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SURGICAL TREATMENT OF INVASIVE VULVAR CANCER

HIRURŠKO LEČENJE INVAZIVNOG KARCINOMA VULVE

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Summary – This paper presents the surgical treatment of invasive cancer of the vulva at the Department of Gynecology and Obstetrics in Novi Sad in the period from 2000 to 2010. Forty-one patients underwent different surgical procedures depending on their stage of the disease, age and general physical condition assessed according to the International Federation of Gynecologists and Obstetricians: wide excision to the healthy area with negative edges of 10 mm, simplex - radical vulvectomy or hemivulvectomy, block dissection of the vulva by Way, one-sided or bilateral lymphadenectomy and skin-muscle flap to cover the resulting skin defects. The number of removed lymph nodes on one side ranged from 8 to 19, the average being 12.6. Various postoperative complications (inflammation and wound dehiscence, lymphorrhoea, lymphocyst and limb lymphedema) developed in 9 (21.9%) and the local regional recurrence was recorded in 7 (17%) patients. The outcome was lethal in 4 (9.8%) surgically treated women. The primary surgical procedure is always individually planned and the choice of individual plans depends on three main factors: the size and position of the primary tumor in relation to the center line of the vulva (clitoral area - anus) and the involvement of regional lymph nodes. In order to reduce the psychosexual morbidity the preference is nowadays widely given to the local excision with adequate and histopathologically confirmed negative edges of the tumor together with determining the presence of metastases in sentinel lymph nodes.
Key words: Vulvar Neoplasms; Surgical Procedures, Operative + methods; Female; Neoplasm Staging; Postoperative Complications; Mortality; Lymph Node Excision; Sentinel Lymph Node Biopsy

Introduction

Cancers of the vulva come to 3-5% of all malignant tumors of the female genital system and usually occur after the age of 60 years. Squamous cell carcinoma accounts for about 90% of all malignant tumors of the vulva, malignant melanoma makes 3-5%, while adenocarcinoma of Bartholin gland, sarcoma, and basal cell carcinomas rarely occur [1, 2]. It is clinically manifested in the form of exofitic mass, or ulceration or hyperpigmented whitish changes above the skin. In about 5-10% of cases, malignant lesions develop on the previously altered skin of the vulva in patients with extensive dystrophic changes, which have not been adequately treated [3]. The risk factors include human papillomavirus (HPV) infection of the lower genital system, the presence of associated "non neoplastic" epithelial lesions (dystrophy) or intraepithelial neoplasia (VIN), early menopause and old age [4]. The definitive diagnosis is made according to the histological examination after the targeted and multifocal bioptically obtained tissue samples with adequate depth of several mm. When cancer of the vulva is in question, there is no concept of micro-invasive cancer as the invasion means any penetration of over 1 mm in depth. The most important independent prognostic factor is the presence of metastases in the lymph nodes [5]. The new system of International Federation of Gynecologists and Obstetricians (FIGO) classification of cancer of the vulva has been applied since 2009 and the biggest changes are related to stage III of the disease, which is based on accurate histopathological findings [6]. The concept of surgical treatment of vulvar cancer always involves an individual approach to each patient with the choice of procedure depending on three main factors: the size of the primary tumor, regional lymph node involvement and tumor position in relation to the center line of the vulva seen from the middle of the clitoris to the anus [7]. The aim of study was to review the various surgical procedures and the overall results of surgical treatment of vulvar cancer performed at the Surgical Ward, Department of Gynecology and Obstetrics, Clinical Center of Vojvodina in Novi Sad (2000-2010) and compare the results of treatment from the previous period (1985-1999).

Material and Methods

Forty-one women were operated for invasive cancer of the vulva at the Surgical Ward, Department of Gynecology and Obstetrics, Clinical Center of Vojvodina in Novi Sad in the period from 2000 to 2010. The definitive diagnosis was based on the histological examination of bioptic samples of vulva. The age of the operated patients ranged from 38 to 89 years, the average being 66.3 years. The length of hospitalization

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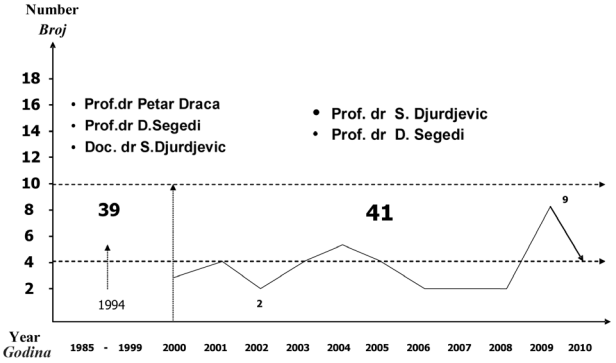
Abbreviations

