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TREATMENT OF VULVAR CANCER

LIJEČENJE RAKA STIDNICE

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Review

Key words: chemoradiation, inguino-femoral lymphadenectomy, radical vulvectomy, sentinel lymph node biopsy, vulvar cancer

Summary. ***Objective.*** Treatment modalities for vulvar cancer includes: surgical, radio- and chemo-therapeutical options. In this paper we discuss the impact of new staging classification (2009) on the treatment modalities. ***Methods.*** We reviewed the available literature on treatment of invasive vulvar cancer and compared with own results on 114 squamous vulvar cancer patients. ***Results.*** The cornerstone of primary treatment remains surgery. There is a trend to introduce less radical surgery, especially in early disease (wide excision). In patients with advanced primary disease, treatment criteria for the use of chemo/radiotherapy are still not completely defined. ***Conclusions.*** Less radical approach in surgical management of early stages with implementation of sentinel node identification techniques, the use of triple incision in radical vulvectomy decrease treatment associated morbidity with similar outcome results. Advanced disease requires individualized approach including combination of chemoradiation option and surgery associated with increased complication rate and undefined benefit in final outcome. The centralization of cases will facilitate the use of optimal treatment and patient recruitment for clinical studies. Finally, a new staging system adopted in 2009 whould be applied in all cases with invasive vulvar cancer.

Pregled

Ključne riječi: biopsija limfnog čvora čuvara, ingvinofemoralna limfadenektomija, kemoiradijacija, radikalna vulvektomija, rak stidnice

Sažetak. ***Cilj.*** U liječenju raka stidnice koriste se kirurška terapija, radioterapija i kemoterapija odnosno njihove razne kombinacije. Cilj ovog članka je istražiti i prikazati utjecaj nove klasifikacije (FIGO 2009.) na liječidbeni postupak raka stidnice. ***Metode.*** Pregledali smo dostupnu literaturu o liječenju invazivnog raka stidnice i usporedili s našim rezultatima na uzorku od 114 bolesnica sa skvamoznim rakom stidnice. ***Rezultati.*** Temelj primarnog liječenja je i dalje kirurški zahvat. Postoji težnja da se smanji radikalitet kirurških postupaka, poglavito u ranom stadiju bolesti (široka ekscizija). U bolesnica s uznapredovalom bolešću kriteriji za primjenu kemo/radioterapije još uvijek nisu jasno definirani. ***Zaključak.*** Manje radikalan kirurški pristup u liječenju ranih stadija bolesti, uvođenje metoda identifikacije limfnog čvora čuvara, te primjena tri separatna reza pri radikalnoj vulvektomiji smanjili su morbiditet kao posljedicu liječenja bolesti, bez bitnih promjena u ishodu samog liječenja. Bolesnice s uznapredovalom bolešću zahtijevaju individualizirani pristup uključujući kombinaciju kemoiradijacije i kirurgije povezane s povećanom stopom komplikacija i nejasnom korisnošću što se tiče završnog ishoda liječenja. Centralizacija bolesnica s rakom stidnice omogućit će primjenu optimalnog liječenja i dostupnost bolesnica za kliničke studije. Na kraju, nova FIGO klasifikacija bolesti iz 2009. godine trebala bi se koristiti u svim slučajevima invazivnog raka stidnice.

Introduction

Cancer of the vulva is a rare malignancy that increases progressively with age. Age-standardized incidence averages between 1 and 2 per 100,000 women in Western countries and rises steadily with advancing age. The incidence among 75-year old women is reported to be 20 per 100,000 per year. However, vulvar cancer has been rarely diagnosed also in very young women.[1] Ninety percent of all vulvar cancers are squamous cell carcinomas in origin. Melanoma and adenocarcinoma each account for about 5% of cases.[2] Histopathological, molecular and epidemiological studies have revealed two subsets of vulvar squamous neoplasia, which are distinguished by their association with human papilloma viruses and patient demographics. The pathway to both human papilloma virus positive and negative vulvar cancers may involve not only obvious precancerous lesions but also biological events in the vulvar mucosa that precede the onset of morphological atypia.[3] There is no recognized procedure with protective as well as therapeutic action direct to papiloma virus present on the vulvar skin. Furthermore, there is no screening test available for vulvar cancer although a number of precursor lesions are recognized including vulvar intraepithelial neoplasia (VIN) and Paget's disease of the vulva. It should also be underlined that women who develop a vulvar cancer are at increased risk of developing other genital cancers, particularly cervical cancer.

