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Prevalence and factors associated with inadequate margin of conization specimens at King Chulalongkorn Memorial Hospital

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ABSTRACT

Objective To study the prevalence of inadequate margin of cold knife conization specimens at King Chulalongkorn Memorial Hospital.

Study design Descriptive study.

Setting Department of Obstetrics & Gynecology, Faculty of Medicine, King Chulalongkorn Memorial Hospital.

Subjects Sixty-five patients who had been treated with cold knife conization between June 1, 1999 and May 31, 2001.

Method The prospective data collection of patients on age, menopausal status, parity, body mass index, histology of colposcopic directed biopsies and conization specimens, surgeon and adequacy of cold knife conization margin were analysed.

Main outcome measures Percentage of inadequate margin of conization specimens.

Results In 65 patients treated with cold knife conization, twenty-seven (41.5%) exhibited inadequate surgical margins. Median age of the patients was 38 years (range 22-74). Eight (80 %) nulliparous patients displayed surgically inadequate margins, whereas nineteen (39.6%) multiparous patients displayed surgically inadequate margins. Nulliparity was the only factor associated with inadequate margins ($p<0.05$); while the other studied factors were not.

Conclusion The prevalence of inadequate cold knife conization margin in this study population was 41.5 %. Nulliparity was the only factor associated with inadequate margin of conization specimens.

Key words: Inadequate conization margin, cold knife conization

Conization of the uterine cervix is a common diagnostic and therapeutic procedure, using for cervical intraepithelial neoplasia and early stage carcinoma of cervix. It is useful in management of patients with abnormal cytology and inconclusive colposcopic evaluation.[1] Clinical management problems occur when squamous or glandular lesions extended beyond the excision margins, which correlated with residual as well as recurrent diseases reported by many authors.[2-7] Moreover, the optimal protocol for post-conization management in such cases remain controversial.[8] The prevalence of inadequate

conization margin in the literature is extremely variable, ranging from 13.5 to 41%.[9-15] However, the information concerning the significance of surgical margins in cervical tissue obtained from cold knife conization is limited. This study was undertaken to evaluate the prevalence of inadequate margin of cold knife conization specimens and to determine the associated factors of this condition.

Material and methods

Patient

Between June 1, 1999 and May 31, 2001, 65 patients had been treated with cervical cold knife conization at King Chulalongkorn Memorial hospital. The indications for conization were 1). Lesion cannot be totally visualized with colposcopy. 2). The squamo-columnar junction is not seen at colposcopy. 3). Positive endocervical curettage (histology report from Endocervical curettage was at least CIN II) 4). There is lack of correlation between cytology and colposcopy results. 5). Microscopic invasion is suspected based on biopsy, colposcopy, or cytology results. 6). The colposcopist is unable to rule out invasive cancer.

The medical records of the patients were review on age, parity, body weight, height, menopausal status, pre-operative cervical cytologic and histologic reports, indications for conization, histology of conization specimens, surgical margins of the specimens (both ectocervical and endocervical margins), and surgeon.

Approval for the study was obtained from the Ethical committee, Faculty of Medicine, Chulalongkorn University.

Operative techniques

All cases were performed under spinal anesthesia. Colposcopic examination was done by gynecologic oncology staff or second years oncologic fellow, using 3% acetic acid to delineate abnormal epithelium. Standard conization was performed in the following manner. 1) Schiller's solution was painted on the cervix. 2). Lateral suture was placed at 3 and 9 o'clock for traction and hemostasis. 3). Endocervical curettage (ECC) was performed only in cases with unsatisfactory colposcopic finding to exclude squamous intra epithelial neoplasia of the upper endocervical canal or endometrium. 4). A uterine sound was placed in the endocervix to guide the depth of the resection. 5). Under visual inspection the specimen should be resected in toto, and only the stroma should be handled to avoid destroying the epithelial surface. 6). After excision, the specimen was tagged at the 12 o'clock position and sent immediately to the pathologic laboratory. 7). Hemostatic suture was sutured by either sturmdof suture or vertical interrupted suture to control bleeding. These procedures were performed in operative room by the faculty staffs or the third year residents under the faculty staffs' supervision. Not all conization was done by the colpologist who performed the colposcopy

