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THE EFFECT OF EARLY CERVICAL CANCER DIAGNOSIS

UČINEK ZGODNJE DETEKCIJE CERVIKALNEGA KARCINOMA

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Abstract

Background   *Treatment effectiveness and clinical outcome of patients with cervical carcinoma FIGO stage IA1 and IA2 are analyzed in three different time period at the Department of Obstetrics and Gynecology Rijeka, Croatia.*

Methods   *Retrospective analysis of the hospital chart of all cervical cancer patients between 1991 and 2005 was conducted with five-year follow up.*

Results   *Data on cervical cancer distribution by stage and five-year survival are presented. Separately analyzed age, histology type and treatment modalities in stage FIGO IA1 and IA2 during three consecutive five-year periods are presented.*

Conclusions   *Conservative surgical approach – conization alone in stage IA1 of the squamous cell carcinoma is reasonable and safe treatment option for reproductive active women. During observed periods conization became the most used surgical technique applied in almost two third of FIGO IA1 cervical cancer patients. Lymph vascular space invasion in stage IA1 lead to adjunct pelvic lymphadenectomy with unclear clinical benefit. In cervical cancer patients stage IA2 simple hysterectomy and pelvic lymphadenectomy could be accepted as a standard treatment. In these patients further studies are recommended to evaluate other less radical surgical techniques – simple and radical trachelectomy with or without pelvic lymphadenectomy. Radical hysterectomy in both stages IA1 and IA2, based on personal experience and literature data represents a surgical overtreatment and should be abandoned.*

Key words   *cervical cancer; conization; hysterectomy; FIGO; radical hysterectomy*

Izvleček

Izhodišča   *Prikazujemo uspeh zdravljenja bolnic z mikroinvazivnim rakom materničnega vratu (RMV) stadija IA1 in IA2 po standardu FIGO v treh različnih obdobjih na Kliniki za ginekologijo in porodništvo Rijeka, Hrvaška.*

Metode   *Retrospektivna analiza popisov bolezni ter 5-letnega sledenja (follow up) bolnic z RMV, obravnavnih v letih 1991 do 2005.*

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Rezultati   *V prispevku prikazujemo podatke o porazdelitvi bolnic z RMV glede na stadij in njihovo petletno preživetje. Starost bolnice, histopatološki tip in vrsta zdravljenja pri RMV stadija IA1 in IA2 analiziramo ločeno glede na 3 zaporedna petletna obdobja.*

Zaključek   *Konzervativno kirurško zdravljenje – konizacija – pri stadiju IA1 je smiselna in varna izbira za ženske v rodnem obdobju. Med opazovanim obdobjem je postala konizacija najpogostejša izbira zdravljenja in smo jo uporabili pri skoraj dveh tretjinah bolnic z mikroinvazivnim RMV stadija IA1. Pri ugotovljenem vdiranju v limfno-žilni prostor (LVSI – limfo-vaskularna infiltracija) smo pri bolnicah napravili pelvično limfadenektomijo, vendar klinična korist tega postopka ni povsem jasna. Pri stadiju IA2 bi bila histerektomija s pelvično limfadenektomijo lahko standardno zdravljenje. Pri teh bolnicah so za oceno manj radikalnih konzervativnih kirurških tehnik – enostavne ali radikalne trahelektomije – potrebne nadaljnje raziskave. Radikalna histerektomija je tako po izkušnjah avtorjev kot po podatkih iz literature čezmerno kirurško zdravljenje bolnic z mikroinvazivnim RMV stadijev IA1 in IA2, zato jo je treba opustiti.*

Ključne besede   *rak materničnega vratu; konizacija; histerektomija; FIGO; radikalna histerektomija*

Introduction

The last FIGO revision of cervical carcinoma in 1994 defined microinvasive cervical cancer as stage IA1 and IA2 (1). Lesions were determined with a depth of stromal invasion of maximal 3 mm and 5 mm with a maximal horizontal spread of 7 mm, respectively. The depth of stromal invasion should be measured from the base of the epithelium, either squamous or glandular. The diagnostic, still unresolved, problem represents isolated foci of atypical cell in the stroma. Lymph vascular space involvement (LVSI) does not alter the stage, but represents a risk factor for either recurrence or metastases. At the same time LVSI may alter the treatment decisions widening the surgical procedure on the cervix and necessitating pelvic lymphadenectomy because of the risk of pelvic lymph node metastases. The diagnosis is based exclusively on microscopic examination of the cone specimen.

