

THE RATIONALE FOR HYSTERECTOMY AFTER UTERINE CERVIX CONIZATION

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Summary. *Our aim was to investigate the incidence, most common indications and adequacy of hysterectomy after uterine cervix conization. We have retrospectively analyzed the patients with conization treated at the Clinic of Gynecology and Obstetrics in Niš from 2000 to 2004. There were 306 uterine cervix conizations performed in total. In 54 patients, on the average in 17.64% hysterectomy was done after conization. Out of all the indications for hysterectomy after conization, the most common was microinvasive and invasive uterine cervix carcinoma in 59.25% and positive conization margins in 27.77%. The analysis of histopathologic findings obtained at hysterectomy following conization demonstrated that hysterectomy was too extensive in 70.37% of the cases, since in 27.77% the findings were benign and in 42.59% of the cases cervical intraepithelial neoplasia (CIN) was identified, for which surgical reintervention would have been sufficient. In the cases of microinvasive and invasive carcinoma, hysterectomy (radical) was demonstrated to be adequate (and that is of statistical significance), since in 80% the findings were identical at hysterectomy. Conclusion. The most common indication for hysterectomy after conization is microinvasive and invasive uterine cervix carcinoma, immediately followed by positive conization margins. Hysterectomy is not an adequate surgical reintervention for positive conization margins, since in 70.37% of the cases it proved to be a too extensive surgery.*

Key words: *Hysterectomy, conization, conization margins*

Introduction

Uterine cervix conization is an independent diagnostic and therapeutic procedure for the treatment of high stage intraepithelial lesions (HSIL) and selected cases of microinvasive carcinoma Ia1 in young patients with unfulfilled reproductive function where the depth of invasion is 1 mm and where there is no lymphovascular invasion. This excision technique enables tissue sampling for subsequent histopathologic analysis (HP). Since biopsy of the uterine cervix is a subjective method and there is agreement as to the biopsy site among those who perform colposcopy in only 77.4% and by biopsy we obtain just one small piece of tissue, there is a disagreement of histopathologic findings of biopsy and conization (1). New papers present data that the total agreement of HP findings of biopsy and conization is 55.26%, while the conization finding is larger in 19.28% and smaller in 24.89% (2).

If the colposcopic finding is unsatisfactory or if pathologic colposcopic finding involves uterine cervix channel, it is necessary to combine cervical biopsy with cervical channel curettage (ECC) for more precise diagnosis. This is the way to improve HP diagnosis reliability related to cervical biopsy by 21% (3).

The aim of uterine cervix conization is to demonstrate the relationship of epithelial lesion with stroma and cervical glands in the excised lesion. Conization thus enables inspection of a larger tissue volume with more sections compared to biopsy, and it has been proven as reliable in verifying the possible presence of invasive disease. If there is invasion, conization enables precise determination of invasion depth, which further dictates disease staging and possible treatment.

Depending on the type, i.e. the site of a lesion, eversion of the borderline of the cylindrical and squamous epithelium of the uterine cervix and age of the patient, the length and shape of the cone are adjusted. Pathologic epithelium rarely spreads more than 1-2 cm into the cervical channel. It is essential that by conization we remove the whole transformation zone with the healthy tissue margin at least 2 mm thick. As for the cone depth, it is important that the treatment involve at least 7-10 mm depth beneath the surface, thus avoiding the possibility of residual disease in the cervical glands which can be affected at the depth of 5.2 mm, and which are involved in cervical intraepithelial neoplasm (CIN) disease stage III in 88.6% of the cases (4). In cases with pathologic change involving ectocervix and the patient is young, the cone should be shallow and broad, which is achieved with almost horizontal cutting through the

cervix, in contrast to the changes involving the cervical channel, for which the cone should be narrow and long. In order to avoid cutting through the involved glands, initial incision should run parallel to the channel before turning inwards, thus forming the dome formation which is better than cone formation, since the narrow cone tip could cut the crypts of the glands with CIN, leaving residual disease within the cone bed (5). After the cervical cone is removed, it is important to perform the curettage of the rest of the uterine cervix, since it is an important predictive factor in residual disease detection and possible relapse.