FIGO – International Federation of Gynaecologists and Obstetricians

was from 5 to 55 days, i.e. 12.6 days on average. The distribution by the FIGO staging system of disease was as follows: stage I - 21 (54%), stage II - 9 (21.9%), stage III - 9 (21.9%) and stage IV - 2 (4.8%). In relation to the histopathological type there were 39 (95.12%) patients with squamous cell carcinoma and one (2.44%) with malignant melanoma and basal cell carcinoma (2.44%), each. Surgical treatment was carried out after the thorough preoperative preparation which included the control of laboratory analysis of blood and urine, lung X-ray, ultrasound inguinal examination with probe for soft tissues and pelvic computerized tomography examination, anesthetic, and internist examination. The main criteria for surgical treatment were: histopathologically confirmed cancer of the vulva, a written report by internal medicine specialist and anesthesiologist stating that the patient had no contraindications for surgical treatment and the patient's written consent to accept the proposed treatment. Surgical procedures were applied separately to the external genitalia (vulva) and in the area of one or both inguinums depending on the histological type, size and position of the primary tumor in relation to the center line of the vulva (clitoris-anus). The following procedures were performed on the vulva: wide excision into the healthy area with 10 mm negative edges, "simplex" vulvectomy, radical hemivulvectomy, radical vulvectomy, V-Y or a local skin transpositioned flap. Unilateral or bilateral superficial and/or deep inguinofemoral lymphadenectomy with removal of superficial and deep inguinal lymph node group and ligation or preservation of the large veins grafts (*v. saphena magna*) were done in the inguinal area. Only one patient with packages of bilaterally enlarged and fixed lymph nodes underwent block dissection of vulva with inguinal lymphadenectomy, the technique by Way. The adequate surgical procedure carried out on the vulva included histological confirmation of the presence of negative edges around the primary tumor of 10 mm. When performing inguinofemoral lymphadenectomy we used the so-called "S" section taken from the opus of plastic surgery and described into details in a previously published study [3]. Before surgery, all patients received antibiotic and anticoagulant prevention (1.0 g iv of cephalosporin 30 min. before surgery, Fraxiparin 0.3 ml sc. 2 hours before surgery) and had the lower limbs bandaged. The statistical analysis was performed by software package SPSS version 17.0. In addition to the methods of descriptive statistics for the incidence of surgically treated patients with vulvar cancer, complications and lethal outcome in the period 2000-2010 and comparison with the period 1985-1999, we used Fisher's exact indicator of the likelihood and Pearson's chi-squared test (χ^2). A significant difference was defined for p value less than 0.05.

Results

The **Graph 1** shows the number of surgically treated patients and the incidence of cancer of the vulva at the Department of Gynecology and Obstetrics in Novi Sad in the period from 1985 to 2010. There is a statistically significant difference (χ^2=9777, df=1, p=0.002) between the two studied periods in the number of women operated for cancer of the vulva. The type of surgical procedures conducted in the period 2000-2010 is presented in **Table 1.** The most frequently applied operating procedure was radical vulvectomy with bilateral inguinofemoral lymphadenectomy, which was done in 13 (31.7%)



Graph 1. Incidence of female patients operated at the Department of Gynecology and Obstetrics of the Clinical Center of Novi Sad due to invasive vulvar carcinoma (1985-2010)

Grafikon 1. *Incidencija hirurški lečenih pacijentkinja zbog invazivnog karcinoma vulve na operativnom odeljenju Klinike sa ginekologiju i akušerstvo u Novom Sadu (1985-1999)*

Table 1. Type of operative approaches in surgical treatment of vulvar cancer

Tabela 1. *Vrsta operativnih postupaka u hirurškom lečenju karcinoma vulve*

Type of Operation *Vrsta operacije*	Period 1985− 1999 : 39 operations *1985−1999 godine : 39 operacija*			Period 2000−2010 : 41 operations *2000−2010 godine : 41 operacija*		
	Bilateral *Obostrana*	One sided *Jednostrana*	No lymphad *Bez limf*	Bilateral *Obostrana*	One sided *Jednostrana*	No lymphad *Bez limf*
radical vulvectomy/*radikalna vulvektomija*	6	-	-	13	-	2
blok dissection of vulva s.Way/*blok disekcija vulve po Way-u*	20	-	-	1	-	-
radical hemivulvectomy/*radikalna hemivulvektomija*	-	2	-	3	4	2
simple vulvectomy/*simpleks vulvektomija*	1	1	3	-	1	1
tumor excision/*ekscizija tumora*	-	-	3	-	3	3
V-Y plastic of cutan lobus/*V-Y kožni režnjevi*	-	-	-	1	2	2
tumor excision + TCT irradiation/*ekscizija tumora+TCT zračenje*	-	-	3	-	-	3
Total/*Ukupno*	27	3	9	18	10	13