The incidence of microinvasive cervical cancer increases affecting at predominantly women under fifty years. The treatment policy in early stage of the disease is still controversial. Conization, hysterectomy, radical hysterectomy as well as radical trachelectomy are applied in the treatment of stage IA1, while hysterectomy, radical hysterectomy or radical trachelectomy in stage IA2.[2-6] The significant FIGO statistics showed that the patient outcome in stage IA1 and IA2 are very satisfactory, 97.5 % and 94.8 %, respectively.[7]

The aim of this single centre retrospective study was to assess the incidence rate, mode of treatment and five-year survival of microinvasive (IA1 and IA2) cervical cancer patients in our institution during 15 years period.

Methods

The hospital records of all cervical cancer patients treated during the period from January 1991 to December 2005 at the Department of Obstetrics and Gynecology, Clinical Hospital Centre of Rijeka, Croatia were reviewed. A total of 746 records of the patients with cervical cancer were selected.

The patients underwent standard protocol for diagnosis and evaluation of distant disease according to the FIGO recommendation. All patients staged IA1 and IA2 underwent one of the standard surgical procedures as conization or hysterectomy. Those patients with stage IB1 and above were staged according to the surgical pathological staging, while those treated primary with oncologic treatment (radiotherapy, chemoterapy and combined treatment) were staged according FIGO clinical recommendation. Cases treated before 1995 were retrospectively staged according to the 1994 FIGO nomenclature.[1] FIGO stage and analyzed clinical data included patient's age and type of definitive surgical procedures were stored in apposite data base.

Histopathologic examination was performed in standard means. The surgical margins of each cone specimen was marked with ink and bisected along to axis of the endocervical canal. Each half was additionally cut at 4–5 mm intervals in a plane parallel to the axis of the canal. Each block was serially sectioned. According to the dimension, from each cone 40–90 sections were obtained. The cervices of the extirpated uteri were opened longitudinally and sectioned along the axis at 3–4 mm intervals in separate blocks. From each block 5 sections were cut. Histologic evaluation comprised depth of invasion and lateral spread of the tumor, LVSI and involvement of the surgical margins.

Mean duration of follow-up was 80 months. During follow-up period we examined the number of death and five-year survival rate.

The data were analyzed using the MedCalc Version 9.5.2.0. The results are expressed by means, standard deviation, median, minimum, maximum, as well as percent. The statistical significance is calculated using t-test, chi-test or two tailored Fisher's exact test. Kaplan Meyer product limit method was applied in analysis of five-year survival rate.

Results

The distribution of FIGO stage among cervical cancer patients in the three time periods, the survival in each stage and the survival per entire group is

Table 1. *Distribution of cervical cancer patients in Rijeka (n = 746) according to FIGO standard.*

Tab. 1. *Porazdelitev bolnic z rakom materničnega vratu z Reke po FIGO standardu (št. = 746).*

	1991–1995		1996–2000		2001–2005		Statistical significance Statistična značilnost
	(N) (Št)	Survival Preživetje	(N) (Št)	Survival Preživetje	(N) (Št)	Survival Preživetje	
IA1	(81)	100.0 %	(83)	97.6 %	(129)	99.2 %	NS
IA2	(7)	100.0 %	(3)	100.0 %	(4)	100.0 %	NS
IB1	(55)	79.0 %	(50)	93.8 %	(78)	97.2 %	**P = 0.003**
IB2	(12)	64.2 %	(14)	49.4 %	(18)	87.4 %	NS
IIA	(6)	66.7 %	(6)	80.0 %	(5)	80.0 %	NS
IIB	(34)	42.7 %	(20)	45.0 %	(16)	40.2 %	NS
IIIA	(2)	0.0 %	(2)	0.0 %	(0)		NS
IIIB	(32)	25.7 %	(43)	17.2 %	(24)	31.4 %	NS
IVA	(2)	0.0 %	(1)	0.0 %	(6)	16.7 %	NS
IVB	(1)	0.0 %	(4)	0.0 %	(8)	0.0 %	NS
Total Skupaj	**(232)**	**71.3 %**	**(226)**	**72.0 %**	**(288)**	**85.4 %**	P = 0.0001