It is essential that after the conization the pathologist should report on the state of the conizate margins, curettage of the rest of the cervical channel and possible invasion and its precise depth. These parameters determine the need for an additional surgery (hysterectomy, classical or radical).

If the conizate margins of 2 mm into the healthy tissue are negative, without pathologic changes, there is no basal membrane involvement and the curettage of the remaining cervical channel is negative, the treatment is complete with this minor surgical intervention.

Some authors state that residual disease was found in 2-10% of the cases with negative conization margins (6). On the other hand, in about 40% of the patients with positive margins, residual disease could not be found on surgical reintervention (hysterectomy) (7).

In order to avoid iatrogenic tissue traumas with surgeries associated complications, especially ones influencing fertility of young patients, it is better to decide on surgical reintervention – a more conservative approach, reconization.

Aim of the paper

We aim at analysing the incidence and most common indications for hysterectomy after uterine cervix conization, as well as to establish the rationale of hysterectomy in patients with previous uterine cervix conization.

Method

In order to realise the above mentioned goals, a retrospective clinical study was conducted at the Clinic of Gynecology and Obstetrics, Dept. of Surgery.

The investigation enrolled all the patients with uterine cervix conization in the five year interval from 2000 through to 2004. The data required were collected retrospectively from the relevant documentation, surgical registries, patient histories and histories from the Council for Early Detection of Cancer.

The information was collected from all patients on their age and preoperative histopathologic findings on biopsy specimens. These biopsy findings were related to final histopathologic findings of the tissue obtained at conization and curettage of the rest of the cervical channel. The uterine cervix biopsy findings were compared to conizate findings. In addition to histopathology, we analysed the state of the lateral margins, conizate top and findings of endocervical curettage. Based on these

findings, the patients were divided into two groups: one group with uninvolved conizate margins (healthy; negative margins); and the other group with conizate margins and/or curettage findings of the rest of the channel involved with changes (positive, involved margins).

If further treatment consisted of surgical reintervention (hysterectomy), histopathologic findings of the specimen removed at second intervention were separately analysed. The results were investigated related to age, site of the changes and other parameters.

Histopathologic analysis of biopsy specimens and cervical tissue removed at conization and reconization was done at the Clinic of Pathology, Clinical Centre Nis. Biopsy or conizate tissue specimens were fixed in 10% formaldehyde water solution for 12 hours. Biopsy or conizate tissue specimens were then sectioned into sequential 5 µm thick blocks, HE and AB-PAS stained and examined according to the standard protocols. The cone was sectioned into at least 8-12 blocks, by Hazel Gore technique. Histopathologic findings were classified into the following categories: benign findings, CIN I, CIN II, CIN III, microinvasive and invasive carcinoma. Subclinical HPV (human papilloma virus) changes, inflammatory changes and metaplasia were considered benign. The Bethesda classification was used alongside in order for us to easily compare the data obtained. Negative conizate margins at histopathology were encountered in patients with resection margins of up to 2 mm into the healthy tissue, without pathologic changes.

The information was statistically processed using Student's t-test and chi square test. The results were presented in tables and graphs.

Results

Table 1 shows the distribution of hysterectomies after conization by the study years. There is no statistically significant difference in the number of hysterectomies after conization by the study years, since $\chi^2_e = 1.72 < \chi^2_{0.05} = 7.815$.

