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Prevalence and Correlation of Margin Status and Residual Disease in Subsequent Hysterectomized Specimens Following Loop Electrosurgical Excision Procedure (LEEP)

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ABSTRACT

Objectives: To evaluate the prevalence of residual disease in the subsequent hysterectomy specimens after loop electrosurgical excision procedure (LEEP) and its correlation with adequacy of margins in the previous specimens.

Materials and methods: Medical records and pathologic reports of patients who were diagnosed of squamous intraepithelial lesion (low grade squamous intraepithelial lesion: LSIL, high grade squamous intraepithelial lesion: HSIL and carcinoma in situ: CIS) or microinvasive squamous cervical carcinoma (MIC) in the LEEP specimens from November 2010 to July 2012 at Sawanpracharak Hospital, Nakhonsawan Province were reviewed. All patients had subsequent hysterectomy within 6 months after the diagnosis.

Results: The prevalence of residual disease was 66.2%. Among 227 women with positive LEEP margins, 171 (75.3%) had residual disease in subsequent hysterectomy specimens, while 17 (29.8%) of 57 women with negative LEEP margins had residual lesions. There was a significant correlation of margin status and residual disease in the subsequent hysterectomy specimens following LEEP ($p<0.0005$).

Conclusion: The prevalence of residual disease in the subsequent hysterectomy specimens after LEEP was high. Positive margin in LEEP specimen was the significant predictor of residual disease in hysterectomy specimen.

Keywords: LEEP, margin status, residual disease

Introduction

Cancer has been the common cause of death in Thailand. With regard to the leading cancers in Thailand for female population, the highest incidence falls into cervical cancer, followed by breast, liver and bile duct, bronchus and lung, colon and rectum, and ovarian cancer, respectively[1]. Loop electrosurgical excision procedure (LEEP) is a conservative management commonly used for both diagnostic and therapeutic purposes for squamous intraepithelial lesions[2]. It has

risks of missing disease progression or losing the patients to follow-up. Previous studies showed that 38.3-46.8% of the subsequent hysterectomy specimens had residual disease[3-5]. Most clinicians requested information on margin status. Some studies found a direct correlation between positive margin and residual disease[4,6] but others failed to confirm[3,7]. Management of patients with positive margins of resection is well defined. The objectives of this study were to assess the prevalence of residual disease and correlation of the margin status of LEEP specimen and residual disease.

Materials and methods

Medical records and pathologic reports of patients who had squamous intraepithelial lesion (low grade squamous intraepithelial lesion: LSIL, high grade squamous intraepithelial lesion: HSIL and carcinoma in situ: CIS) or microinvasive squamous cervical carcinoma (MIC) in LEEP specimens at the Department of Obstetrics and Gynecology, Sawanpracharak Hospital, Nakhonsawan Province from November 1, 2010 to July 31, 2012, were reviewed. All patients had subsequent hysterectomy within 6months after the procedure. The indications for subsequent hysterectomy in the negative margin or LSIL cases were other gynecologic conditions (i.e. myoma, adenomyosis). The present study was approved by Sawanpracharak Hospital's Ethic Committee. The LEEP was performed under local anesthesia with 2 ml of 2% xylocaine, injected at 3, 5, 7 and 9 o'clock peripheral to the cervix. The electrosurgical unit (ESU)(Ellman Surgitron F.F.P.F. EMG) was preset at 65 Watts for the blended cut waveform-1 and at 60 Watts for the coagulation waveforms. The LEEP procedure was performed in five steps:

1) The tip of the loop electrodes was placed at the cervix.

2) The ESU was activated.

3) The loop electrode was rotated for 360 degrees.

4) The electrode and the excised specimen were removed.

5) Haemostatic was achieved by fulguration using the ball electrodefrom the same supplier.

All pathologic reports were reviewed by an experienced pathologist at the Department of Pathology, Sawanpracharak Hospital. Negative margin was defined as the specimens that show no evidence of human papilloma virus infection, intraepithelial neoplasia of squamous or glandular origin, or invasive disease in all margins. LSIL and HSIL were reported using the criteria of Bethesda System. MIC was divided into stage IA1 or "minimal microscopic stromal invasion", and stage IA2 or "tumor with invasive component of 5 mm or less in depth taken from the base of the epithelium and 7 mm or less in horizontal spread. Descriptive statistics (chi-square, p-value) were used to calculate the prevalence and statistical significance.

Results

From November 1, 2010 to July 31, 2012, a total of 284 patients were available for analysis. Mean age (±SD) was 43.8 (±7.4) years. Majority of the patients were parous (97.2%). Median duration between the LEEP and hysterectomy was 79 days, ranging from 40-125 days. HSIL was the most common pathologic diagnosis in LEEP specimens (78.2%). Most common site of positive margin was ectocervix (73.9%). Prevalence of the residual disease in subsequent hysterectomy specimens after LEEP was 66.2% (188 out of 284 cases) (Table 1).