presented in Table 1. Staging is the most important predictor of survival, reflecting the extent of the disease with the risk of death being higher as a stage increases. Comparing total survival between the three periods, there is a clear significant higher five-year survival rate among patients treated in the third time period. However, patients distribution per stage (Chi square 40.5; p = 0.0018) shows statistical difference. In the third period patient's stage IA1 and IB1 were more frequent present. The evaluated patient age (48.7 vs. 51.1 vs. 46.2 years) is equal in the first and second time period. However, patients in the third time period are significantly younger (period 1 vs. period 3 P = 0.004; period 2 vs. period 3 P = 0.0002). All patients within the same FIGO stage show equal survival rate between three time periods except patients staged FIGO IB1.The mentioned group of patients treated in the second and third period had significantly better survival rate than the patients treated in the first period.

The ratio of group of patients staged IA1, combined stages IB1, IB2 and IIA as well as stages IIB and higher were different in the three time period (Chi square 14.3; P = 0.0065). The results are shown in Table 2. Ratio of patients staged IA1 show borderline increase in the third period (Chi square 6.7; P = 0.058), while combined group IB1 to IIA was equally distributed throughout the observed time periods. The group of advanced cervical cancer stage IIB and higher show significant decrease in the third time period (Chi-square 13.8; P = 0.0002). Survival was equal in the group of patient's stage FIGO IA1 and the group FIGO IIB and higher in the three analyzed time periods. Patients group FIGO IB1 – IIA show better five-years survival in the second and third observed time period (Chi square 12.0; P = 0.0024).

In our study, FIGO stage IA1 was present in 293 (39.3 %) patients out of 746. In the second time period we found an increase from 34.9 % to 36.7 %, while 44.8 % of patients were present in the third time (Tab. 2). The types of patient treatment in stage IA1 are presented in the Table 3. An increase in conservative surgical treatment is identifies during three time periods, from 48.1 % in the first time period to 63.6 % in the third time period. Statistical significance is reached comparing the ratio of conization vs. all type of hysterectomy between first and third time period (Chi square 4.2; P = 0.04).

Table 2. *Cervical cancer patients distribution and five-year survival during three observation periods.*

Tab. 2. *Porazdelitev bolnic z rakom materničnega vratu v treh opazovalnih obdobjih in petletno preživetje.*

	1991–1995	1996–2000	2001–2005
IA1	81 (34.9 %)	83 (36.7 %)	129 (44.8 %)
5-year survival Petletno preživetje	**100.0 %**	**97.6 %**	**99.2 %**
IB1-IB2-IIA	73 (31.5 %)	70 (31.0 %)	101 (35.0 %)
5-year survival Petletno preživetje	**75.5 %**	**84.9 %**	**94.7 %**
IIB-IIIA-IIIB-IVA-IVB	71 (30.6 %)	70 (31.0 %)	54 (18.8 %)
5-year survival Petletno preživetje	**32.1 %**	**22.3 %**	**27.8 %**

Table 3. *Surgical procedures in cervical cancer patients stage IA1 during three observation periods.*

Tab. 3. *Vrsta kirurškega zdravljenja pri bolnicah z rakom materničnega vratu stadija IA1 v treh opazovalnih obdobjih.*

	1991–1995	1996–2000	2001–2005
Conization Konizacija	39 (48.1 %)	43 (51.8 %)	82 (63.6 %)
Hysterectomy Histerektomija	26 (32.1 %)	21 (25.3 %)	27 (20.9 %)
Hysterectomy with lymphadenectomy Histerektomija z limfadenektomijo	14 (17.3 %)	13 (15.7 %)	14 (10.9 %)
Radical hysterectomy Radikalna histerektomija	2 (2.5 %)	6 (7.2 %)	6 (4.7 %)
Total Skupaj	**81 (100 %)**	**83 (100 %)**	**129 (100 %)**

Simplex hysterectomy, hysterectomy with concomitant pelvic lymphadenectomy and radical hysterectomy show decrease during the observed time.