Table 2. Distribution of postoperative complications after primary surgical treatment
Tabela 2. *Distrubucija postoperativnih komplikacija posle primarnog hirurškog lečenja*

Type of complications *Vrsta komplikacije*	Period/*Period* 1985–1999	Period/*Period* 2000–2010
Wound dehiscence/*Dehiscencija rane*		
Partial/*Delimična*	9	5
Complete/*Potpuna*	5	0
Lymphocyst/*Limfocista*	0	1
Lymph edema of leg/*Limfedem noge*	2	2
Lymphorrhoea longer than 15 days *Limforeja duže of 15 dana*	0	1
Tromboemboly of lungs/*Tromboembolija pluća*	2	0
Stricture of vulva and vagina *Striktura vulve I vagine*	1	0
Uretrovaginal fistula/*Uretrovaginalna fistula*	1	0
Total/*Ukupno*	20 (51.3%)	9 (21.9%)

patients and their number was significantly reduced (χ^2=9777, df=1, p=0.002) compared to the period from 1985 to 1999 if we include the number of radical vulvectomy by Way. **Table 2** shows the type and frequency of complications after surgery. There is a statistically significant difference (χ^2=7441, df=1, p=0.006) between the two studied periods in the number of complications. The number of removed lymph nodes on one side ranged between 8 and 19 and the average number of removed lymph nodes in the overall sample was 12.6. The average number of removed lymph nodes during the period 1985-1999 was 16.3, of which one in seven (26.9%) cases was positive. Lethal outcome in the postoperative period was recorded in 4 patients operated in both periods **(Table 3)**. Fisher's exact test demonstrated no statistically significant difference (p=0.615) in lethal outcome between these two periods. **Figure 1** illustrates the deep inguinofemoral lymphadenectomy showing elements of Scarp triangle, and **Figure 2** shows V-Y skin flaps placed on both sides to cover the resulting defects.

Table 3. Extirpated lymph nodes, recurrence rate, mortality and 5 year survival
Tabela 3. *Odstranjeni limfni čvorovi, recidivi, letalni ishod i preživljavanje*

Examined parameters *Ispitivani parametri*	Period 1985–1999	Period 2000–2010
Average number of removed lymph nodes *Prosečan broj odstranjenih limfnih čvorova*	16.3	12.6
Recurrences/*Recidivi*	5 (12.8%)	7 (17 %)
Lethal outcome/*Letalni ishod*	4 (10.3%)	4 (9.8 %)
Total five year survival *Ukupno petogodišnje preživljavanje*	65.3 %	85.4%

Discussion

Radical vulvectomy with bilateral lymphadenectomy was first described by Bassett in 1912, and in 1948 Sir Stanley Way introduced the modifications in the form of block dissection of the vulva and inguinal

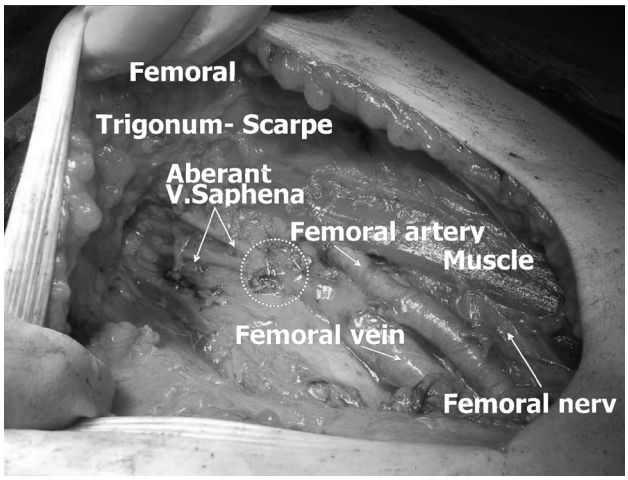


Fig. 1. Deep inguinofemoral lymphadenectomy with elements of Skarp's triangle
Slika 1. *Duboka ingvinofemoralna limfadenektomija sa elementima Skarpovog trougla*