Table 1. Margin status and residual disease in subsequent hysterectomy specimens.

Margin status / Residual disease	MIC		HSIL		LSIL	
	Positive margin	Negative margin	Positive margin	Negative margin	Positive margin	Negative margin
Residual disease	0	0	79	66	41	2
No residual disease	0	2	53	23	3	15

There was a significant difference of the residual lesions in the uterus between positive and negative margins of LEEP specimens ($p < 0.0005$). Among 227 women with positive LEEP margins, 171 (75.3%) had residual diseases, while only 17 of 57 women (29.8%) with negative LEEP margins had residual diseases (Table 2).

Table 2. Correlation between margin status of the LEEP specimens and residual disease.

Margin status / Residual disease	Positive margin	Negative margin	p
Residual disease	171	17	< 0.0005
No residual disease	56	40	

There was no invasive cervical cancer in the hysterectomy specimens. In all 57 negative margin specimens, none had residual lesion more severe than the lesions in the LEEP specimens. However, 14 out of 151 positive margin specimen had more severe lesions of the residual disease than the margin pathology (Table 3).

Table 3. Severity of margin status of LEEP specimens and residual disease.

Margin status / Residual disease		MIC	HSIL	LSIL	No residual disease
MIC	Negative margin	0	0	0	2
	Positive margin	0	0	0	0
HSIL	Negative margin	0	13	2	23
	Positive margin	0	116	14	53
LSIL	Negative margin	0	0	2	15
	Positive margin	0	14	27	3

Free margin = Negative margin

Not free margin = Positive margin

Discussion

The positive endocervical margins mean that the excision is not deep enough. The positive ectocervical margins mean that the excision is not wide enough. In this study, 73.9% of positive margin specimens were at ectocervical margin. The prevalence of residual disease

in this study was 66.2%, which was higher than those in the previous reports (38.3-46.8%)[3-5]. It may be due to higher rate of positive margins in LEEP specimens (78.5%) compare to other studies (39.7-61.3%)[3-5]. The present study found that positive margin in LEEP specimens was the significant predictor for residual disease which was the same as previous studies[4,6,7] contrary to the other studies. Fifty six of 171 positive margins in the LEEP specimens had no residual lesion. A positive margin was not always associated with residual disease, possibly because of the eradication of residual lesions by the immune response, vaginal acidity, destruction of residual dysplastic cell by cauterization for hemostasis[9] and false positive margin status produced by the oblique section during specimen preparation[10-13]. However, negative margin in LEEP specimens cannot guarantee the absence of residual lesion. There were residual diseases in 29.82% of negative margin specimens comparable with the study by Kupasano et al. (37.7%)[3]. Possible explanation for the presence of residual disease after apparently complete LEEP were friable dysplastic cells stripped off the cervical stroma by LEEP, the lesions may be originally multifocal in nature or reactivation of HPV-infected tissue at the excised crator[14].

However, the main weak point of this study is that subsequent hysterectomy was not performed in all cases after LEEP. This could have some effects to the prevalence of the residual lesions in our study. Further studies are needed to support these findings in order to to establish the appropriate guidelines of management. In conclusion, 66.2% of hysterectomy specimens after the LEEP had residual disease. The positive margin of the LEEP specimens was the significant predictor of residual disease. However, negative margins of the LEEP specimens could not rule out residual disease.