There is an obvious difference in patients age among group of patients underwent conization and the group of patients with hysterectomy/radical hysterectomy (Tab. 4). The mean age of patients underwent conization (N = 164) during all time periods is 35.5 (SD = 6.6), significantly younger (t-test = 9.2; P < 0.0001) than the group of patients underwent hysterectomy/radical hysterectomy (N = 129) with mean age of 44.5 (SD = 10.0) years (data not shown in the tables).

Table 4. *Age distribution among cervical cancer patients stage IA1 according to three different time periods.*

Tab. 4. *Starostna porazdelitev bolnic z rakom materničnega vratu stadija IA1 glede na različna časovna obdobja.*

	1991–1995	1996–2000	2001–2005
Conization Konizacija	35.2 ± 5.8 (Min 25, Max 51)	35.9 ± 6.5 (Min 23, Max 54)	35.5 ± 7.2 (Min 21, Max 53)
Hysterectomy Histerektomija	42.2 ± 7.9 (Min 34, Max 68)	46.7 ± 9.6 (Min 33, Max 71)	48.7 ± 11.1 (Min 31, Max 77)
Hysterectomy with lymph-adenectomy Histerektomija z limf-adenektomijo	40.4 ± 9.5 (Min 30, Max 64)	39.8 ± 4.8 (Min 29, Max 49)	45.9 ± 12.5 (Min 31, Max 82)
Radical hyste-rectomy with lymphadenectomy Radikalna histe-rektomija z limfadenektomijo	46.0 ± 15.6 (Min 35.0, Max 57.0)	40.0 ± 10.5 (Min 31, Max 57)	48.2 ± 8.6 (Min 38, Max 60)
Total Skupaj	**38.6 ± 8.0 (Min 25, Max 68)**	**39.5 ± 8.6 (Min 23, Max 71)**	**40.0 ± 10.6 (Min 21, Max 82)**

The histologic characteristic of the groups of patient stage IA1 during three time periods are shown in the table 5. There is no difference in the presence of adenocarcinoma, stromal invasion and lymph-vascular space involvement.

Table 5. *Histopathologic characteristics in the specimens of cervical cancer stage IA1 during three different time periods.*

Tab. 5. *Histopatološke značilnosti pri raku materničnega vratu stadija IA1 v treh časovnih obdobjih.*

	1991–1995	1996–2000	2001–2005
Planocellular cancer Ploščatocelični rak	80 (98.8 %)	82 (98.8 %)	123 (95.3 %)
Adenocarcinoma Adenokarcinom	1 (1.2 %)	1 (1.2 %)	6 (4.7 %)
Cervix stromal invasion ≤ 1 mm Stromalna invazija v cerviks ≤ 1 mm	67 (82.8 %)	63 (76.0 %)	106 (82.2 %)
Cervix stroma invasion > 1 to ≤ 2 mm Stromalna invazija v cerviks > 1 do ≤ 2 mm	7 (8.6 %)	10 (12.0 %)	15 (11.6 %)
Cervix stromal invasion > 2 to ≤ 3 mm Stromalna invazija v cerviks > 2 do ≤ 3 mm	7 (8.6 %)	10 (12.0 %)	8 (6.2 %)
Lymph-vascular space invasion (LVSI) Invazija v limfo-vaskularni prostor	1 (1.2 %)	6 (7.2 %)	5 (3.9 %)
Total Skupaj	**81 (100 %)**	**83 (100 %)**	**129 (100 %)**

The surgical option in the treatment of stage IA2 patients during three time period and histologic characteristics are shown in the table 6 and 7, respectively. There are no positive lymph nodes, neither parametrial invasion among cervical cancer patients stage IA1 and IA2.

