac and obturator lymph nodes. When the superficial lymph nodes are involved (>3), it is recommended to irradiate the entire inguinal and iliac lymph nodes to the dose of 50 Gy with a boost dose to the involved nodes to the total dose of 60 Gy using intensity-modulated radiation therapy (IMRT) in order to reduce the risk of radiation reactions in the adjacent organs (skin, urinary bladder, rectum, intestine and femoral heads). In patients with advanced T3 and T4 disease, neoadjuvant chemoradiotherapy to 45–50 Gy can be considered. This enables tumor mass reduction and allows radical and less mutilating resection.

Tab. 1. Vulvar carcinoma. FIGO staging system (2009)

Stage I	Tumor contained to the vulva
IA	Lesions ≤ 2 cm in size, confined to the vulva or perineum and with stromal invasion ≤ 1.0 mm, no nodal metastasis
IB	Lesions >2 cm in size confined to the vulva or perineum or with stromal invasion >1.0 mm, no nodal metastasis
Stage II	Tumor of any size with extension to adjacent structures (1/3 lower urethra, 1/3 lower vagina, anus), no nodal metastasis
Stage III	Tumor of any size with or without extension to adjacent structures (1/3 lower urethra, 1/3 lower vagina, anus) with positive inguino-femoral lymph nodes
IIIA	with 1 lymph node metastasis (≥ 5 mm), or 1–2 lymph node metastases (<5 mm)
IIIB	with ≥ 2 lymph node metastases (≥ 5 mm), or ≥ 3 lymph node metastases (<5 mm)
IIIC	with positive nodes with extracapsular spread
Stage IV	Tumor invades other regional structures (2/3 upper urethra, 2/3 upper vagina) or produces distant metastases
IVA	Tumor invades any of the structures: upper urethra and/or mucosa of the upper vagina, bladder mucosa, rectal mucosa, or fixed to pelvic bone fixed or ulcerated inguino-femoral lymph nodes
IVB	Tumor with distant metastasis, including pelvic lymph nodes

Chemotherapy is applied as an element of a combined therapy in primary treatment of advanced vulvar carcinoma (FIGO III and IV) and in relapses. The most common cytostatics are 5-fluorouracil, cisplatin, mitomycin C and taxol.

Local relapses are the most common treatment failure in vulvar carcinoma [9]. The recurrence rate ranges from 15% to 30% in patients after primary surgery. Recurrences within the vulva account for 43% to 70% of cases, in the inguinal region: 24–30% of cases and in the pelvis minor: approximately 5% of cases. Distant metastases are observed in 22%–34% of cases. Inguinal relapses usually develop sooner, typically within 12–24 months after surgery. In 80% of patients, local vulvar recurrences occur within 2 years, but they can also develop after even 5 years of surgery. Treatment outcomes in patients with recurrences that develop after more than 3 years are similar to those after primary treatment [10].

Factors predisposing to relapse include:

- the lymph node status depending upon the location of the primary lesion (clitoris, urethra, vagina, rectum, midline), tumor diameter, depth of stromal infiltration (over 1 cm), nature of invasion (infiltrative growth), cancer infiltration of the regional outflow vessels;
- healthy tissue margin <1 cm;
- multifocal vulvar lesions;
- cancer cell mitotic activity;
- histological grade (G2 and G3);
- too small extent of the primary surgery (e.g. regional lymph node dissection only on the side of the tumor).

Surgery is crucial in the treatment of vulvar carcinoma recurrences. The choice of a repeated procedure depends on the type of the primary surgery, the location of the recurrent lesion and its size. The aim is to remove the tumor completely with a safe healthy tissue margin. Local recurrences that can be treated surgically are characterized by the highest cure rate from 50% to 70%. If surgery is not radical, adjuvant radiotherapy and/or chemotherapy should be implemented. In the case of inoperable recurrences, radiotherapy alone is applied (either tele- or brachytherapy). Vulvar recurrences of <5 cm and nodal recurrences of <2 cm in diameter present a good prognosis. The site of the recurrent tumor is one of the decisive factors in vulvar cancer relapse. Five-year survival of patients with a vulvar recurrence ranges from 50% to 60%, while it is 0–15% in patients with

recurrences in the inguinal region. In the case of recurrences located in the pelvis minor and/or distant metastases, survival is not longer than 28 months. Time from the primary therapy to recurrence is crucial. Recurrences that occur within 4 months are associated with significantly lower chances for survival. After treatment, each patient must be closely observed. In the first year, gynecological follow-up examinations should be conducted every 2 months due to the risk of relapse, which usually occurs within the first 12–24 months after treatment. Subsequently, patients are followed-up every 3–4 months for 5 years due to the risk of recurrences and dissemination.

AIM

The aim of the study was to evaluate the efficacy and clinical usefulness of vulvar electroresection with inguinal lymphadenectomy as surgical treatment of early vulvar carcinoma (FIGO IB–II).

MATERIAL AND METHOD

From March 2016 to February 2017, 16 patients with FIGO IB–II vulvar carcinoma received surgical treatment in the Centre of Woman's and Child's health in Zabrze, Poland. The patients' age ranged from 47 to 81 years. All patients were referred from the Institute of Oncology in Gliwice where they were initially deemed eligible for surgery after a global clinical analysis of each case based on gynecological assessment, histopathological evaluation of vulvar specimens and imaging findings (abdominal and pelvic CT conducted for confirmation or exclusion of pelvic and inguinal lymph node involvement). Chest radiography and an SCC level were assessed in each patient. Keratinizing squamous cell carcinoma was preoperatively diagnosed in 11 women, 4 women were diagnosed with non-keratinizing squamous cell carcinoma and 1 patient had squamous cell carcinoma.