Histopathological techniques

All surgical raw surface of the specimens were thoroughly inked and vertically cut at 12 o' clock. After fixation with 10% formalin solution the specimens were serially cut about 2-3 mm in each section thickness. After labelling, all pieces of specimen sections were normally processed as routine histologic technique and stained with hematoxylin and eosin. All glass slides were reviewed by two gynecologic pathologists. Therefore, if the margin of the specimen was suspected the other gynecologic pathologist will confirm the diagnosis. In these cases, inadequate margin was defined as cervical intraepithelial neoplasia or HPV-infection feature, at the inked resected margin. Cervical intraepithelial lesion was graded by using the CIN system.

Study aims

The study had two end points. First, we analyzed the determinant of inadequate margin in one category. Second, we specifically analyzed the factors associated with inadequate margin.

Statistics

Percentage was used to determine prevalence of inadequate margin. Chi-square test and Fisher's exact correction were used to determine the association between studied factors and surgical margin of the specimens. We used SPSS for Windows, release 10.0, for statistical analyses. P values less than 0.05 were considered significant. Calculation of the sample size showed that a minimum of 57 patients is needed to be included for this study.

Result

All 65 patients undergone conization during the study period. No missing data occurred. The median age of the patients was 38 years (range from 22 to 74). The mean weight, height, and BMI were 55.0 kg (range from 41 to 91), 156.2 cms (range from 145 to 169), and 22.5 kg/m^2 (range from 16.2 to 31.8), respectively.

Demographic characteristics and pathological findings were shown in table 1. The mean age of menopausal group was 53.6 years (range 49 to 58). The majority (58.1 %) of indications for conization was discrepancy between cytology, biopsy and colposcopic findings, and majority of conization pathology results in this group was CIN III 26 (60.5%).

Table 1. Characteristic of population

Factor	Number of patient (%) N = 65
Menopausal status	
Premenopausal status	53 (81.5%)
Postmenopausal status	12 (18.5%)
Parity	
Nulliparity	10 (15.4%)
Multiparity	55 (84.6%)
Pap smear	
Suspicious	23 (35.4%)
Very suspicious	21 (32.3%)
Positive	21(32.3%)
Colposcopic biopsy	
Cervicitis	6 (9.2%)
CIN I,II	5 (7.7%)
CIN III	45 (69.2%)
MIC	9 (13.9%)
Indication for conization	
Unsatisfy colposcopic	12 (18.5%)
Discrepancy	43 (66.1%)
MIC	10 (15.4%)
Conization pathology	
Cervicitis	3 (4.6%)
CIN I,II	9 (13.8%)
CIN III	32 (49.3%)
MIC	18 (27.7%)
Invasive	3 (4.6%)
Surgeon	
Faculty staff	21(32.3%)
Third-year resident	44(67.7%)

Fig. 1. Prevalence of inadequate margin.

As shown in Fig.1, the total frequency of inadequate margin was 27 (41.5%). Table 2 show the association of endocervical and/or ectocervical inadequate margin of conization specimens. The inadequacy of the ectocervical margin and endocervical margin were 14 (51.9%) and 16 (59.3%), respectively. Three patients (11.1%) had inadequate margin both endocervical and ectocervical margins, which were CIS, MIC and frank invasive carcinoma, respectively. Tables 3 show the univariate analysis of demographic data and surgical margin of the specimens. In this study, the number of patients who had cervicitis was too small; therefore we combined the number of this group with CIN I & II group. We found that nulliparity was the only statistically significant factor associated with inadequate conization margin ($P<0.05$), while the other factors such as age, parity, body mass index, menopausal status, preopertive cytology and histology, indication for conization, histology of conization specimens and surgeon were not associated with inadequate margin.