Table 6. *Surgical procedures in cervical cancer patients stage IA2 during three observation periods.*

Tab. 6. *Vrsta kirurškega zdravljenja pri bolnicah z rakom materničnega vratu stadija IA2 v treh opazovalnih obdobjih.*

	1991–1995	1996–2000	2001–2005
Hysterectomy Histerektomija	5 (71.41 %)	1 (33.3 %)	0 (20.9 %)
Hysterectomy with lymphadenectomy Histerektomija z limfadenektomijo	1 (14.3 %)	0	1 (25.0 %)
Radical hysterectomy Radikalna histerektomija	1 (14.3 %)	2 (66.7 %)	3 (75.0 %)
Total Skupaj	**7 (100 %)**	**3 (100 %)**	**4 (100 %)**

Table 7. *Histopathologic charecteristics in the specimens of cervical cancer stage IA2 during three different time periods.*

Tab. 7. *Histopatološke značilnosti pri raku materničnega vratu stadija IA2 v treh časovnih obdobjih.*

	1991–1995	1996–2000	2001–2005
Planocellular carcinoma Ploščatocelični karcinom	7	1	3
Adenocarcinoma Adenokarcinom	0	2	1
Cervix stromal invasion > 3 to ≤ 4 mm Stromalna invazija v cerviks > 3 do ≤ 4 mm	3	2	2
Cervix stromal invasion > 4 to ≤ 5 mm Stromalna invazija v cerviks > 4 do ≤ 5 mm	4	1	2
Lymph-vascular space invasion (LVSI) Invazija v limfo-vaskularni prostor	3 (42.9 %)	0	3 (75.0 %)
Total Skupaj	**7**	**3**	**4**

There is no statistical significance between three analyzed different period groups.

Discussion

The diagnosis of stage IA1 and IA2 cervical cancer has to be established by microscopic examination of cone specimen. An alternative surgical technique could be a large loop excision of the transformation zone (LLETZ). Taking into account the actual FIGO classification stromal invasion as well as horizontal spread represents one of major prognostic factors. At the same time it should be a guide in treatment option and prognosis. Other two risk factors represent

marginal status and lymph vascular space involvement (LVSI). The presence of stromal invasion less than 3 mm without LVSI and those with invasion greater than 3 mm or presence of LVSI irrespective to stromal depth from the therapeutic point of view in practice represents two distinct entities. Both entities have very high survival rate and it seems that former doesn't carry a risk of parametrial and nodal involvement, as shown also in our series of patients.

In our institution a total of 164 patients with micro-invasive cervical cancer stage IA1 were treated with conization alone as a definitive surgical procedure during three separate time periods. It represents 56 % of all cervical cancer patients stage IA1. Microinvasive disease has been managed historically with a variety of procedures that ranged from radical hysterectomy with lymphadenectomy to total hysterectomy.[8] From our results, the younger patients and especially those with uncompleted reproduction are candidates for conservative management. The mean age of 35 years compared to the older patients in whom hysterectomy is offered and performed introduce a logic and acceptable surgical approach to the early cervical cancer stage FIGO IA1, an easy controllable disease. Based on our results as on the results of the great FIGO statistics,[7] five-year survival is excellent confirming the conservative approach for the younger patients.

Cervical cancer patients stage IA1 in our material comprises about 40 % of all cervical cancer patients.[9] More than two thirds of the patients with less than 1 mm of stromal invasion, while only small proportion of patients had invasion between 3 and 5 mm. Our results shows relative increase in microinvasive cervical cancer compared with the FIGO statistics,[7] but is in accordance with other single centre reports.[3, 10] Partial explanation of observed phenomenon could be related to the great number of serial sections (40–70) through the paraffin blocks of cone specimens, routinely obtained in our laboratory.

