

RESEARCH ARTICLE

Risk Factors for Incomplete Excision after Loop Electrosurgical Excision Procedure (LEEP) in Abnormal Cervical Cytology**Treerin Yingyongwatthanawitthaya, Watcharin Chirdchim*, Chanya Thamrongwuttikul, Panya Sananpanichkul****Abstract**

Objective: To investigate the risk factors related to incomplete excision after loop electrosurgical excision procedure (LEEP) in abnormal cervical cytology. **Methods:** This retrospective cohort study was performed during September 2010 to February 2017. The study population was patients with abnormal cervical cytology who treated by LEEP at Prapokklao hospital, Chanthaburi. From the medical records, data were collected include age, menopausal status, parity, body mass index, HIV infection, history of smoking, cervical cytology and characteristics of LEEP histopathology such as number of specimen, size and glandular involvement. Risk factors were investigated using multivariable risk ratio from risk ratio regression. **Result:** Five hundred cases of LEEP were done during this period and 322 cases were analyzed. Complete excision of the LEEP specimens found nearly half of the cases (46.9%). Multiple pieces of specimen was the risk factor for incomplete excision of LEEP (adjusted risk ratio [aRR] = 1.29, 95% confidence interval [CI] = 1.06-1.58; P = 0.013). **Conclusion:** The number of specimen from LEEP more than one piece was the risk factor for incomplete excision. Alternative methods such as cold knife conization (CKC), needle excision of the transformation zone (NETZ) or contoured loop excision of the transformation zone (C-LETZ) should be justified when all lesions could not be operated by single sweep.

Keywords: Abnormal cervical cytology- incomplete excision- LEEP

Asian Pac J Cancer Prev, **18 (9)**, 2569-2572

Introduction

New cases of cervical cancer found 528,000 per year in world population. Cervical cancer is the second most common cancer found in Thai women after breast cancer. The statistics in 2012 from the International Agency for Research on Cancer (IARC) showed that the age-standardized incidence rate in Thailand was 17.8 per 100,000 women. In Thailand, new cases and death from cervical cancer were 8,000 and 4,500 each year, respectively. Actually, cervical cancer is still public health problem in Thailand (Ferlay et al., 2013).

Cervical cancer screening is a secondary prevention aimed to find the precancerous lesion for treatment before developing to cancer. The lesion with cervical intraepithelial neoplasia (CIN) is classified the severity as CIN 1, CIN 2 or CIN 3. In the CIN 2 and 3 groups, the usually recommended treatment is excisional procedure such as loop electrosurgical excision procedure (Geneva: World Health Organization., 2014). If the lesion is founded at the margin of specimen (incomplete excision), indicate the higher chance of the persistent or recurrent of the disease than no lesion left (Zaitoun et al., 2000; Gonzalez et al., 2001; Fogle et al., 2004; Ghaem et al., 2007; Serati et

al., 2012). The choices of treatment in case of incomplete excision of LEEP are (1) follow-up at 4-6 months with cytology and endocervical curettage, (2) repeat excision and (3) hysterectomy (Massad et al., 2013). As a result, reduction of incomplete excision will decrease the complication resulting from treatment, expense and time consuming of patient during follow-up period.

Many factors contribute to incomplete excision of the LEEP specimen such as cone length of less than 10 mm, invasive cancer on cytology, invasive cancer on LEEP histopathology (Kietpeerakool et al., 2005), multiparity and glandular involvement of LEEP specimen (Kanjanasirirut et al., 2015). Increase number of the procedure is also increase number of the specimen. This may from difficulty of the operation and abnormal large of the cervical lesion. This research aimed to find other factors associated to incomplete excision from LEEP in our population.

Materials and Methods

This research was conducted using retrospective cohort study focusing on etiologic study at Department of Obstetrics and Gynecology, Prapokklao hospital,

*Department of Obstetrics and Gynecology, Prapokklao Hospital, Chanthaburi, Thailand. *For Correspondence: watcharinchirdchim@hotmail.com*

Chanthaburi, Thailand during September 2010 to February 2017. Inclusion criteria were all the population treated by LEEP because of abnormal cervical cytology. This study was conducted after approval of Prapokklao hospital ethical committee. From the medical records, data were collected include age, menopausal status, parity, body mass index, HIV infection, history of smoking, cervical cytology and characteristics of LEEP histopathology such as number of specimen, size and glandular involvement. The exclusion criteria were incomplete data and pathological report from LEEP showed no abnormal lesion.

Abnormal cervical cytology was reported as 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) and cancer.

Colposcopy examination was done in case of abnormal cervical cytology by gynecologist. Cervical biopsy was performed in case of high grade precancerous cervical lesion. Endocervical curettage (ECC) was done if indicated. The indications to perform cervical conization were as follows:

cytopathologic discrepancy; histological diagnosis of at least CIN 2, 3; histological diagnosis of CIN 1 persistent for more than 2 years.

All of the LEEPs were conducted by gynecologic residents under supervision of the staff at operation room under intravenous sedation. The procedure was initiated by selection the size of the loop based on size of the lesion after application with lugol's solution. There are 3 sizes of loop; 15 mm, 20 mm and 25 mm. In some cases, additional excision will be conducted to cover all lesions. The LEEP specimen was sent for pathological report at department of pathology, Prapokklao hospital. If the result showed incomplete excision, the further management is based on doctor and patient decision. The choices of management are (1) follow-up at 4-6 months with cytology and endocervical curettage, (2) repeat excision and (3) hysterectomy.

