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Prevalence and Risk Factor of Incomplete Cervical Excision in Chonburi Hospital

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ABSTRACT

Objective: To determine the prevalence and risk factors of incomplete cervical excision in Chonburi hospital.

Materials and Methods: Descriptive analytical study was conducted in Chonburi Hospital, Thailand. Medical records of patients who had positive (incomplete) cervical margins after loop electrosurgical excision procedure (LEEP) or conization from January 2007 to December 2011 were reviewed.

Results: There were 2,526 patients undergoing excision procedure and291 patients (11.52%) had positive margins. One thousand four hundred and fifty one cases (57.44%) underwent conization and 175 cases (42.56%) underwent LEEP. Patient age ranged from 17 to 89 years (mean 41.56 ± 13.5 years). Mean body weight and height were 58.28 ± 9.5 kg and 153 ± 6 cm, respectively. Body mass index ranged from 14.67 to 40.81 kg/m^2 (mean 24.88 ± 4.4 kg/m^2). Ninety two percent were multiparous and sixty eight percent were premenopause. Preoperative cytology was high grade squamous intraepithelial lesion (HSIL) in 1,109 cases (43.9%). Three hundred and fifty nine cases (14.2%) had unsatisfied colposcopic findings. The margin involvement was significantly associated with nulliparity, post menopause, history of HIV, history of smoking, type of the operation, experience of the surgeon, preoperative cytology, unsatisfactory colposcope and preoperative histology.

Conclusions: The prevalence of a positive cone margin was rather high and depended on population, operativeprocedure, experience of the surgeon, preoperative cytology and histology. Physicians who perform cervical excision should take into account the risk factors in the management of cases with abnormal cytological screening for cervical cancer.

Keywords: cervical intraepithelial neoplasia, incomplete excision, positive margin, LEEP, conization

Introduction

Cervical cancer is the second most common cancer in Thai women. From International Agency for Research on Cancer (IARC) base statistical data on the year 2008, CA cervix cause 14.9% of all cancer death[1].

Detection of preinvasive cervical lesions and appropriate treatment are the way for cervical cancer reduction[2]. The treatment for cervical intraepithelial neoplasia (CIN) is surgical excision, either by loop electrosurgical excision procedure (LEEP) or conization, Because this procedure helps exclude unsuspected

invasive cancer, is cost-effective and has lower complication[3-6].

The presence or absence of CIN in the specimen margins represented the adequacy of treatment. The importance of margin involvement in establishing the risk of post-treatment disease is controversial[2-4]. Evidence suggested that patients with positive cone margins have significantly higher chance of having disease persistence and/or progression to squamous cell carcinoma than those with negative margins[7]. Several reports hasshown that there were predictive factors associated with residual disease in subsequent hysterectomy specimen[7-10]. However, the great attention should be focused on the possibility of complete excision. There were scarce information concerning the prevalence and risk factors of the positive margin from cervical excision procedure. Therefore, we are interested in the risk factors of having residual disease at the margin of the specimen (positive margin).

Many studies have reported the prevalence of positive surgical margin, varying from 3 to 47%[2]. The difference may be explained by the characteristics of study population, hospital, surgeon and histological type. Our study was to determine the prevalence and risk factors of positive cervical cone margin in Chonburi hospital.

Materials and methods

This was a retrospective observational study. Medical record of the patients who underwent diagnotic and therapeutic cervical excision (LEEP or conization) at Department of Obstetrics and Gynecology, Chonburi hospital, Thailand from January 1st, 2007 to December 31st, 2011 were reviewed. The cervical excision was performed by gynecologic residents under supervision of staffs of our department. The study protocol was approved by the research ethics committee of the institution.

Eligible patients presented with cervical dysplasia who met the criteria for diagnostic or therapeutic cervical excision were enrolled. Indications for cervical excision were abnormal cervical cytology with unsatisfied colposcopic findings, positive endocervical curettage, suspecious of microinvasive disease and discordant results between Pap smear and colposcopic biopsy. For LEEP, the cervix was stained with Lugol's iodine solution to identified pale area. Local anesthetic consisted of 1% lidocaine hydrochloride with adrenaline 1:100,000 dilutions was infiltrated into the cervix circumferentially. Excision was performed using electrodes 15 - 25 mm loop, 1/16" shaft diameter. For conization, the cervix was stained with Lugol's solution to outline the lesion, and a scalpel No.11 is used to cut the cone. Conizations were completed using a Sturmdorf procedure. Gynecologic residents performed the procedure under staff supervision.