Actually rates of parametrial and lymph node involvement are negligible and the patients can be treated with simple hysterectomy without lymphadenectomy. Conization, as surgical procedure in stage IA1 cervical cancer patients remains recommended. According to the literature data, cervical cancer patients stage IA1 indicate that approximately 96 % of cases treated conservatively are alive and disease free after 5 years. In this group of patients recurrence rate ranged from 2.7 % to 9 %.[11-13] The actual guidelines for conservative treatment of cervical cancer patients should consider only the histological characteristic of the cone biopsy specimen. Significance of increasing age, positive endocervical curettage, positive cone margins and increasing neoplastic severity were attributed to the presence of residual disease on hysterectomy specimen after conization (14). Same authors explained the menopausal status as a risk factor that could be related to the relative difficulty of eradicating the lesion completely in older patients due to the retracted transformation zone. We did not perform routinely endocervical curettage after conization, and in our material we did not take into account the menopausal status. However, the conization, as therapeutic approach

was infrequently used in postmenopausal women. A cooperative study of Gadducci et al.[15] show that among north italian institutions, conization was performed in 30 (21 %) out of 143 patients, significantly lesser than in our study. In the same paper hysterectomy (49.4 %) and radical hysterectomy with pelvic lymphadenectomy (32.5 %) were applied more frequently as compared with our results.

Positive resection margin (lateral and endocervical) for CIN, should be considered as risk factors for further conservative management.[16, 17] Furthermore, apical clearance defined as a distance from tumor margin and the lateral margin and apex of the cone biopsy could be used as additional parameter to optimize the conservative management of stage IA1 cervical cancer patients.[12] Irrespective to several reports that showed the role of dysplastic lesions on the resection margin to be responsible of recurrence, on hysterectomy specimens performed for this indications a histological defined cervical lesion was found only in 40 % of cases[18, 19]

However, residual lesions were also found in 8–24 % of patients with negative resection margins precluding politopic disease development in the uterine cervix.[2, 20] Furthermore, patients treated only with conization and without present positive margin(s) are not exempted from the risk of recurrence. The use of human papillomavirus status detection after loop electrosurgical conization combined with classical surgical margins status in patients with cervical intraepithelial neoplasia could allow subvision of patients at different risk of recurrence, requiring new tailored surveillance procedures,[21] but further studies are necessary to evaluate the precise role.

There was a low risk for lymph node metastases, recurrence and death in microinvasive cervical carcinoma.[2, 11, 22] In our material there were no positive lymph nodes among 55 and 8 patients staged IA1 and IA2, respectively. However, a wide range of incidence of lymph node metastases in stage IA disease was reported, from 0 %[23] to 5.5 %.[24] No consensus regarding the significance of LVSI in predicting lymph node metastases was achieved. The risk of lymph node metastases was present in 0.3 % in microinvasive cervical cancer with less than 3 mm of stromal invasion and no LVSI, as compared with 2.6 % if the LVSI was present.[25] Other investigators found higher incidence of pelvic lymph node metastases – 1.7 % in stage IA1 but without correlation with LVSI.[26] LVSI as a parameter not considered in actual FIGO classification, in our opinion, irrespective to our finding, should remain a risk factor and only further evaluation would clarify its precise meaning and prognostic significance.

Involvement of the parametrial has not been extensively reported in the literature, and was similar to our results, i.e. no parametrial involvement was detected. Parametrial resection may not be necessary in microinvasive cervical cancer. If we accepted such point of view, then a standard therapeutic approach in cervical cancer stage IA2 could be a simple hysterectomy with pelvic lymphadenectomy. Conservative treatment in patients who did not reach complete reproduction

could include wide conization or amputation of the cervix (simple trachelectomy without parametrial resection) with pelvic lymphadenectomy. Parametrial dissection during radical trachelectomy than can represent some degree of overtreatment. Three studies[27-29] incorporate results of conservative approach in cervical cancer stage IA2, indicating possible conservative surgery. However, there is no conclusive recommendation, firstly due to very small number of patients and miscellaneous stage (IA1-IA2-IB1), histologic subtypes (squamous-adeno) and different treatment modalities. Informations of such approach are needed on large number of patients with IA2 cervical cancer before such approach would be widely adopted.