Diagnosis

Diagnosis of vulvar cancer is made exclusively using histologic evaluation of the tumor specimens. Early diagnosis is of vital importance to assure the appropriate therapeutic option with the best survival results. Any vulvar symptom(s) should require a prompt examination of the lower genital tract. Factors contributing to

the primary care doctors in making or suspecting a diagnosis include: elderly woman, vulvar pain, burning, pruritus and soreness which all can be associated with vulvar cancer. However, a lack of symptoms does not exclude invasive disease since some tumors are asymptomatic. Warts are uncommon in elderly women and should be regarded with suspicion. In pre-menopausal women »warts« may initially be treated as condylomata accuminata but persistent warts should be referred for an excision biopsy. It is recommended that referral should be made if any of the following changes are detected: a swelling, polyp, lump or ulcer, color change (whitening or pigment deposition), elevation and/or irregularity or surface contour, a clinical »wart«, irregular fungating mass, an ulcer with raised rolled edges and enlarged groin nodes.

If invasive disease is suspected then the patient should be referred to a Gynecological Oncology Centre (GOC) or clinician with an interest in vulvar disease. Colposcopy and especially *Collins test* using toluidin blue staining can be only helpful for localization of the suspect area. It is important that relevant histological material should be sent to the pathologist in the GOC.

Diagnosis whould in most cases be confirmed by a biopsy prior to definitive surgery. Occasionally, where the clinical situation dictates, definitive surgery to the lesion may be performed. In general, surgery to the groin nodes should not be performed prior to pathological confirmation of invasive disease. If lesions are small (<2cm in diameter) then it is sometime appropriate to excise the whole of the lesion as a diagnostic biopsy. It is important to keep detailed notes regarding the site and size of the lesion in case further treatment is required. It may be helpful to take a clinical photograph prior to surgery in these circumstances, with the patient's consent.

Additional radiographic and endoscopic studies should be considered for those with large primary tumors or suspected metastases. Potentially useful studies include proctosigmoidoscopy, colonoscopy, cystourethroscopy, computed tomography (CT) scan and intravenous pyelogram, magnetic resonance (MRI) and finally there are the possibilities of positron emission computed tomography (PET-CT) use. Fine-needle aspiration biopsy from sites of suspected metastases may be used with intention to avoid the need for surgical exploration.

Table 1. FIGO staging for vulvar epidermoid cancer (1994) and associated survival

Tablica 1. FIGO klasifikacija raka stidnice (1994.) i odgovarajuće preživljenje

Description – Clinical/Pathologic findings Opis – Kliničko/patološki nalaz		Survival Preživljenje	
Stage 0 **Stadij 0**	Carcinoma in situ, intraepithelial carcinoma Karcinom in situ, intraepitelni karcinom	Rijeka#	*FIGO 2006**
Stage I **Stadij I**	Tumor 2 cm or less in greatest diameter, confined to the vulva or perineum; nodes are negative Tumor promjera 2 cm ili manji, ograničen na stidnicu ili međicu; čvorovi su negativni	85.9%	*78.5%*
IA	As above with stromal invasion 1.0 mm or less Kao gore sa stromalnom invazijom 1.0 mm ili manjom	100.0%	
IB	As above with stromal invasion more than 1.0 mm Kao gore sa stromalnom invazijom dubljom od 1.0 mm	77.4%	
Stage II **Stadij II**	Tumor confined to the vulva and/or perineum, greater than 2 cm in greatest dimension, nodes are negative Tumor ograničen na stidnicu i/ili međicu, najvećeg promjera većeg od 2 cm, čvorovi su negativni	43.8%	*58.8%*
Stage III **Stadij III**	Tumor of any size with 1. Adjacent spread to the lower urethra and/or the vagina and/or the anus 2. Unilateral regional lymph node metastasis Tumor bilo koje veličine s 1. Širenjem u donji dio mokraćne cijevi i/ili rodnice i/ili anus 2. Pozitivnim jednostranim regionalnim limfnim čvorovima	50.5%	*43.2%*
Stage IV **Stadij IV**		8.3%	*13.0%*
IVA	Tumor invades any of the following: Upper urethra, bladder mucosa, rectal mucosa, pelvic bone, or bilateral regional node metastasis Tumor invadira bilo što od sljedećeg: gornji dio mokraćne cijevi, sluznicu mokraćnog mjehura i/ili rektuma, zdjeličnu kost ili s obostrano pozitivnim regionalnim limfnim čvorovima		
IVB	Any distant metastasis including pelvic lymph nodes Udaljene metastaze uključujući pozitivne zdjelične limfne čvorove		