Table 1. Hysterectomy after conization by the year of study

Study years	Number of conizations done	Number of hysterectomies after conization	Percent
2000	53	9	19.68%
2001	52	8	15.38%
2002	73	12	16.43%
2003	62	13	20.63%
2004	66	12	18.18%
Total	306	54	17.64%

Distribution of the examinees with hysterectomy after conization was shown in Table 2. The highest percentage of hysterectomy-treated patients, of statistical significance, were over 45 years of age, since $\chi^2_e = 37.11 > \chi^2_{0.01} = 13.27$.

Table 2. Age-group distribution of patients with hysterectomy after conization

Age (years)	Number	Percent
< 25	2	3.70%
25 - 34	5	9.25%
35 - 44	19	35.18%
45 - 54	24	44.44%
>54	4	7.40%
Total	54	100.00%

Table 3 demonstrates that the most common indication for hysterectomy after conization was microinvasive and invasive carcinoma in 59.25% patients, while positive margins were the indication in 27.77%. The difference is of statistical significance, since $\chi^2_e = 6.14 > \chi^2_{0.05} = 3.84$.

The total correlation of HP findings at biopsy and conizate is shown in Table 4; in patients with hysterectomy after conization it is weak, since the kappa coefficient of correlation was 22.22, weak correlation ($r = 21-40$).

Table 4. Histopathologic finding at biopsy and conization in cases with biopsy after conization

H.P conizate	CIN II	CIN III	MIC	IC	Total
H.P biopsy					
CIN II	2	10	5	4	21
CIN III	0	10	8	12	30
MIC	0	0	0	3	3
Total	2	20	13	19	54

H.P – histopathologic finding, CIN – cervical intraepithelial neoplasia, MIC – microinvasive carcinoma, IC –invasive carcinoma

The correlation of findings in patients without hysterectomy after conization was $r = 88.09$, which is very strong correlation (0.81–1.00). Statistically, it was proven that significantly higher percentage of patients with hysterectomy after conization has a lesser degree of correlation of HP findings at biopsy and conization compared to the patients without hysterectomy after conization, since $\chi^2_e = 83.76 > \chi^2_{0.01} = 6.63$.

Table 5 shows that hysterectomy as a mode of re-intervention was adequate treatment for 16, and inadequate (over-) treatment for 38 patients, so that hysterectomy was significantly inadequate mode of surgical re-intervention, since $\chi^2_e = 8.96 > \chi^2_{0.01} = 6.63$. In case of invasive carcinoma correlation is 80%, so that radical hysterectomy was adequate mode of surgical re-intervention and of statistical significance, since $\chi^2_e = 6.36 > \chi^2_{0.05} = 3.84$.

Table 3. Indications for hysterectomy after conization by the study years

Year	CIN	Close to marg.	Posit. lat. marg.	Posit. apex	Posit. curettage	Microin. Ca. Ia1	Microin. Ca. Ia2	Invasive Ca.	Total
2000	2	0	2	2	0	1	0	2	9
2001	3	0	1	0	0	1	0	3	8
2002	1	1	0	1	1	4	0	4	12
2003	1	0	1	1	0	3	1	6	13
2004	0	1	2	2	0	3	0	4	12
Total	7	2	6	6	1	12	1	19	54

Table 5. Histopathologic finding at hysterectomy in cases with hysterectomy after conization

H.P hysterectomy	Benign	CIN	MIC	IC	Total
H.P conizate					
CIN III	1 (14.28%)	6 (85.71%)	0	0	7 (12.96%)
Close to margin	2 (100.00%)	0	0	0	2 (3.70%)
Positive lat. margins	2 (33.33%)	4 (66.66%)	0	0	6 (11.11%)
Positive apex	1 (16.66%)	5 (83.33%)	0	0	6 (11.11%)
Positive curettage	1 (100.00%)	0	0	0	1 (1.85%)
Microinvasive carcinoma	7 (53.84%)	5 (38.40%)	1 (7.69%)	0	13 (24.07%)
Invasive carcinoma	1 (5.26%)	3 (15.78%)	0	15 (78.94%)	19 (35.81%)
Total	15 (27.77%)	23 (42.59%)	1 (1.85)	15 (22.77%)	54 (100%)

The highest percent of benign HP findings at hysterectomy (Table 6) was obtained for the conizate finding of microinvasive carcinoma; it was of statistical significance since $\chi^2_e = 14.49\% > \chi^2_{0.05} = 12.59$. There is no statistically significant difference in the proportion of benign HP findings in microinvasive carcinomas related to age, since $\chi^2_e = 0.42 < \chi^2_{0.05} = 7.81$.