Finally, it should be emphasized the need for individualization of the treatment in microinvasive cervical cancer patients. Individualization should includes multiple factors, some of them related to the patients and other based exclusively on the comprehensive evaluation of cone specimens. Patient age, childbearing desire, cancerphobia and compliance to regular follow up should be assessed in conjunction with tumor dimensions and depth of invasion, marginal status and lymph vascular space invasion.

Conclusion

From our results and literature data conservative surgical approach – conization alone in stage IA1 cervical cancer is reasonable and safe treatment option, especially for those who did not reach complete reproduction. Status of the margins is a crucial histologic parameter. Lymph vascular space involvement in our material was not beneficial in identification of lymph node involvement, but we support the idea that it remains a risk factor including the necessity of pelvic lymph node dissection.

The optimal treatment in cervical cancer patients stage IA2 remains unresolved. The use of simple hysterectomy with pelvic lymphadenectomy could be accepted as a standard treatment. In patients with uncompleted reproduction conservative option could be applied – wide conization or cervical amputation – simple trachelectomy without parametrial resection and with pelvic lymphadenectomy. Such treatment modality should be applied on large number of patients before it becomes a standard procedure.

References

1. Creasman WT. New gynecologic cancer staging. Gynecol Oncol 1995; 58: 157–8.
2. Kolstad P. Follow-up study of 232 patients with stage Ia1 and 411 patients with stage Ia2 squamous cell carcinoma of the cervix (microinvasive carcinoma). Gynecol Oncol 1989; 33:265–72.
3. Burghardt E, Girardi F, Lahousen M, Pickel H, Tamussion K. Microinvasive carcinoma of the uterine cervix. (International Federation of Gynecology and Obstetrics Stage IA). Cancer 1991; 67: 1037–45.
4. Benedet JL, Anderson GH. Stage IA carcinoma of the cervix revisited. Obstet Gynecol 1996; 87: 1052–9.
5. Creasman WT, Zaino RJ, Major FJ, DiSaia PJ, Hatch KD, Homesley HD. Early invasive carcinoma of the cervix (3 to 5 mm invasion): risk factors and prognosis. A Gynecologic Oncology Group study. Am J Obstet Gynecl 1998; 178: 62–65.
6. Dargent D, Martin X, Sacchetoni A, Mathevet P. Laparoscopic vaginal radical trachelectomy: A treatment to preserve the fertility of cervical carcinoma patients. Cancer 2000; 88: 1877–82.
7. Quinn MA, Benedet JL, Odicino F, Maisonneuve P, Beller U, Creasman WT. Carcinoma of the cervix uteri. FIGO Annual Report on the Results of Treatment in Gynecological Cancer. Int J Gynecol Obstet 2006; 95 Suppl 1: S43–103.
8. Jones WB, Mercer GO, Lewis JL Jr, Rubin SC, Hoskins WJ. Early invasive carcinoma of the cervix. Gynecol Oncol 1993; 51: 26–32.
9. Haller H, Rupčić S, Krašević M, Begonja R, Stamatović M, Mamula O. Treatment of invasive cervical cancer: Rijeka Experience. Coll Antropol 2007; 31: 139–46.
10. Motta F. Microinvasive squamous carcinoma of the cervix: treatment modalities. Acta Obstet Gynecol Scand 2003; 82: 505–9.
11. Van Nagell J, Greenwell N, Powell D, Donaldson ES, Hanson MB, Gay EC. Microinvasive carcinoma of the cervix. Am J Obstet Gynecol 1983; 145: 981–91.
12. Raspagliesi F, Dito A, Quattrone P, Solima E, Fontanelli R, Dousias V, et al. Prognostic factors in microinvasive cervical squamous cell cancer: long term results. Int J Gynecol Cancer 2005; 15: 88–93.
