Thai Journal of Obstetrics and Gynaecology
March 1998, Vol. 10, pp. 47-54

GYNAECOLOGY

Management and Result of Patients with Positive Cone Margin at Rajavithi Hospital.

Suwat Boonwisut MD,
Pornsom Hutacharern MD.

Department of Obstetrics and Gynaecology, Rajavithi Hospital, Bangkok Thailand.

ABSTRACT

Objective To evaluate the results of the management of patients with positive cone margin after cervical conization.

Design Retrospective study.

Setting Department of Obstetrics and Gynaecology, Rajavithi Hospital.

Subjects 136 patients with positive cone margin after cervical conization

Results From 1985-1995, a total of 601 patients had cervical conization by cold knife conization and large loop excision of the transformation zone. Out of these patients, 465 (77.37%) had negative margin, and the remaining 136 patients (22.62%) had positive margin.

In the latter group, 92 patients underwent simple hysterectomy, 18 patients had radical hysterectomy with or without lymphadenectomy, 9 patients followed up with Papanicolaou smear, and 4 patients had radiation therapy. Of the remainder, 12 did not come for continued treatment and one was beyond further treatment.

Of the 92 patients who underwent simple hysterectomy, 82.61% were found to have residual disease in the hysterectomy specimen. The histology showed that 53.26% of residual disease in the hysterectomy specimens were the same as conization, 6.52% were higher grade and 40.22% were lower grade. The hysterectomy specimens of those patients in cervical intraepithelial neoplasia grade III from conization revealed that 2.17% had microinvasive carcinoma and a further 2.17% had invasive carcinoma.

In the group of patients who underwent radical hysterectomy, 16 patients or 88.89% were found to have residual disease. Of which 66.67% showed the same histologic finding as conization, 5.56% were higher grade and 27.78% were lower grade.

Three patients in the simple hysterectomy group and one patient in the radical hysterectomy group had repeated conization. 75% of these repeated conization still had residual disease.

In the group of 9 patients who had continued treatment by Pap smear, 11.11% were found to be positive.

Four patients had radiation therapy because 3 patients with microinvasive were obese that the operation cannot be performed and another one had positive nodes.

All the patients except 12 cases who lost follow up still follow until January 1998.

Conclusion One hundred and thirty six patients with positive cone margins were diagnosed and treated during 1985-1995 and were followed until 1998. Only 9% were lost followed up. The remainder 124 patients, 92 patients underwent simple hysterectomy, 18 patients had radical hysterectomy with or without lymphadenectomy, 9 patients were followed with Pap smear and 4 patients had radiation. 82.61% and 88.89% were found to have residual disease in the first and second group. In the follow up group with Pap smear, 11.11% had positive result. For the patients who had repeated conization, 75% of the cases still had residual disease. The patients who had positive cone margin should be followed up regularly. Also the patients who had completed families should be investigated to rule out invasive carcinoma in residual disease before hysterectomy due to high percentage of residual disease in the incomplete conization.

Key words : positive cone margin, incomplete conization, results

Cervical conization is the method for diagnosis and therapeutic treatment for cervical precancerous lesion. It was indicated in cases of abnormal Pap smear, normal Pap smear with cervical erythroplakia after undergoing colposcopic examination, cervical biopsy and endocervical curettage (ECC) with no distinction between microinvasive and invasive carcinoma and for the treatment of cervical intraepithelial neoplasia (CIN) grade III. Even when conization was performed by experienced doctors, the disease could still be found in the cone margins. The acceptable management of patients who had positive cone margins can be summarized as follows :[1]

1. Those patients who want to have more children and are able to have regular follow up can have cervical cytology (Pap smear) taken for at least 3 years.

2. Those patients who had CIN III or more from conization with extensive lesion and where invasive carcinoma cannot be ruled out, repeat conization should be performed. Repeat conization however has inherent risks and complications. The second cervical resection margin may again reveal residual disease and future fertility may be impaired.

3. Hysterectomy is indicated in those patients who had CIN III who do not want more children or where other indications for hysterectomy exist.

The purpose of this retrospective study was to evaluate the results of management of patients with positive margins after cervical conization.