– own five-year survival based on 114 epidermoid vulvar cancer patients – naše 5-godišnje preživljenje na 114 slučajeva
* – Reference 7

Staging

A clinical staging system based on TNM classification was adopted by the *International Federation of Gynecology and Obstetrics* (FIGO) in 1969. The staging was based on clinical evaluation of primary tumor and of regional lymph nodes and a limited search for distant metastasis. In 1988, FIGO introduced a new surgical/pathological staging system, replacing a clinical staging system for vulvar carcinoma. The final diagnosis is dependent upon thorough histopathologic evaluation of the operative specimen (vulva and lymph nodes). A surgical staging system was instituted because of the clinical inaccuracy of estimating node status and the prognostic significance of histologically proven inguinal node. Modifications were made in 1994 with Stage I further divided into IA and IB; the staging system with survival results is presented in *Table 1*.[4] Sixteen years later, in 2009 FIGO Committee on Gynecologic Oncology introduced revised FIGO staging for carcinoma of the vulva, cervix and endometrium[5] (*Table 2, 3 and 4*). Major changes are made regarding the extent of inva-

Table 2. FIGO staging (2009) for carcinoma of the vulva
Tablica 2. FIGO klasifikacija (2009.) karcinoma stidnice

Stage I	**Tumor confined 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 or with stromal invasion >1.0 mm*, confined to the vulva or perineum, with negative nodes
Stadij I	**Tumor ograničen na stidnicu**
IA	Lezije ≤2 cm u promjeru, ograničene na stidnicu ili međicu sa stromalnom invazijom ≤1.0 mm*, bez metastaza u limfnim čvorovima
IB	Lezije >2 cm u promjeru ili sa stromalnom invazijom >1.0 mm*, negativni limfni čvorovi
Stage II	**Tumor of any size with extension to adjacent perineal structures (1/3 lower urethra, 1/3 lower vagina, anus) with negative nodes**
Stadij II	**Tumor bilo koje veličine sa širenjem u okolne strukture (donja trećina mokraćne cijevi, donja trećina rodnice ili anus), negativni limfni čvorovi**
Stage III	**Tumor of any size with or without extension to adjacent perineal structures (1/3 lower urethra, 1/3 lower vagina, anus) with positive inguino-femoral lymph nodes**
Stadij III	**Tumor bilo koje veličine sa/bez širenja u okolne strukture (donja trećina mokraćne cijevi, donja trećina rodnice ili anus) s pozitivnim ingvinofemoralnim limfnim čvorovima**
IIIA	(i) With 1 lymph node metastasis (≥5 mm), or (ii) 1–2 lymph node metastasis(es) (<5 mm) (i) S jednom metastazom u limfnom čvoru (≥5mm), ili (ii) 1-2 metastaze u limfnim čvorovima (<5mm)
IIIB	(i) With 2 or more lymph node metastases (≥5 mm), or (ii) 3 or more lymph node metastases (<5 mm) (i) S 2 ili više metastaza u limfnim čvorovima (≥5mm), ili (ii)3 ili više metastaza u limfnim čvorovima (<5mm)
IIIC	With positive nodes with extracapsular spread Pozitivni limfni čvor s ekstrakapsularnim širenjem
Stage IV	**Tumor invades other regional (2/3 upper urethra, 2/3 upper vagina), or distant structures**
IVA	Tumor invades any of the following: (i) upper urethral and/or vaginal mucosa, bladder mucosa, rectal mucosa, or fixed to pelvic bone, or (ii) fixed or ulcerated inguino-femoral lymph nodes
IVB	Any distant metastasis including pelvic lymph nodes
Stadij IV	**Tumor invadira ostale regionalne (gornje 2/3 mokraćne cijevi, gornje 2/3 rodnice) ili udaljene strukture**
IVA	Tumor invadira bilo što od sljedećeg: (i) gornje 2/3 mokraćne cijevi i/ili rodnice, sluznicu mokraćnog mjehura, sluznicu rektuma ili je fiksiran za zdjeličnu kost (ii) fiksirani ili ulcerirani ingvinofemoralni limfni čvorovi
IVB	Udaljene metastaze uključujući pozitivne zdjelične limfne čvorove