Surgical treatment involved extensive electroresection of the vulva with inguinal lymphadenectomy. The incision line ran along the outer edges of the labia majora in the genitofemoral sulcus downwards and encompassed as much of the perineum as possible. The inner dissection of the vaginal vestibule proceeded from the urethral opening and reached the posterior commissure bilaterally. After partial dissection of the vulva from the surface of the

symphysis, the internal circular incisions were joined with the external incision. The vulvar bed was coagulated. The condition necessary for the wound in this region to heal is the lack of tension of the sutured skin. If, however, tension is noted, approximately 1 cm long transverse incisions can be made on the outer edges of the wound. Subsequently, inguinal lymph nodes were reached from separate incisions and excised. In each case, a Redon drain was inserted to the inguinal wound in the lower pole. The edges of the wound after inguinal lymphadenectomy were sutured with single sutures. The surgery was not complicated in any of 16 patients. The patients were discharged on the 7th or 8th day after the operation. Local and intravenous antibiotic therapy was used during hospitalization. A local antibiotic (neomycin) was applied to the vulvar wound. Also, Silol and a combined product with a steroid (oxycort) were used. From day 2 after surgery, the patients required low doses of analgesics: NSAIDs, drugs of step II and III of the analgesic ladder, which was associated with nerve ending palsy during vulvar electroresection.

Postoperative complications in the form of massive accumulation of lymph in the inguinal region after lymphadenectomy were noted in 2 patients. In both cases, lymphatic edema reduced significantly upon a puncture procedure. Hospitalization of these patients was longer: up to 12 days. In one patient, the histopathological examination revealed a positive right medial margin. This was an indication for a radical procedure consisting in broad resection of the lesion. The margin was negative in the examination of the postoperative specimen. Two patients were ordered postoperative radiotherapy due to narrow surgical margins (0.3 cm). IMRT was used to deliver 50 Gy to the iliac and inguinal lymph nodes. One patient needed treatment for lymph node metastases reported in a postoperative histopathological examination. The patient also received IMRT. She was administered 50 Gy to the iliac and inguinal lymph nodes with a boost to 60 Gy to the involved region.

The follow-up period is relatively short in our patients. It reaches 12 months in those operated first. In one case, a local recurrence was noted. The patient underwent chemoradiotherapy with 50 Gy and a boost to 60 Gy to the vulvar infiltration with simultaneous treatment with cisplatin. A positive therapy outcome was noted.

DISCUSSION

Multicenter studies [7,11] show that there is no one standard surgical technique to be performed in vulvar carcinoma patients. The clinical assessment of each case should be personalized as much as possible. Patient's age, general state and comorbidities are of significance. Of prognostic factors, the most important is the histopathologically verified presence or absence of metastasis in the inguinal lymph nodes. In our group of patients, all women underwent vulvar electroresection with inguinal lymphadenectomy. This management reflects the current tendency to reduce the extensiveness of surgical treatment in women with vulvar carcinoma. The percentage of extensive radical surgeries, such as Way's surgery, has been decreasing in the past several years to the benefit of less extensive operations. More importantly, no statistically significant differences in survival have been observed [12].

Hospitalization of our patients averaged 7–8 days. Some authors [13] report longer hospitalization periods in vulvar carcinoma patients. These differences may result from the fact that hospitalization time may depend on various factors, such the extensiveness of surgery, comorbidities or patient's age. Literature data on the frequency of relapse in vulvar carcinoma vary considerably. They mostly depend on the follow-up period, the type of surgery and the course of the postoperative period.

Postoperative complications noted in this study were similar to those reported by others [11,13]. Some authors suggest that drains after inguinal lymphadenectomy should remain inserted for a longer period of time to prevent lymph accumulation in the nodal bed. A very useful modality to assess lesions within the inguinal lymph nodes is magnetic resonance imaging [14]. Positron emission tomography (PET), used in certain centers, seems to be an optimal examination to assess the borders and depth of malignant infiltration and potential presence of metastases. This imaging technique delivers global information needed to ultimately determine the stage of vulvar carcinoma. Most American centers recommend PET as an essential examination for patient selection for surgery [15].

At present, radical radiotherapy, chemoradiotherapy and brachytherapy are gaining importance [16,17]. These methods can be used before surgery in patients with advanced disease in order to avoid further radical procedu-

res, e.g. exenteration [10]. Most oncologists and specialists in gynecologic oncology claim that personalized treatment and possibilities of adjuvant therapy will improve treatment outcomes and patients' quality of life [3].

CONCLUSIONS

1. Vulvar electroresection with inguinal lymphadenectomy seems to be an effective surgical treatment method in patients with vulvar carcinoma. No tension of the sutured skin results in better and faster wound healing.
2. Vulvar electroresection with inguinal lymphadenectomy offers shorter hospitalization

(7–8 days) compared to conventional surgery. This reduces treatment costs significantly.

3. The painless postoperative period improves patients' quality of life and eliminates the need to frequently administer potent analgesics.
4. No feeling of mutilation has a positive effect on psychophysical and psychosexual function of patients. The wound is healed completely after 10 weeks, allowing a return to normal life.
5. Too short observation prevents final conclusions concerning efficacy and clinical usefulness of vulvar electroresection. That is why this evaluation is only preliminary.

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