Materials and Methods

The data of 601 cervical conized patients between October 1985 and September 1995 were collected from tumor registration in gynaecologic oncology unit, Department of Obstetrics and Gynaecology and from Department of Pathology at Rajavithi Hospital, Bangkok. Five hundred and fifty eight patients had cold knife conization

whereas 43 patients had large loop excision of transformation zone (LLETZ). The histological report of cervical conization revealed 136 patients with positive margins. Ninety one percents of the patients were followed and treated until January 1998 except 12 patients who lost follow up. All the patients had conization performed due to one of the following indications :

1. Unsatisfactory colposcopic findings without colposcopic biopsy and ECC due to no abnormal cervical lesion evident in abnormal Pap smear with CIN II to invasive carcinoma.

2. Unsatisfactory colposcopic examination with positive ECC.

3. Discrepancy in Pap smear and histology of colposcopic biopsy and ECC.

4. Diagnosis and treatment of cervical lesion due to CIN II or more from colposcopic biopsy or ECC and CIN with extensive lesion.

Conization was performed by cold knife conization and large loop excision of transformation zone (LLETZ) under colposcopic examination. The cervix was marked with methylene blue or Indian ink before conization done and the conization specimens were sent for histology. Histological readings were performed by three pathologists from the department of Pathology. Subsequent abdominal or vaginal hysterectomy was performed six weeks after conization if indicated both from high grade of CIN and other hysterectomy indications such as myoma uteri, prolapsed uteri.

The patients who had conization or hysterectomy will be followed up by Pap smear every 4 months in the first year, 6 months in the second year and annually after that.

The Pap smear was reading as according to Richart's scheme[2]

All the data were counted and calculated as percentage.

Results

Of the total of 601 patients had cervical conizations, cold knife conization was performed in 558 cases (92.85%) and large loop excision of the transformation zone (LLETZ) in the remaining 43 cases (7.15%). Four hundred and sixty five (77.37%) of the 601 patients had negative margin (440 or 78.85% from cold knife conization, and 25 or 58.14% from LLETZ). The remaining 136 patients (22.63%) had positive margin, of which 118 or 21.15% were from cold knife conization and 18 or 41.86% from LLETZ (Table 1). The mean age of the patient was 38.2 years.

Table 1. Complete/incomplete conization by cold knife or large loop excision transformation zone (LLETZ).

Procedure	Complete resection N (%)	Incomplete resection N (%)	Total N (%)
Cold knife conization	440 (78.85)	118 (21.15)	558 (92.85)
LLETZ	25 (58.14)	18 (41.86)	43 (7.15)
Total	465 (77.37)	136 (22.63)	601 (100)

The indications for conization were as shown in Table 2.

Table 2. Indications for conization in patients with incomplete resection.

Indications	No of patients (%)
Unsatisfactory colposcopy without colposcopic biopsy and ECC	14 (10.29)
Unsatisfactory colposcopy with positive ECC	13 (9.56)
Discrepancy in cytology and histology	78 (57.35)
Therapeutic	31 (22.90)
Total	136 (100)

Table 3. Results of residual disease from hysterectomy specimens.

Hysterectomy			Hyst. Specimen: Residual disease	Hyst. Specimen: No residual disease
1. Simple Hysterectomy	Post Cone	78 cases	64	14
	Post LLETZ	14 cases	12	2
	Total	**92 cases***	**76**	**16**
2. Radical Hysterectomy	Post Cone	17 cases	15	2
	Post LLETZ	1 case	1	0
	Total	**18 cases****	**16**	**2**

*3 cases were the second conization
**1 case were the second conization

Table 4. Relationship between histological reports of conization and simple hysterectomy.

TAH / Cone	Neg.	CIN I	CIN II	CIN III	MIC	Invasive carcinoma	Total
Neg.	-	-	-	-	-	-	-
CIN I	-	-	-	2*	-	-	2
CIN II	-	1**	-	-	-	-	1
CIN III	14	12	2	46	2	2	78
MIC	2	-	1	5	3	-	11
Invasive	-	-	-	-	-	-	-
Total	16	13	3	53	5	2	92

MIC = microinvasive TAH = Total abdominal hysterectomy
*One case had severe dysplasia from Pap smear, another case had CIS with focal stromal invasion from Colpo. Biopsy.
**Moderate dysplasia from ECC (endocervical curettage)

Of the 136 patients who had incomplete margins, 92 patients underwent simple hysterectomy, 18 patients had radical hysterectomy with or without lymphadenectomy, 9 patients had follow up with Pap smear, and 4 patients had radiation therapy. Of the remainders, 12 did not come for continued treatment and 1 was beyond further treatment.