All LEEP and conization specimens were marked by pins and fixed in formalin and processed with standard procedure. The histologic slides were reviewed by an experienced pathologist at the Department of Pathology in Chonburi Hospital. The positive margin was defined as the presence of cervical intraepithelial neoplasia or invasive cancer at the edges of the specimen.

The medical records of patients who had incomplete data were excluded. The pathologic informations such as cytology and histology were extracted from Chonburi's computer database to check for the validity of the pathological reports. The medical records were included if the pathology reports were unclear or standard reports cannot be arranged. Cytological standard report included ASC-US (Atypical squamous cells of undetermined significance), ASC-H (Atypical squamous cells cannot exclude HSIL), AGC (Atypical glandular cells), LSIL (Low grade squamous intraepithelial lesion), HSIL (High grade squamous intraepithelial lesion), AIS (Adenocarcinoma in situ), CIS (Carcinoma in situ), SCCA (Squamous cell carcinoma) and histological standard report included CIN (Cervical intraepithelial neoplasia) I, II, III, CIS (Carcinoma in situ), AIS (Adenocarcinoma in situ) and microinvasive cancer. The demographic data were also obtained from the medical records. The variables including age, body mass index (BMI), menopausal status, parity, history of smoking, HIV status, Pap smear,

colposcopic result and level of surgeon were collected. If colposcopic result had multiple types of histology, the most severe histologic result were recorded

Continuous variables were presented as mean ±standard deviation. Categorical variables were presented as number of cases and percentage. Univariable analysis was based on either the Chi-square test or student t-test where appropriate. To evaluate the risk factors associated with the positive surgical margin, logistic regression analysis was used. The decision to include the variables in the logistic regression models depended on the results of the univariate analyses. For all statistical tests, p-value of less than 0.05 was considered significant. Statistical analyses were performed using MedCalc for Windows, version 11.0.1.0 (MedCalc Software, Mariakerke, Belgium). Download from http://www.medcalc.org.

A total of 2,526 women who underwent cervical excision for the diagnosis and therapeutic cervical intraepithelial neoplasia at the Department of Obstetrics and Gynecology, Chonburi hospital, Thailand from January 1st, 2007 to December 31st, 2011 were included in the study. Patient age ranged from 17 to 89 years (mean 41.56 ± 13.5 years), average body weight was 58.28 ± 9.5 kgs, and mean height was 153 ± 6 cm. Body mass index ranged from 14.67 to 40.81 kg/m^2 (mean 24.88 ± 4.4 kg/m^2). Most of the patients were parous (92.2%) and premenopause (68.5%). Preoperative cytology was high grade squamous intraepithelial lesion (HSIL) in 1,109 cases (43.9%). Three hundred and fifty nine patients (14.2%) had unsatisfied colposcopic findings. The prevalence of positive cone margin in Chonburi hospital were 11.52%. The characteristics of the patients were presented in Table 1

Result

Table 1. Demographic Data (N=2526)

Characteristics	
Age(years)	41.56 ± 13.5
Body weight (kg)	58.28 ± 9.5
Height (cm)	153 ± 6
BMI	24.88 ± 4.4
- BMI <30	2,200 (87.09%)
- BMI ≥30	326 (12.9%)
Menopause status	
- Premenopause	1,732 (68.56%)
- Menopause	794 (31.4)
History of smoking	
- Yes	28 (1.1%)
- No	2,498 (98.89%)
Underlying HIV status	
- Negative	2,029 (80.39%)
- Positive	497 (19.67%)
Parity	
- Nulliparous	197 (7.79%)
- Parous	2,329 (92.2%)

Data presented as mean ± SD or n (%)