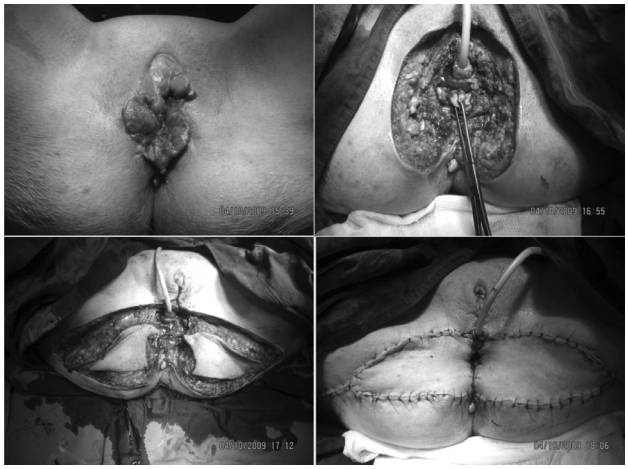


Fig. 2. Covering defects after radical vulvectomy using V-Y skin flaps
Slika 2. *Pokrivanje defekta posle radikalne vulvektomije primenom V-Y kožnih režnjeva*

regions in the shape of a butterfly. Due to the large skin defect and approaching the edge of the wound by expressed tensile force this surgical procedure caused a high percentage of postoperative dehiscence with the formation of extensive scars [8,9]. Since the removal of lymph nodes is performed in flexible inguinal region, various surgical techniques have been applied to reduce morbidity. In 1981 Hacker introduced separate inguinal incisions, which led to reduction in the percentage of total wound dehiscence from 50 to 14% and this is one of the most important modifications in surgical treatment of invasive carcinoma of the vulva [10]. In the same year, Iversen proved that the unilateral localized cancer of the vulva had bilateral lymphogenic metastases in 15%; whereas Stehman suggested inguinofemoral unilateral lymphadenectomy to be performed after wide excision of the tumor with negative edges [11,12]. Bilateral inguinofemoral lymp-

hadenectomy is performed when cancers are closer to the center line of the vulva with the localization of the clitoris or perineum, and the depth of invasion is over 1 mm, while unilateral lymphadenectomy is indicated in well-differentiated tumors without penetration into the lymphatic and vascular system with negative lymph nodes on the side of the tumor [13-15]. This study presents the results of surgical treatment of invasive cancer of the vulva performed at the Surgical Ward, Department of Gynecology and Obstetrics, Clinical Center of Vojvodina in Novi Sad in the period from 2000 to 2010 and compares them with the results obtained at the same institution in the period from 1985 to 1999 [2]. Twenty-six (66.7%) out of 39 patients surgically treated in the latter period underwent radical vulvectomy with bilateral lymphadenectomy, which was performed by the Way method in 20 (51.3%) and by Hacker in 6 (15.3%) patients. Operative wound dehiscence was recorded in 14 (36%) patients. In the period after 2000, there has been an increase in the total number of surgically treated patients and a decrease in the number of vulvectomy with bilateral lymphadenectomy to 13 (31.7%). The number of radical excision of tumor and hemivulvectomy were increased. Partial dehiscence of the inguinum was recorded in 4 cases and of the vulva (12.2%) in 1 case, which was a significant reduction in morbidity by 20% compared to the previous period. A significant decrease of postoperative morbidity was achieved by the application of separate inguinal incision in the shape of the letter ”S”, sharp surgical preparation to form the sharp edges of the wound with a part of the subcutaneous tissue that provides adequate nutrition of the skin, application of vacuum drains and suturing skin with synthetic seaming materials under minimally expressed tension. According to the cumulative results from the literature the total percentage of recurrence after surgical treatment of vulvar cancer ranges from 15 to40% and is related to the size, depth of invasion of malignant lesions and positive regional lymph nodes [16-18]. In our study, recurrences were recorded in 7 (17%) patients, which is slightly higher than in the previous period when five (12.8%) cases were recorded. The increase in the number of relapses can be interpreted by statistically significant reduction in the number of radical surgeries (block dissection of vulva by Way), which resulted in the reduction of morbidity and improvement of quality of life; however, there was a slight increase in recurrences by 4.2%. It should be noted that locoregional relapse was treated on two occasions by a wide excision and V-Y flaps on both sides and by external TCT radiation in one patient. The outcome was lethal in 4 (9.8%) patients, which is slightly less than in the previous period when it was 10.3%. There were no recorded cases of intrahospital mortality in the period from 2000 to 2010; whereas 2 cases were recorded in the period from 1985 to 1999. Three patients died because of early recurrence and metastases dissolution in the period of 6-12 months after surgery with additional radiation therapy applied, and one patient died 4 years after surgery. In the period 1985-1999, two patients died because pulmonary thromboembolism developed on the 25th and 50th postoperative day, and the condition was aggravated by the expressed risk factors (obesity, hypertension, varices of the lower extremities) and long bed confinement due to wound dehiscence and two women died because of diffuse metastases dissolution in the first and fourth postoperative year [2]. Treatment of invasive cancer of the vulva always includes an individual approach, which should be adapted to each patient. Maximally conservative surgical procedure should always be opted for in treatment which would result in healing and control of disease [19,20].