References

1. Wilailak S. Epidemiologic report of gynecologic cancer in Thailand. J Gynecol Oncol 2009;20:81-3.
2. Huang LW, Hwang JL. A comparison between loop electrosurgical excision procedure and cod knife conization for treatment of cervical dysplasia. Residual disease in a subsequent hysterectomy specimens. Gynecol Oncol 1999;73:12-5.
3. Kumpasano T, Triratanachat S. Residual disease in hysterectomy specimens after loop electrosurgical excision or cold knife conization in high grade squamous intraepithelium lesion and microinvasive cervical carcinoma. Thai J Obstet Gynaecol 2011;19:67-73.
4. Natee J, Therasakvichaya S, Boriboonhiunsarn D. Prevalence and risk factors for residual cervical neoplasia in subsequent hysterectomy following LEEP or conization. J Med Assoc Thai 2005;88:1344-8.
5. Saeaib N, Boonyapipat S,Tungsinmunkong K, Liabsuetrakul T. Predictors of the residual disease of high-grade lesions and microinvasive squamous cell carcinoma of the cervix following conization.J Med Assoc Thai 2009;92:1406-12.
6. Sharon J, Pamela E, Charles D, Stephanie K. Margin status on excision of cervical intraepithelial neoplasia. Obstet Gynecol 2000;55:520-7.
7. Alonsoa I, Tornéa A, Puig-Tintoréa L M, Esteveb R, Quintoc L, Campob E et al. Pre- and post-conization high-risk HPV testing predicts residual/recurrent disease in patients treated for CIN 2–3. Gynecol Oncol 2006;103:631-6.
8. Lapaquette TK, Dinh TV, Hannigan EV, Doherty MG, Yandell RB, Buchanan VS. Management of patients with positive margins after cervical conization. Obstet Gynecol 1993;70:529-32.
9. Maluf P, Adad S, Murta E. Outcome after conization for cervical intraepithelial grade III: relation with surgical margins, extension to the crypts and mitoses.Tumori 2004;90:473-7.
10. Lu CH, Liu FS, Tseng JJ, Ho ES. Predictive factors for residual disease in subsequent hysterectomy following conization for CIN III. Gynecol Oncol 2000;79:284-8.
11. Lin H, Chang HY, 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.
12. Park JY, Lee SM, Yoo CW, Kang S, Park SY, Seo SS. Risk factors predicting residual disease in subsequent hysterectomy following conization for cervical intraepithelial neoplasia (CIN) III and microinvasive cervical cancer. Gynecol Oncol 2007;107:39-44.
13. Kietpeerakool C, Khunamornpong S, Srisomboon J, Siriaunkgul S, Suprasert P. Cervical intraepithelial neoplasia II-III with endocervical cone margin involvement after cervical loop conization: is there any predictor for residual disease? J Obstet Gynaecol Res 2007;33:660-4.
14. Buxton E J, Luesley D M, Wade-Evans T, Jorgan J A. Residual disease after cone biopsy: completeness of excision and follow up cytology as predictive factors. Obstet Gynecol 1987;70:529-32.

รอยโรคที่หลงเหลืออยู่ในมดลูกหลังการตัดปากมดลูกด้วยห่วงไฟฟ้า: ความชุกและพยาธิสภาพที่ขอบของปากมดลูกที่ถูกตัดด้วยห่วงไฟฟ้า

สุวรรณา ศรวณีย์

วัตถุประสงค์ *: เพื่อประเมินความชุกของรอยโรคหลงเหลือในมดลูกที่ถูกตัดออกภายหลังการตัดปากมดลูกด้วยห่วงไฟฟ้าและความสัมพันธ์ของพยาธิสภาพที่ขอบของปากมดลูกที่ถูกตัดด้วยห่วงไฟฟ้ากับรอยโรคหลงเหลือในมดลูกที่ถูกตัดออกภายหลัง*

วัสดุและวิธีการ *: เวชระเบียนและรายงานทางพยาธิวิทยาของผู้ป่วยที่ได้รับการตัดปากมดลูกด้วยห่วงไฟฟ้าและผลทางพยาธิวิทยาพบว่ามีเซลล์ผิดปกติระยะก่อนการเป็นมะเร็งและมะเร็งปากมดลูกระยะแรกชนิดสแควมัส และได้รับการตัดมดลูกออกภายใน 6 เดือนหลังจากตัดปากมดลูกด้วยห่วงไฟฟ้า ตั้งแต่วันที่ 1 พฤศจิกายน พ.ศ.2553 ถึง 31 กรกฎาคม พ.ศ.2555 ที่ โรงพยาบาลสวรรค์ประชารักษ์ จังหวัดนครสวรรค์*

ผลการศึกษา *: ความชุกของรอยโรคที่เหลือ คือ ร้อยละ 66.2 ในสตรี 227 รายที่ตรวจพบรอยโรคที่ขอบของชิ้นเนื้อที่ถูกตัดด้วยห่วงไฟฟ้าพบว่า 171 ราย (ร้อยละ 75.3) มีรอยโรคหลงเหลือในมดลูกที่ถูกตัดออกมา ในขณะที่สตรี 57 ราย ที่ตรวจไม่พบรอยโรคที่ขอบชิ้นเนื้อที่ถูกตัดด้วยห่วงไฟฟ้ามีรอยโรคหลงเหลือ 17 ราย (ร้อยละ 29.8) มีความแตกต่างอย่างมีนัยสำคัญทางสถิติของโรครอยโรคหลงเหลือในมดลูก ระหว่างการมีหรือไม่มีพยาธิสภาพที่ขอบของปากมดลูกที่ถูกตัดด้วยห่วงไฟฟ้า ($p<0.0005$)*

สรุป *: มีความชุกสูงของรอยโรคที่เหลือในมดลูกที่ถูกตัดหลังจากการตัดปากมดลูกด้วยห่วงไฟฟ้า และการมีพยาธิสภาพที่ขอบของปากมดลูกที่ถูกตัดด้วยห่วงไฟฟ้าเป็นปัจจัยที่มีนัยสำคัญใช้พยากรณ์รอยโรคที่เหลืออยู่ในมดลูกได้*