Residual disease was found in the hysterectomy specimens of 92 patients of which 3 cases were the second conization, while 18 patients showed no residual disease of which one case was the second conization, as indicated in Table 3.

In Table 4, out of 92 patients who underwent simple hysterectomy due to cervical intraepithelial neoplasia grade II or more, 16 or 17.39% had no residual disease in the hysterectomy specimen, while 76 or 82.61% were found to have residual disease. 2 CIN I and 1 CIN II were operated due to one case with CIN I had pap smear with severe dysplasia and another case had colposcopic biopsy with CIS and focal stromal invasion, one case with CIN II had ECC positive with moderate dysplasia. The histology showed that 53.26% of residual disease in the hysterectomy specimens was the same as in conization, 6.52% were higher grade and 40.22% were lower grade. The hysterectomy specimens of those patients in cervical intraepithelial neoplasia grade III from conization revealed that 2.17% had microinvasive carcinoma and a further 2.17% had invasive carcinoma and received subsequent radiation therapy.

Of the 18 patients who underwent radical hysterectomy with or without lymphadenectomy, 2 patients or 11.11% had no residual disease while 88.89% were found to have residual disease (Table 5). The histology showed that 66.67% of residual disease in the hysterectomy were the same as in conization, 5.56% were higher grade and 27.78% were lower grade. In the group of CIN III from conization 3 patients had radical hysterectomy without lymphadenectomy because of CIN III extended to vagina. In group of microinvasive carcinoma from conization 7 patients underwent radical hysterectomy because of extensive lesion and invasive carcinoma cannot be definitely ruled out.

Three patients in the simple hysterectomy group and one patient in the radical hysterectomy group had repeated conization. 75% of these repeated conization still had residual disease.

Of the nine patients who had Pap smear follow-up, only one patient had positive Pap smear (CIN 1) (Table 6). This follow-up continues up to January 1998 and no progression of the disease is evident.

Four patients had radiation therapy because three patients with microinvasive were obese that the operation cannot be performed and another one had positive nodes.

Twelve cases showing positive disease at conization margins did not return for further treatment, of which ten were CIN III and one was microinvasive carcinoma, one was invasive carcinoma.

One patient was beyond further treatment because of invasive carcinoma metastasized to bone.

Discussion

Cervical conization is performed for diagnostic and therapeutic purposes. The relationship between involvement of the cervical cone margins by cervical intraepithelial neoplasia (CIN) and the presence or absence of CIN as determined by subsequent hysterectomy or cytologic follow up has been the subject of several reviews. The conclusions, however, are divergent. Some stu-

Table 5. Relationship between histological reports of conization and radical hysterectomy.

Cone \ RH	Neg.	CIN I	CIN II	CIN III	MIC	invasive	Total
Neg	-	-	-	-	-	-	-
CIN I	-	-	-	-	-	-	-
CIN II	-	-	-	-	-	-	-
CIN III	-	-	-	3*	-	-	3
MIC	1	-	-	2	3	1	7
Invasive	1	-	-	1	-	6	8
Total	2	-	-	6	3	7	18

MIC = Microinvasion RH = Radical hysterectomy

*without lymphadenectomy

Table 6. Relationship between histology and cytology of patients follow up by Papanicolaou smear.

In-complete Cone-LLETZ \ Pap smear	Neg	CIN I	CIN II	CIN III	MIC	INV. CA.	Total
Neg	1	-	-	-	-	-	1
CIN I	-	-	-	-	-	-	-
CIN II	-	-	-	-	-	-	-
CIN III	7	1	-	-	-	-	8
MIC	-	-	-	-	-	-	-
Invasive CA.	-	-	-	-	-	-	-
Total	8	1	-	-	-	-	9

MIC = Microinvasive INV. CA. = Invasive carcinoma

dies find no association between the histologic criteria of cone clearance and the actual presence of residual disease at hysterectomy.[3] Whereas others claim high degree of accuracy in predicting complete removal of CIN.[4-5]

This study included 136 patients with positive cone margin of which 91% were followed and treated during 1985 to 1998. The numbers of

patients with residual disease after conization vary.[6-7] Deveraux[8] reported 16%, while Schiffer[9] found about 50%. The difference may be when the hysterectomy was delayed, the residual disease in the subsequent hysterectomy decreased.