Table 6. Distribution of the patients with histopathologic finding of microinvasive carcinoma at conization by the years of life with histopathologic finding at hysterectomy after conization

H.P. at hysterectomy	Benign	CIN	MIC	Total	Percent
Years of life					
<40	2 (66.66%)	1 (33.33%)	0	3	27.27%
40-44	2 (50.00%)	1 (25.00%)	1 (25.00%)	4	36.36%
45-49	2 (50.00%)	2 (50.00%)	0	4	36.36%
>49	1 (50.00%)	1 (50.00%)	0	2	18.18%
Total	7 (63.63%)	5 (45.45%)	1 (9.09%)	11	100.00%

H.P- histopathologic finding

Table 7 demonstrates that most of the patients with invasive carcinoma were aged 45-49 years, but the difference was not statistically significant ($\chi^2_e = 7.44 < \chi^2_{0.05} = 7.81$).

Table 7. Distribution of patients with invasive carcinoma finding by years of life

Age (years)	No. of invasive cancer cases	Percent
< 40	3	15.78%
40-44	4	21.05%
45-49	9	47.36%
>49	3	15.78%
Total	19	100.00%

Discussion

Retrospective statistical method was used in this clinical study. In the five year interval 2000-2004 there were 306 conizations of the uterine cervix at the Dept. of Surgery, Clinic of Gynecology and Obstetrics. In 54 patients, in 17.64% on the average hysterectomy was done after conization. We may note in the Table 1 that the percentage of performed hysterectomies was similar by the years of study – from 15.38% in 2001, to 20.63% in 2003 – and the difference was not statistically significant.

If we observe the age of the patients with hysterectomy after conization (Table 2), it is evident that 70% of those were over 45 years of age. The difference was statistically significant and demonstrates that the indications for hysterectomy in younger patients were more strict and critical. This high percentage of hysterectomies in the elderly patients is also influenced by the high proportion of invasive disease in this age group.

As for the indications for hysterectomy after conization, Table 3 demonstrates that most common indications were microinvasive and invasive cancer in 59.25%, while positive conization margins were indication for hysterectomy in 27.77%, and the difference is statistically significant. There are data that in 18% of the examinees hysterectomy was done after conization due to positive margins (8). In 12.96% indication for hysterectomy in our study was CIN III with negative margins in old patients, with some other associated gynecologic indication – myoma.

Table 4 demonstrates that the correlation of biopsy and conization findings in patients with subsequent conization is 22.22 – a very poor correlation ($r = 21-40$). This poor correlation is associated with the fact that it was in fact the reason for hysterectomy (positive margins and invasive disease). The table also shows that invasive disease was present in 31.37% of CIN patients and 100% of those with microinvasion at conization – that is the reason why it is necessary to first perform conization and precise HP diagnosis, avoiding thus inadequate treatment. On the other hand, in patients without hysterectomy after conization, there is a very good correlation of HP findings at biopsy and conization – $r = 88.09$. Statistical analysis demonstrated that there is a better correlation of biopsy

and conization findings in patients without subsequent hysterectomy than in those with hysterectomy.

When we analyzed HP findings obtained at hysterectomy after conization and related them to hysterectomy indications (Table 5), we came to a conclusion that hysterectomy was over-treatment in 70.37% of the cases, since in 27.77% the findings were benign and in 42.59% it was CIN, for which reconization would be sufficient management. Statistical analysis demonstrated that hysterectomy as a mode of surgical reintervention was not appropriate in a statistically significant degree. In cases of invasive carcinoma, on the other hand, hysterectomy was adequate treatment modality in a statistically significant degree, since in 80% of the cases PH findings were identical on hysterectomy too.