* *Note:* The depth of invasion is defined as the measurement of the tumor from the epithelial-stromal junction of the adjacent most superficial dermal papilla to the deepest point of invasion.
* *Opaska:* Dubina invazije je definirana kao dimenzija tumora s epitelno-stromalnog spoja prilježeće najpovršnije dermalne papile do točke najdublje invazije.

sion and size of tumor, as well as the type and metastatic size of lymph node involvement.

For identification of special cases of TNM or pTNM classifications, the suffix »**m**«, »**y**«, »**r**« and »**a**« prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The »**m**« suffix indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

Table 3. TNM staging system compared to the FIGO staging (2009) for vulvar cancer
Tablica 3. TNM klasifikacija i usporedba s FIGO stadijem (2009.) za rak stidnice

TNM categories **TNM kategorija**	*FIGO Stages* *FIGO Stadij*	
TX		Primary tumor cannot be assessed Primarni tumor se ne može evaluirati
T0		No evidence of primary tumor Bez dokaza o primarnom tumoru
Tis		Carcinoma in situ (preinvasive carcinoma) Karcinom in situ (preinvazivni karcinom)
T1a	*IA*	Lesions 2 cm or less in size, confined to the vulva or perineum and with stromal invasion 1.0 mm or less Lezije promjera ≤ 2 cm, ograničena na stidnicu ili međicu sa stromalnom invazijom ≤ 1.0 mm
T1b	*IB*	Lesions more than 2 cm in size or any size with stromal invasion more than 1.0 mm, confined to the vulva or perineum Lezije promjera > 2 cm ili bilo koje veličine sa stromalnom invazijom > 1.0 mm, ogranične na stidnicu ili međicu
T2	*II*	Tumor of any size with extension to adjacent perineal structures (lower/distal 1/3 urethra, lower/distal 1/3 vagina, anal involvement) Tumor bilo koje veličine sa širenjem u okolne structure (donja 1/3 mokraćne cijevi, donja 1/3 rodnice ili anus)
T3	*IVA*	Tumor of any size with extension to any of the following: upper/proximal 2/3 of urethra, upper/proximal 2/3 vagina, bladder mucosa, rectal mucosa, or fixed to pelvic bone Tumor bilo koje veličine sa širenjem u: gornje 2/3 mokraćne cijevi, gornje 2/3 rodnice, sluznicu mokraćnog mjehura, sluznicu rektuma ili je fiksiran za zdjeličnu kost

The »**y**« prefix indicates those cases in which classification is performed during or after initial multimodality therapy. The cTNM or pTNM category is identified by a »y« prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The »y« categorization is not an estimate of tumor before multimodality therapy.

The »**r**« prefix indicates a recurrent tumor when staged after a disease-free interval and is identified by the »r« prefix: rTNM.

The »**a**« prefix designates the stage determined at autopsy: aTNM.

In classification from 2009 an additional descriptor used to define residual disease. Residual tumor (**R**) is defined as the absence or presence of residual tumor after treatment. In some cases when treated with surgery and/or neo-adjuvant therapy, there will be residual tumor at the primary site after treatment because of incomplete resection or local and regional disease that extends beyond the limit of ability of resection. **RX** – Presence of residual tumor cannot be assessed. **R0** – No residual tumor. **R1** – Microscopic residual tumor. **R2** – Macroscopic residual tumor.