Table 2. Preoperative cytology

Cytology	Number (%)
ASC-US	235 (9.3)
ASC-H	288(11.4)
LSIL	277(10.96)
HSIL	1,109(43.9)
AGC	182(7.2)
AIS	115(4.55)
SCCA	320(12.66)

ASC-US = Atypical squamous cells of undetermined significance, ASC-H = Atypical squamous cells cannot exclude HSIL, LSIL = Low grade squamous intraepithelial lesion, HSIL = High grade squamous intraepithelial lesion, AGC = Atypical glandular cells, AIS = Adenocarcinoma in situ, SCCA = Squamous cell carcinoma

Colposcopic findings were satisfactory in 2,167 patients (85.78%), CIN I in 411 patients (16.27%), CIN II in 150 patients (5.93%), CIN III in 973 patients (38.5%), AIS in 172 patients (6.8%), CIS in 535 patients (21.1%) and microinvasive cancer in 126 patients (4.98%). There were no CIN in 159 patients (6.29%). (Table 3)

Table 3. Preoperative histology

Histology	Number (%)
CIN I	411 (16.27)
CIN II	150 (5.93)
CIN III	973 (38.5)
AIS	172 (6.8)
CIS	535 (21.1)
Microinvasive cancer	126 (4.98)
No CIN	159 (6.29)

CIN = Cervical intraepithelial neoplasia, AIS = Adenocarcinoma in situ, CIS = Carcinoma in situ

Table 4 represented factors associated with negative and positive margin. The result of logistic regression analysis showed that factors associated with positive margin were nulliparity, postmenopause, underlying HIV, smoking, unsatisfactory colposcopy, preoperative histology of CIN I, II, III, AIS, CIS and microinvasive cancer, operative method and experience of the surgeon (1st and 2nd year residents).

Table 4. Factors associated with positive margin

RISK FACTORs	Number Negative margin N=2,526	(%)	Number Positive margin N=291	(%)	95% CI	p-value
Demographic data						
Nulliparous	158	7.07	39	13.4	1.39 to 2.95	0.0002*
Postmenopause	672	30.06	122	41.92	1.25 to 2.06	0.0002*
Obesity (BMI≥30)	291	13.02	35	12.02	0.62 to 1.33	0.6348
HIV	375	16.78	122	41.92	2.76 to 4.63	<0.0001*
Smoking	10	0.45	18	6.18	6.70 to 32.10	<0.0001*
Preoperative cytology						
ASC-US	201	8.99	34	11.68	0.77 to 1.66	0.5272
ASC-H	266	11.90	22	7.56	0.38 to 0.95	0.0299*
LSIL	241	10.78	36	12.37	0.81 to 1.72	0.3746
HSIL	959	42.91	150	51.55	1.59 to 2.61	<0.0001*
AGC	164	7.34	18	6.18	0.47 to 1.29	0.3339
AIS	114	5.10	1	0.34	0.01 to 0.46	0.0063*
SCCA	290	12.97	30	10.30	0.52 to 1.15	0.1995
Unsatisfactory colposcopic	290	12.97	69	23.71	1.43 to 2.58	<0.0001*
Histologic diagnosis						
No CIN	156	6.97	3	1.03	0.04 to 0.44	0.0008*
CIN I	399	17.85	12	4.12	0.11 to 0.36	<0.0001*
CIN II	112	5.01	38	13.05	1.93 to 4.21	<0.0001*
CIN III	832	37.23	141	48.45	1.24 to 2.03	0.0002*
AIS	170	7.60	2	0.68	0.02 to 0.34	0.0005*
CIS	452	20.22	83	28.52	1.19 to 2.07	0.0012*
Microinvasion	22	0.87	104	4.12	0.02 to 0.34	<0.0001*
Operation						
LEEP	1244	49.2	207	8.19	1.50 to 2.56	<0.0001*
Conization	991	39.2	84	3.32	0.39 to 0.66	<0.0001*
Surgeon level						
1st year resident	117	5.23	2	0.68	0.03 to 0.51	0.0037*
2nd year resident	385	17.22	78	26.80	1.32 to 2.33	0.0001*
3rd year resident	1611	72.08	195	67.01	0.60 to 1.02	0.072
Staff	122	5.46	16	5.49	0.58 to 1.72	0.9777

ASC-US = Atypical squamous cells of undetermined significance, ASC-H = Atypical squamous cells cannot exclude HSIL, LSIL = Low grade squamous intraepithelial lesion, HSIL = High grade squamous intraepithelial lesion, AGC = Atypical glandular cells, AIS = Adenocarcinoma in situ, SCCA = Squamous cell carcinoma, CIN=: Cervical intraepithelial neoplasia, CIS= Carcinoma in situ, LEEP= Loop electrosurgical excision procedure .