From this study, the 136 out of 601 cases (22.63%) with incomplete resection paralleled to the Ostergard's report[3] which the figure was 23%. The incidence of resolution of CIN after conization with positive margin was 16 cases (17.39%) (82.61% of the patients had persistent CIN) of the simple hysterectomy specimens and similar to radical hysterectomy group (88.89% of the patients had persistent CIN and 11.11% had no residual disease). There was invasive carcinoma in 2 patients (2.17%) who had simple hysterectomy due to CIN III from conization. It should be confirmed that there is no invasive carcinoma in residual disease by colposcopic examination, repeated biopsy, ECC or repeated cone before hysterectomy is performed.

Radical hysterectomy was performed in seven patients who had microinvasive carcinoma because of extensive lesion and invasive carcinoma could not be ruled out in the residual disease. In nine cases might be considered as overtreatment (Table 5).

There are several explanations for the absence of expected residual disease in the hysterectomy specimen when the cone line of resection are involved with CIN. Some relate to the handling of cervical cone and the hysterectomy specimens. The performance of endometrial curettage after conization may remove a significant amount of disease, a smaller effect may result from the use of cautery for hemostasis which caused necrosis and inflamation of the involved margins. Only one of the author's 9 patients with CIN involving cone margins developed a positive cytology during follow up (Table 5). Eight of nine patients (88.89%) were negative cytology. This shows that the patients with CIN involving margins could be follow up by cytology.

The management of patients with positive cone margins after cervical conization depends on grade of CIN, extent of cervical lesion, parity and condition of patients. Continued follow-up by Pap smear should be performed on patients who can come for follow up regularly. Repeated conization has inherent risks and complications. Furthermore the second resection margin may again reveal positive margin. The hysterectomy should be performed on patients who have completed families or high grade of CIN due to the high percentage of residual disease. Also before simple hysterectomy is performed in high grade of CIN, invasive carcinoma should be excluded.

Conclusion

One hundred and thirty six patients with positive cone margins were diagnosed and treated during 1985-1995 and were followed until 1998. Only 9% were lost followed up. The remainder 124 patients, 92 patients underwent simple hysterectomy, 18 patients had radical hysterectomy with or without lymphadenectomy, 9 patients were followed with Pap smear and 4 patients had radiation. 82.61% and 88.89% were found to have residual disease in the first and second group. In the follow up group with Pap smear 11.11% had positive result. For the patients who had repeated conization still had residual disease 75% of the cases. The patients who had positive cone margin should be followed up regularly. Also the patients who had completed families should be investigated to rule out invasive carcinoma in residual disease before hysterectomy due to high percentage of residual disease in the incomplete conization.

References

1. Husseinzadeh N, Shbaro I, Wesseler T. Predictive value of cone margins and post-cone endocervical curettage with residual disease in subsequent hysterectomy. Gynecol Oncol 1989 ; 33 : 198-200.
2. Richart RM. Natural history of cervical intraepithelial neoplasia. Clin Obstet Gynecol 1967 ; 10 : 748-84.
3. Ostergard DR. Prediction of clearance of cervical intraepithelial neoplasia byconization. Obstet Gynecol 1980 ; 56 : 77-80.
4. Burghart E, Holzer E. Treatment of carcinoma in situ : evaluation of 1,609 cases. Obstet Gynecol 1980 ; 55 : 539-45.
5. Ahlgren M, Ingermarsson I, Lindberg LG, Nordquist S. Conization as a treatment of carcinoma in situ of the uteri cervix. Obstet Gynecol 1975 ; 45 : 135-40.
6. Benedet JL, Anderson GH, Sampson ML, Shaw D. Colposcopy conization and hysterectomy practices : a current perspective. Obstet Gynecol 1982 ; 60 : 539-45.
7. Garcia RL, Bigelow B, Demopoulos RI, Beckman EM. Evaluation of cone biopsy in the management of carcinoma in situ of the cervix. Gynecol Oncol 1975 ; 3 : 32-9.
8. Deveraux WP, Edwards CL. Carcinoma in situ of the cervix : applicability of diagnostic and treatment methods in 632 cases. Am J Obstet Gynecol 1967 ; 98 : 497-508.
9. Schiffer MH, Greene HJ, Pomerance W, Moltz A. Cervical conization for diagnosis and treatment of carcinoma in situ. Am J Obstet Gynecol 1965 ; 93 : 889-95.