Conclusion

An increase in the total number of patients operated for cancer of the vulva was recorded in the last ten years (2000-2010) at the Department of Gynecology in Novi Sad in comparison to the previous period (1985-1999), with the peak in 2009 when 9 patients were operated. The number of radical vulvectomy with bilateral lymphadenectomy was reduced in the same period from 66.6% to 31.7%, and the number of radical excision of tumor and hemivulvectomy increased. The postoperative complications, which had amounted to 51.3% in the period from 1985 to 1999, were significantly decreased by 29.3% in the period from 2000 to 2010. Five-year survival was 65.3% in the period from 1985 to 1999 and 85.4% in the period from 2000 to 2010. Lethal outcome was almost the same in both time periods, and there was no statistically significant difference.

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Sažetak

Uvod

Karcinomi vulve čine 3–5% svih malignih tumora ženskog genitalnog sistema. Primarni hirurški postupak uvek se planira individualno a izbor zavisi od tri glavna faktora: veličine i položaja primarnog tumora u odnosu na centralnu liniju vulve i zahvaćenosti regionalnih limfnih čvorova. Cilj rada je prikaz različitih hirurških postupaka i ukupnih rezultata hirurškog lečenja invazivnog karcinoma vulve na ginekološko-akušerskoj Klinici u Novom Sadu, od 2000. do 2010. godine i njihova komparacija sa rezultatima iz perioda 1985–1999. godine na Klinici.

Materijal i metode

U periodu 2000–2010, lečena je ukupno 41 žena zbog invazivnog karcinoma vulve. Sprovođeni su sledeći hirurški postupci: široka ekscizija do u zdravo sa negativnim ivicama od 10 mm, simpleks radikalna vulvektomija ili hemivulvektomija, blok disekcija vulve po Way-u, jednostrana ili obostrana limfadenektomija i kožno-mišićni režnjevi za pokrivanje nastalih kožnih defekata.

Rezultati

Najčešće primenjen operativni postupak bila je radikalna vulvektomija sa obostranom ingvinofemoralnom limfadenektomijom kod 13 ili 31,7% pacijentkinja. Broj odstranjenih limfnih čvorova po jednoj strani iznosio je 8–19, prosečno 12,6. Različite postoperativne komplikacije bile su zastupljene kod 9 (21,9%) a pojava lokoregionalnog recidiva zabeležena je kod 7 pacijentkinja. Letalni ishod evidentiran je kod 4 ili 9,7% operisanih žena.

Zaključak

U periodu 2000-2010. godine na Klinici za ginekologiju i akušerstvo u Novom Sadu,u odnosu na period 1985–2000. godine povećan je broj ukupno operisanih pacijentkinja od karcinoma vulve. Smanjen je broj radikalnih vulvektomija sa obostranom limfadenektomijom sa 66,6% na 31,7% uz povećanje broja radikalnih hemivulvektomija i ekscizija tumora. Značajno su smanjene postoperativne komplikacije za 29,3%. Sa ciljem smanjenja psihoseksualnog morbiditeta, danas se prednost daje širokoj lokalnoj eksciziji tumora sa adekvatnim i patohistološki potvrđenim negativnim ivicama u zajednici sa određivanjem prisustva metastaza u sentinealnim limfnim čvorovima.

Ključne reči: *Karcinomi vulve; Operativne hirurške procedure + metode; Žensko; FIGO klasifikacija tumora; Postoperativne komplikacije; Mortalitet; Ekscizija limfih čvorova; Biopsija sentinel limfnog čvora*

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