Discussion

Prevalence of positive margin in Chonburi Hospital was 11.52% which was different from other studies in Thailand. Panna, et al reported 26.8% of positive margin at Srinagarind Hospital[11]. This result were varied as expected as described in introduction part. Panna, et al reported that purpose of conization, surgeon's skill, type of cervical excision, and histological diagnosis were significantly associated with the margin involvement[11]. Samneangsanoh, et al reported that nulliparity was associated with inadequate conization specimen[12]. Our study showed that factors associated with positive margin were nulliparity, postmenopause, history of HIV and smoking.

Lu, et al reported postmenopause was the risk factor associated with positive margin. The squamocolumnar junction after menopause is usually within the endocervical canal[8]. Boardman, et al reported HIV-positive women were more likely to undergo conization for an abnormal endocervical curettage specimen, persistent CIN I or inadequate colposcopic examination. Analysis revealed that HIV-positive women had a two-fold increase risk of having a positive cone biopsy margin compared with HIV-negative women[13]. Several studies showed that CD4 level was associated with the rate of recurrent disease and potency to have residual disease[14]. Smoking was the risk factor associated with cervical cancer[15]. Some evidence mentioned about effect of smoking on cervical epithelium and our study found an association of smoking and positive cervical margin. Several studies reported that LEEP can replace conization due to more safety, bloodless and no significant difference in histological report[3-6]. According to LU, et al, Fanning J, Zeng SY, our study showed that LEEP was associated with higher rate of positive margin compare with conization[8,16-19]. However, our study did not collect the site of positive margin (endocervical or exocervical), operative time and estimated blood loss. We suggest thar further study should address all these factors.

Operations performed by the 1st and 2nd year residentswere associated with significant higher rate of positive margin. Chonburi hospital were training institute, as resident training level resident 2nd were learning and practicing. However, this is the valuable result to reflect our institute for improvement of surgeon skill. In our study showed that the result would come from the experience of surgeons.

In the univariate analyses, surgeon skill, operative procedure, preoperative cytology and histological diagnosis were related to the positive cone margin. According to these findings, no factors have consistently been reported as a risk of the positive cone margin. This may be from the difference in the study design, sample size, factors of interest, setting, and study population. A multicenter, prospective cohort or randomized controlled trials which take all potential factors into account for analysis would be beneficial and clearly identify risk factors of positive cone.

For clinical perspective, physician should be aware that the margin involvement is rather common. Identification of the risk factors is simple and may help predict the result.

Conclusion

The prevalence of a positive cone margin is rather high and depends on population, operative procedure, experience of the surgeon, preoperative cytology and preoperative histology. Physicians who perform cervical excision should take into account the risk factors in the management of cases with abnormal cytological screening for cervical cancer.

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ความชุกและปัจจัยเสี่ยงของการตัดปากมดลูกที่มีผลรอยโรคที่ขอบชิ้นเนื้อในโรงพยาบาลชลบุรี