Table 4. Regional lymph node staging (N)
Tablica 4. Klasifikacija regionalnih limfnih čvorova (N)

N	*FIGO*	
NX		Regional lymph nodes cannot be assessed Regionalni limfni čvorovi se ne mogu evaluirati
N0		No regional lymph node metastasis Nema metastaza u regionalnim limfnim čvorovima
N1		One or two regional lymph nodes with the following features Jedan ili dva pozitivna limfna čvorova sa sljedećim karakteristikama:
N1a	*IIIA*	One or two lymph node metastases each 5 mm or less Jedna ili dvije metastaze u limfnim čvorovima, svaka promjera ≤ 5 mm
N1b	*IIIA*	One lymph node metastasis 5 mm or greater Jedna metastaza u limfnom čvoru promjera > 5 mm
N2		Regional lymph nodes metastasis with the following features Metastaze u regionalnim limfnim čvorovima sa sljedećim karakteristikama
N2a	*IIIB*	Three or more lymph node metastases each less than 5 mm Tri ili više metastaza u limfnim čvorovima svaka promjera < 5 mm
N2b	*IIIB*	Two or more lymph node metastases 5 mm or greater Tri ili više metastaza u limfnim čvorovima promjera ≥ 5 mm
N3	*IVA*	Fixed or ulcerated regional lymph node metastasis Fiskirana ili ulcerirana metastaza u regionalnim limfnim čvorovima

An effort should be made to describe the site and laterality of lymph node metastases
Treba opisati lokalizaciju i lateralnost metastaza limfnih čvorova

Table 5. Distant metastases (M)
Tablica 5. Udaljene metastaze (M)

M	*FIGO*	
M0		No distant metastases Nema udaljenih metastaza
M1	*IVB*	Distant metastases (including pelvic lymph node metastases) Udaljene metastaze (uključujući pozitivne zdjelične limfne čvorove)

Single-center restaging analysis showed better reflection of prognosis for patients with squamous vulvar cancer,[6] but there are no multicenter published survival results according to the new classification.

Surgery

The principles guiding the management of women with vulvar cancer are evolving. Since the presentation of vulvar cancer may vary enormously, each case needs to be judged on its own merits and may involve surgery, radiotherapy or chemotherapy and in some cases a combination of all three. There is also an increasing use of plastic surgery techniques. This may lessen the surgical morbidity by allowing closure of tissues without undue tension and could reduce long-term psycho-sexual morbidity associated with the scarring that follows the standard radical approach. Many factors will influence decisions regarding management including the site and size of the primary tumor and its histological features, the presence or absence of nodal metastasis, the fitness of the patient and her informed decision.

Primary treatment target in the case of vulvar cancer represents primary site of disease and the potential lymph node metastases. The extent of vulvar malignancy determinates a primary surgical approach, and actually two clinical entities could be recognized: an early and advanced disease.

Among early stage diseases, microinvasive vulvar cancer (**FIGO stage IA**) can be managed by radical wide tumor excision only. The risk of lymph node metastases is negligible and therefore lymph node dissection can be omitted.[8] Recognized risk factors at this stage are the status of surgical margin(s) and histologic grade.[9]

Stage IB (lesion greater than 2 cm or lesion 2 cm or less in width but with stromal invasion greater than 1 mm) is treated by radical wide local incision completed by an inguino-femoral node dissection.

Stage II should be treated with radical vulvectomy and bilateral inguinal-femoral lymphadenectomy. The main aim of the surgery is to remove the primary tumor with minimum of 1cm clinical margins of disease-free tissue in all directions, including also a negative deep margin by excising the lesion down to the fascia. A radical wide local excision facilitates obtaining a margin 1 cm that corresponds to 8 mm margin in microscopic view on histopatologic specimen.[10] Although several

Table 6. Lymph node metastases according to the T stage among squamous cell vulvar carcinoma (own unpublished statistics – based on FIGO classification 1994)
Tablica 6. Metastaze u limfnim čvorovima u odnosu na T stadij među skvamoznim karcinomima stidnice (neobjavljena statistika na našem uzorku – zasnovana na FIGO klasifikaciju 1994.)

T stage T stadij	No *(Number and* survival) *(Broj i* preživljenje)		N1 *(Number and* survival) *(Broj i p*reživljenje)		N2 *(Number and s*urvival *(Broj i p*reživljenje)		**Total Ukupno** *(Number and* survival) *(Broj i p*reživljenje)	
T1b	*(13)*	83.9%	*(1)*	100.0%	*(0)*		*(14)*	**85.1%**
T2	*(19)*	58.5%	*(10)*	77.8%	*(6)*	16.7%	*(35)*	**55.5%**
T3	*(3)*	66.7%	*(2)*	50.0%	*(3)*	0.0%	*(8)*	**37.5%**
Total Ukupno	*(35)*	**68.7%**	*(13)*	**75.5%**	*(9)*	**11.1%**	**(*57*)**	**60.3%**
Statistics – Distribution: Statistika – Distribucija:	Chi-square 9.96; **P=0.0411** Hi-kvadrat 9.96; **P=0.0411**							

studies showed that pathological margin distance of more than 8 mm is an important predictor for local recurrence,[11] other could not support.[12]