13. Ostor AG. Studies on 200 cases of early squamous cell carcinoma of the cervix. Int J Gynecol Pathol 1993; 12: 193–207.
14. Lin H, Chang Y, Huang CC, Changchien CC. Prediction of disease persistence after conization for microinvasive cervical carcinoma and cervical intraepithelial neoplasia grade 3. Int J Gynecol Cancer 2004; 14: 311–6.
15. Gadducci A, Sartori E, Maggino T, Landoni F, Zola P, Cosio S, et al. The clinical outcome of patients with Stage Ia1 and Ia2 squamous cell carcinoma of the uterine cervix. A Cooperation Task Force (CTF) study. Eur J Gynaecol Oncol 2003; 24: 513–6.
16. Phongnarisorn C, Srisomboon J, Khunamornpon S, Siriaungkul S, Suprasert P, Charoenkwan K, et al. The risk of residual neoplasia in women with microinvasive squamous cervical carcinoma and positive cone margins. Int J Gynecol Cancer 2006; 16: 655–9.
17. Park JY, Lee SM, Yoo CW, Kang S, Park SY, Seo SS. Risk factors predicting residual disease in subsequrnt hysterectomy following conization for cervical intraepithelial neoplasia (CIN) III and microinvasive cervical cancer. Gynecol Oncol 2007; 107: 39–44.
18. Morris M, Mitchell M, Silva E, Coppeland L, Gershenson D. Cervical conization as a definitive therapy for early invasive squamous carcinoma of the cervix. Gynecol Oncol 1993; 51:193–6.
19. Monk A, Pushkin S, Nelson A, Gunning J. Conservative management of options for patients with dysplasia involving cervical margins of cervical cone biopsy specimen. Am J Obstet Gynecol 1996; 174: 1695–700.
20. Greer BE, Figge DC, Tamimi HK, Cain JM, Lee RB. Stage IA2 squamous carcinoma of the cervix: difficult diagnosis and therapeutic dilemma. Am J Obstet Gynecol 1990; 162: 1406–9.
21. Prato B, Ghelardi A, Gadducci A, Marchetti I, Di Cristofano C, Di Coscio G, et al. Correlation of recurrence rates and times with posttreatment human papillomavirus status in patients treated with loop electrosurgical excision procedure conization for cervical squamous intraepithelial lesions. Int J Gynecol Cancer. 2008; 18: 90–4.
22. Takeshima N, Yanoh K, Tabata T, Nagai K, Hirai Y, Hasumi K. Assessment of the revised International Federation of Gynecology and Obstetrics staging for early invasive squamous cervical cancer. Gynecol Oncol 1999; 74: 165–9.
23. Sedlis A, Sall S, Tsukada Y, Park R, Mangan C, Shingleton H, et al. Microinvasive carcinoma of the uterine cervix: a clinical-pathologic study. Am J Obstet Gynecol 1979; 133: 64–74.
24. Maiman MA, Fruchter RC, DiMaio TM, Boyce JC. Superficially invasive squamous cell carcinoma of the cervix. Obstet Gynecol 1988,72: 399–403.
25. Copeland LJ, Silva EG, Gershenson DM, Morris M, Young DC, Wharton JT. Superficially invasive squamous cell carcinoma of the cervix. Gynecol Oncol 1992; 45: 307–12.
26. Lee KB, Lee JM, Park CY, Lee KB, Cho HY, Ha SY. Lymph node metastasis and lymph vascular space invasion in microinvasive squamous cell carcinoma of the uterine cervix. Int J Gynecol Cancer 2006; 16:1184–7.

27. Rob L, Charvat M, Robova H, Pluta M, Strnad P, Hrehorcak M, et al. Less radical fertility-sparing surgery than radical trachelectomy in early cervical cancer. Int J Gynecol Cancer 2007; 17:304–10.
28. Landoni F, Parma G, Peiretti M, Zanagnolo V, Sideri M, Colombo N, et al. Chemo-conization in early cervical cancer. Gynecol Oncol 2007; 107 Suppl 1: S125–6.
29. Bisseling KC, Bekkers RL, Rome RM, Quin MA. Treatment of micro-invasive adenocarcinoma of the uterine cervix: a retrospective study and review of the literature. Gynecol Oncol 2007; 107: 424–30.