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วัตถุประสงค์ *: เพื่อศึกษาความชุกและปัจจัยเสี่ยงของการตัดปากมดลูกที่มีผลรอยโรคที่ขอบชิ้นเนื้อในโรงพยาบาลชลบุรี*
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วิธีการวิจัย *: ศึกษาข้อมูลย้อนหลังของผู้ป่วยที่ได้รับการตัดปากมดลูกในโรงพยาบาลชลบุรี 2,526 คน ในช่วงเวลา 1 มกราคม 2550 ถึง – 31 ธันวาคม 2554 แบ่งกลุ่มตัวอย่างเป็น 2 กลุ่ม คือ ผู้ป่วยที่มีผลรอยโรคที่ขอบชิ้นเนื้อ และผู้ป่วยที่ไม่มีผลรอยโรคที่ขอบชิ้นเนื้อ เปรียบเทียบข้อมูลการมีบุตรวัยหมดประจำเดือน ประวัติการสูบบุหรี่ ประวัติการเป็นโรคภูมิคุ้มกันบกพร่อง ดัชนีมวลกาย ผลเซลล์ปากมดลูก และชิ้นเนื้อที่ได้จากการส่องกล้องก่อนผ่าตัด ประเภทของการผ่าตัดและระดับของผู้ผ่าตัดเปรียบเทียบโดยใช้ความสัมพันธ์ระหว่างปัจจัยต่างๆ กับการมีรอยโรคที่ขอบชิ้นเนื้อวิเคราะห์โดยใช้ Logistic regression*
ตัววัดที่สำคัญ *: ค่าความสัมพันธ์ระหว่างการมีรอยโรคที่ขอบชิ้นเนื้อและปัจจัยต่างๆ วัดโดยค่าความเชื่อมั่นที่ 95 เปอร์เซนต์*
ผลการวิจัย *: ผู้ป่วยที่มารับการตัดปากมดลูกที่โรงพยาบาลชลบุรีจำนวน 2,526 คนพบว่า ได้รับการผ่าตัดปากมดลูกเป็นรูปกรวย 1,451 คน คิดเป็นร้อยละ 57.44 ได้รับการตัดปากมดลูกด้วยห่วงไฟฟ้า 1,075 คนคิดเป็นร้อยละ 42.56 อายุเฉลี่ยตั้งแต่ 17 ถึง 89 ปีค่ามัธยฐานของอายุคือ 41.56 ปี ส่วนสูงและน้ำหนักเฉลี่ยเท่ากับ 1.53 ± 0.06 ซม. และ 58.28 ± 9.5 กก. ตามลำดับดัชนีมวลกายเฉลี่ยเท่ากับ 24.88 ± 4.4 ดัชนีมวลกายที่มากกว่า 30 เท่ากับ 326 คน คิดเป็นร้อยละ 12.9 ส่วนใหญ่ของผู้ป่วยเป็นสตรีวัยมีประจำเดือน 1,732 คน คิดเป็นร้อยละ 68.56 มีประวัติสูบบุหรี่ 28 คน คิดเป็นร้อยละ 1.1 เป็นโรคภูมิคุ้มกันบกพร่อง 497 คนคิดเป็นร้อยละ 19.67 มีบุตรแล้ว 2,329 คน คิดเป็นร้อยละ 92.2 มี 291 คน ที่มีรอยโรคที่ขอบชิ้นเนื้อคิดเป็นร้อยละ11.52 ปัจจัยที่มีความสัมพันธ์กับผู้ป่วยที่มีรอยโรคที่ขอบชิ้นเนื้อและมีนัยสำคัญทางสถิติได้แก่การไม่มีบุตรสตรีวัยหมดประจำเดือนเป็นโรคภูมิคุ้มกันบกพร่องประวัติสูบบุหรี่ผลเซลล์ชิ้นเนื้อปากมดลูก วิธีการผ่าตัด ระดับของผู้ผ่าตัด*
สรุป *: การมีรอยโรคที่ขอบชิ้นเนื้อปากมดลูกมีความชุกที่หลากหลายขึ้นอยู่กับกลุ่มประชากร โรงพยาบาล ชนิดการผ่าตัด ผู้ผ่าตัด ผลเซลล์และชิ้นเนื้อปากมดลูกก่อนผ่าตัดดังนั้นในการวางแผนการรักษาผู้ป่วยที่มีรอยโรคก่อนการลุกลามผู้ผ่าตัดควรคำนึงถึงปัจจัยที่มีความสัมพันธ์กับการที่มีรอยโรคที่ขอบชิ้นเนื้อ เพื่อการวางแผนในการผ่าตัดและคำนึงถึงผลการรักษาที่จะเกิดขึ้นด้วย*