Appropriate groin node dissection is one of the most important steps in identification of a risk factor associated with vulvar cancer mortality. The predictable spread pattern of vulvar cancer to regional lymphatics has allowed for improvements in survival largely due to radical surgical intervention. However, significant morbidity from radical surgery has led to the search for better prognostic indicators and complementary therapeutic modalities to modify the extent of surgery in both early and advanced disease. *En bloc* radical vulvectomy and bilateral inguinal-femoral lymphadenectomy are rarely performed today. An early invasive stage has been defined where only limited excision is required. The extent of and the indications for inguinal lymphadenectomy for various vulvar tumors and role of separate incisions (three separate incisions) have been clarified.

Our results on incidence of lymph node metastases according to the T stage and related five-year survival are presented in *Table 6*.

However, the morbidity associated with lymphadenctomy is considerable including wound dehiscence, wound infection, lymphocysts, lymphedema, prolonged hospital stay.[13]

Actually, there is no preoperative diagnostic technique showing acceptable results in predicting lymph node metastases; including clinical palpation with sensitivity of 57% and specificity of 62%, high frequency ultrasound detecting change in size and shape of lymph nodes, Doppler detecting changes in nodes perfusion, ultrasound guided fine needle aspiration cytology (FNAC) presenting high false negative rate; magnetic resonance imaging (MRI) detecting size and shape of nodes with high degree of specificity but sensitivity is low, T1 and T2 signal intensity is not useful in differentiation between benign and malignant nodes, MR lymphography using ultra-small-iron-oxide-particles (USIOP) – the results are awaited – and finally positron emission tomography (PET) and computed tomogaphy (CT) have yet to show any promise in the detection of groin node metastases in vulvar cancer).[14] When disease has spread to more than one inguinal node adjuvant radiotherapy has replaced pelvic lymphadenectomy as the standard treatment. Inguinal radiotherapy without groin dissection does not appear to be adequate therapy for most patients.

Sentinel lymph node mapping appears to be feasible in patients with primary vulvar cancer. The utility of newer techniques of sentinel node mapping is also being evaluated in squamous cancer and melanoma to limit the extent of lymphadenectomy in patients with clinically normally lymph nodes. It seems that the actual protocol provides a step forward toward less invasive, oncologically safe and more convenient and accurate procedures in the surgical management of the stage I and II vulvar cancer patients, but we should wait for definitive conclusion.[15,16]

Advanced disease

Radical surgery has resulted in impressive cure rates in women with locally advanced vulvar carcinoma. Unfortunately, morbidity mostly related to wide ablative techniques as inguinofemoral lymphadenectomy, is common. Some innovative techniques are used in the management of vulvar disease with attempts to reduce attendant morbidity. The most important success in the treatment of vulvar cancer in recent years is the maintenance of high survival rates despite considerably less extensive surgical treatment, resulting in lower complications rates. However, in advanced cases, the ablation of wide involved external female genitalia aims to achieve local disease control, and at the same time to restore the form and function of these organs. Despite a growing trend to reduce the extent of surgical resection, impaired quality of life after surgery due to severe sexual dysfunction and disturbed body image is common. The integration of surgical techniques for vulvar reconstruction into primary treatment after demolishing surgery would improve aesthetic and functional results and therefore quality of life. Actually there is a lot of applied techniques including various skin flaps, both with random vascularisation and those based on vascular territories (ie, axial pattern, fasciocutaneous, musculocutaneous, and bowel flaps), they can restore important parts of vulvovaginal form and function with acceptable morbidity at the donor and recipient sites. Appropriate vulvovaginal reconstruction necessitates specialists who are familiar with general principles of reconstructive surgery to master many techniques to select the optimum procedure for the individual patient.[17]

An important challenge for the near future will be the improvement of the management of advanced disease. The reduction of treatment requires a considerable effort in education of both health care workers and the general public.