Since the highest percentage of benign HP findings at hysterectomy was obtained for microinvasive carcinoma (in 53.84%), we separately presented in Table 6 the cases with this diagnosis and distributed them by the factor of age. We did not detect any difference in incidence for various age groups, but in 27.77% of the cases below 40 years of age with diagnosis of microinvasive carcinoma, hysterectomy findings were normal. These data indicate that a more conservative approach is required when treating younger patients, especially those with Ia1 stage without lymphovascular invasion, with conization margins into the healthy tissue.

Table 7 presents all invasive cancers at hysterectomy and distributed them according to the patient age. Patients aged 45-49 years were commonly diagnosed with invasive carcinoma – it is necessary to pay attention to this age group. Similar data on age and invasion status were presented by Kobak, who found that 31% of those with positive margins had invasive cancer at reintervention (9).

Conclusion

On the average, hysterectomy after conization was done in 17.14%. Those were mainly women over 45 years of age, which indicates that indications for hysterectomy were more critical and strict in younger cases. Most common indications for hysterectomy after conization were microinvasion and invasion – in 59.25%, and positive cone margins – in 27.77%. General correlation of the biopsy and conization findings in patients with hysterectomy after conization is very poor – $r = 22.22$, due to the fact that it was the reason for hysterectomy in the first place (positive margins and invasive disease).

Hysterectomy was not appropriate mode of surgical reintervention in patients with positive conization margins – in 70.37% of the cases it was over-treatment. Since in 27.27% of patients below 40 with microinvasive carcinoma hysterectomy findings were normal, it is necessary to be more conservative and critical in deciding on reintervention. Patients aged 40-45 years more commonly had invasive disease at hysterectomy – it is necessary to pay special attention to this age group when deciding on reintervention.

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OPRAVDANOST HISTEREKTOMIJE NAKON KONIZACIJE GRLIĆA MATERICE

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Kratak sadržaj: Cilj rada je da ispita učestalost, najčešće indikacije i opravdanost histerektomije nakon konizacije grlića materice. Korišćenjem retrospektivne metode analizirali smo bolesnice sa konizacijom, operisane na Ginekolo-akušerskoj klinici (GAK) u Nišu od 2000. – 2004. godine. Načinjeno je ukupno 306 konizacija grlića materice. Kod 54 bolesnice, prosečno u 17,64% je nakon konizacije urađena histerektomija. Najčešća indikacija za histerektomiju nakon konizacije je mikroinvazivni i invazivni karcinom grlića materice u 59,25% i pozitivne ivice konizata u 27,77% bolesnica. Analiza histopatoloških nalaza dobijenih na histerektomiji posle konizacije, kod bolesnica sa pozitivnim ivicama konizata, je pokazala da je histerektomija kao način lečenja bila preobimna za 70,37% bolesnica, jer je u 27,77% nađen benigni nalaz, a u 42,59% cervikalna intraepitelna neoplazija (CIN) za koji bi rekonizacija bila dovoljna hirurška reintervencija. U slučaju mikroinvazivnog i invazivnog karcinoma histerektomija (radikalna) se pokazala kao statistički značajno adekvatnim načinom hiruške reintervencije jer je u 80% nalaz bio identičan i na histerektomiji. Najčešća indikacija za histerektomiju nakon konizacije je mikroinvazivni i invazivni karcinom grlića materice i pozitivne ivice konizata. Histerektomija nije adekvatna hiruška reintervencija kod pozitivnih ivica konizata, jer je u 70,37% bila preobimna hiruška reintervencija.

Ključne reči: Histerektomija, konizacija, ivice konizata