Table 2. Number of inadequate margin defined as ectocervcal and / or endocervical location

	Ectocervical margin		
Endocervical margin	**Inadequate margin**	**Adequate margin**	**Total**
Inadequate margin	3	11	14
Adequate margin	13	0	13
Total	16	11	27

Table 3. Univariated analysis of factor associated with inadequate margin in cold knife conization

Studied factors	**Number(%) of Inadequate margin**	**Number(%) of Adequate margin**	**X^2**	**P value**
Menopausal status				
Premenopause(53)	21(39.6%)	32(60.4%)		
Postmenopause(12)	6(50.0%)	6(50.0%)	0.534	0.366
Parity				
Nulliparous (10)	8(80%)	2(20%)	0.012	0.010
Multiparous(55)	19(34.4%)	36(65.5%)		

Studied factors	Number(%) of Inadequate margin	Number(%) of Adequate margin	X^2	P value
Body mass index (kg/m^2)				
< 25 (46)	21(45.7%)	25(54.3%)	1.097	0.295
>25 (19)	6(31.6%)	13(68.4%)		
Colposcopic biopsy				
Cervicitis,CINI&CINII (11)	2(18.2%)	9(81.8%)	2.99	0.224*
CIN III (45)	21(46.7%)	24(53.3%)		
MIC(9)	44(44.4%)	5(55.6%)		
Indication for conization				
Unsatisfy colposcopic(11)	2(18.2%)	9(81.8%)	1.771	0.413
Discrepancy(43)	19(44.2%)	24(55.8%)		
MIC(10)	5(50.0%)	5(50.0%)		
Conization pathology				
Cervicitis,CINI&CINII(12)	3(25%)	9(75%)	3.672	0.159*
CIN III (32)	12(37.5%)	20(62.5%)		
MIC(18)	10(55.6%)	8(44.4%)		
Invasive (3)	2(66.7%)	1(33.3%)		
Surgeon				
Faculty staff (21)	7(33.3%)	14(66.7%)	8.60	0.354
Third-year resident (44)	20(45.5%)	24(54.5%)		

Note * Fisher's exact correction were used to determine the association of parameter.

From this study, the mean age of nulliparous women with inadequate margin was 38.5 years (29-58). The conization pathologic reports in this group were CIN III 4 (50%) cases and MIC 4 (50%) cases, inadequate margin at ectocervical and endocervical area were 3 (37.5%) and 5 (62.5%), respectively.

Discussion

Conization is an effective diagnostic and therapeutic tool.[7,14] The status of the excision margin is of interest to clinician to determine the need for additional therapy or appropriate follow up. The prevalence of positive margin after cold knife conization in this study was 41.5%, however, the prevalence from previous reports were ranging from 13.5 to 41%.[9-15] Interestingly, the prevalence of inadequate margin in this study was so high. The possibility were bias in case selection because conization was done frequently than LEEP in high grade- CIN and our hospital is a referal center. However, it should alert us to improve our operative quality such as defining the lesion before conization. The colpologists should be the ones who perform conization in the same case or conization should be done under colposcopic examination

The only characteristic factor associated with inadequate margin reported by Chang et al[3] and Costa et al[16] was severity of lesions. In our study, it was not significantly different. This might be due to the sample size of this study is quite small compared with other previous studies. (172 by Chang et al[3] and 718 by Costa et al[16])

The only significantly associated factor was nulliparity. This might be due to smaller size of the cervix and difficult to identify squamocolumnar junction. Interestingly, severity in the group of inadequate conization margin were rather high grade, almost were CIN III.

This study supports that surgeon experience[9] and age of the patient[13] were not associated with

inadequate margin and there were no difference among menopausal status, BMI, Papanicolaou smear, and histology of colposcopic directed biopsy, indication for conization and conization pathology

The limitation of this study, which is the descriptive study, was that some informations may not be accurate from error in medical records. In this study, the sample size is quite small compared to other previous study and limitation in time of this study.

The recommendation from this study was when nulliparous patients were performed conization, we should be aware of our intraoperative procedure. The inadequate conization margin should be reduced by carefully studying colposcopic finding.

We did not know whether the patients with inadequate margin had significantly higher chances of having residual lesions compared with those who had negative margin. The other point of view is that how to management the patients with inadequate margin, because of limitation in time.

Further studies should be done in order to clarify residual diseases in patients with inadequate margin and risk factors of inadequate margin to reduce problems in management and follow up after conization.

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