Radiotherapy

The criteria for the use of radiotherapy as adjuvant therapy after radical vulvectomy are still unclear and undefined. Adjuvant radiotherapy is generally applied in cases when the primary tumor is not completely resected, in presence of lymph node metastases, when primary tumor is large, with invasion of lymph-vascular spaces, all associated with the increased risk of local recurrence.[18]

Chemoradiation

Combined chemoradiation is used in the cases of advanced vulvar cancer where radical surgery obtaining clear margins cannot be applied. Neoadjuvant chemoradiation has a primary role to reduce tumor volume achieving resectability with standard radical surgery. A GOG phase II chemoradiation study with cisplatin and 5-fluorouracil, obtained 48% patients had no visible tumor and additional 34% had complete pathologic remission.[20] Information on neoadjuvant chemoradiation

in vulvar cancer are limited, recommendation regarding the optimal drug regimen is unresolved. The main disadvantage of combined chemoradiation is increased morbidity. Surgical interventions after completed chemoradiation have high complication rates and the impact of tumor bed resection in cases of complete remission is unclear.[18] A Cochrane review of five studies on neoadjuvant chemoradiation showed considerable toxicity, therefore cautious indication of this treatment modality was recommended.[21]

Chemotherapy

Chemotherapy as a single treatment modality is actually not recommended in a primary vulvar cancer treatment. However, in metastatic recurrent disease after radiotherapy combination with cisplatin and vinorelbin resulted in progression free survival of 10 months and overall survival of 19 months.[22]

Our results

Five-year survival among patients with negative inguinofemoral nodes is 70–93% compared to 25–41% in patients with positive nodes.[19] Our results showe five-year survival of 68.7% among squamous cell vulvar cancer patients in stage IB or more with negative nodes (N=35) and 47.2% with positive nodes. Significantly better outcome rate had patients with unilateral positive node (N=13; survival rate of 75.5%), compared to the patients with bilateral positive nodes (N=9; survival rate of 11.1%). There are conflicting results regarding the impact of the number of metastatic lymph-nodes and the effectiveness of radiotherapy in survival. Current recommendations include the use of adjuvant radiotherapy of the inguinofemoral region in the cases of two or more affected lymph-nodes without extracapsular involvement. The value of adjuvant radiotherapy in case with single intranodal metastasis remains unresolved as well as the therapeutic option in cases with micrometastasis detected during ultrastaging procedure; similar is the problem of increased pelvic lymphatic involvement in cases with inguinofemoral positive lymph nodes.[18]

Conclusion

Vulvar cancer is a rare disease with a good prognosis only in cases of early stage. Less radical approach in surgical management of early stages with implementation of sentinel node identification techniques and the use of triple incision in radical vulvectomy, decreased treatment associated morbidity with similar outcome results.

Advanced disease requires individualized approach including combination of chemoradiation option and surgery, but it is associated with increased complication rate and undefined benefit in final outcome.

The centralization of cases will facilitate the use of optimal treatment and patient recruitment for clinical studies.

Finally, a new staging system adopted in 2009 should be applied in all cases with invasive vulvar cancer.

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VIJESTI
NEWS

2. HRVATSKI KONGRES GINEKOLOŠKE ONKOLOGIJE
Zagreb, Hotel »Dubrovnik«, 15.–17. XI. 2012.

Organizator. Hrvatsko ginekološko onkološko društvo (HGOD) uz European Society of Gynaecological Oncology (ESGO) Session

Voditelj kongresa. Prof. dr. Vlastimir Kukura, Klinika za ženske bolesti i porode, KB »Merkur«, Zagreb, Zajčeva 19.

Teme kongresa.

I. Preinvazivne lezije stidnice, rodnice i vrata maternice (Dubravko Barišić)
II. Rak stidnice, rodnice i vrata maternice (Ante Čorušić)
III. Rak endometrija (Herman Haller)
IV. Rak jajnika i jajovoda (Vladimir Kukura)
V. Rak dojke (L. Markulin-Grgić)

Pozivna predavanja, slobodna priopćenja, posteri, videoprezentacije, satelitski simpoziji.

Kotizacija. Do 15. rujna 2012. za članove HGOD (s plaćenom članarinom) 1000 Kn, za ostale 1200 Kn. Od 16. rujna i na mjestu za članove HGOD 1300 Kn, za ostale 1500 Kn. Specijalizanti, umirovljeni liječnici i medicinske sestre 800 Kn a osobe u pratnji i izlagači 500 Kn.

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