Continuous characteristics were showed as mean and standard deviation. Categorical characteristics were presented as number of cases and percentage. Continuous variables were compared by t-test while categorical data

Table 1. Demographic Characteristics of the Study Population

Characteristics	Total N=322	Incomplete excision N=171 (N, (%))	Complete excision N=151 (N, (%))	p-value
Mean age (years)	42.3±10.0	43.2±10.1	41.3±9.8	0.087
Postmenopausal status	73(22.7%)	44(25.7%)	29(19.2%)	0.103
Multiparity	285(88.5%)	152(88.9%)	133(88.1%)	0.478
BMI ≥ 25 kg/m ²	122(37.9%)	65(38.0%)	57(37.8%)	0.527
HIV infection	71(22.1%)	43(25.2%)	28(18.5%)	0.098
History of smoking	30(9.3%)	19(11.1%)	11(7.3%)	0.162

were compared by the Fisher's exact test. All the factors which had p-value less than 0.05 in univariable analysis were entered into the multiple regression analysis. Statistical significance was considered for p < 0.05.

Incomplete excision defined as the presence of at least cervical intraepithelial neoplasia at the margin of LEEP specimen.

Piece of LEEP specimen defined as the number of specimen from LEEP pathological report.

Results

The total of 500 cases of abnormal cervical cytology underwent LEEP during study period. One hundred and seventy eight cases were excluded because of 158 women with incomplete data and 20 women with pathological report of normal lesion. Finally, 322 patients were enrolled to the study. Mean age of the population was 42.3±10.0 year old. Postmenopausal status was identified nearly one-fourth of the population. Most of the patients were multiparous while nearly 40% of the population was overweight (BMI equal to or greater than 25 kg/m²). HIV infection found one-fifth of the patient and 9.3% of the population had history of smoking. Cases of complete excision were identified nearly half of the population (151 cases of 322 cases). There is no statistic difference of the demographic characteristics between incomplete and complete excision group (Table 1).

Table 2 shows comparison of the cytopathologic characteristics between incomplete and complete excision group. The specimens were not complete free margin at ectocervix, endocervix and both (31.58%, 43.27% and 25.15%, respectively). In incomplete excision group, there were significantly higher cases of invasive cancer by cytology, carcinoma in situ and invasive cancer on pathology than in complete excision group. Multiple pieces of LEEP specimen also show significant difference between the both groups in multivariable analysis. Incomplete excision group has 1.29 times more case of multiple pieces of specimen than complete excision group (aRR = 1.29, 95%CI = 1.06-1.58; P = 0.013) (Table 3).

Table 2. Cytopathologic Characteristics

Characteristics	Incomplete excision N=171 (N, (%))	Complete excision N=151 (N, (%))	p-value
Cytology:			
Invasive cancer	11 (6.4%)	2 (1.3%)	0.018*
Pathology:			
CIN 1	16 (9.4%)	13 (8.6%)	0.486
CIN 2 and CIN 3	123 (71.1%)	121 (80.1%)	0.056
CIS and invasive cancer	32 (18.7%)	17 (11.3%)	0.043*
Multiple pieces of LEEP	70 (40.9%)	41 (27.2%)	0.006*
Mean length (cm)	2.6±0.6	2.6±0.6	0.853
Mean width (cm)	1.8±0.5	1.8±0.5	0.577
Glandular involvement	73 (42.7%)	60 (39.7%)	0.336

* Statistically significant; CIN, cervical intraepithelial neoplasia; CIS, carcinoma in situ

Table 3. Adjusted Risk Ratio of Characteristics Associated Incomplete Excision Specimen

Characteristics	RR (95%CI)	Adjust RR (95%CI)	p-value
Invasive cancer on cytology	1.63 (1.17-2.29)	1.41 (0.95-2.11)	0.09
Carcinoma in situ and invasive cancer on pathology	1.28 (1.01-1.64)	1.16 (0.88-1.53)	0.302
Multiple pieces of LEEP	1.32 (1.08-1.61)	1.29 (1.06-1.58)	0.013*

* Statistically significant; CIS, carcinoma in situ

Discussion

Nowadays, as a public concern, the cervical cancer screening coverage is only 60.2% (Bruni et al., 2017). So, cervical cancer in Thailand is a still public health problem. The improvement of cervical cancer screening and prompt treatment for precancerous lesion is an essential topic.

This study aimed to find factors associated to incomplete excision specimen from LEEP. From the study, multiple pieces of LEEP specimen would increase the incidence of incomplete excision. The higher number for excision specimen came from large area of abnormal lesion seen after Schiller's test and the procedure could not be done in the single sweep. Moreover, this risk factor was 80% of the power calculation (one tailed test, $\alpha = 0.05$). This study is consistent with another research that found the relation of the recurrent CIN ≥ 2 within multiple sweeps lesion (Ayhan et al., 2016). To correct multiple pieces of LEEP specimens in selected cases, alternative procedure would be used such as cold knife conization (CKC), needle excision of the transformation zone (NETZ) or contoured loop excision of the transformation zone (C-LETZ) (Chan et al., 1997; Sadek, 2000; Panoskaltis et al., 2004; Chen et al., 2009; Panna et al., 2009; Boonlikit and Thitisagulwong, 2012; Zeng et al., 2012; Chaijindaratana and Lomdee, 2013). Our oncologic staff will use these techniques in selected case while gynecologic resident will be trained to improve the skill of operation in the future.

Other factors in univariate analysis which had the same result to other study were invasive cancer on cytology (Kietpeerakool et al., 2005), carcinoma in situ on LEEP pathology (Chen et al., 2009) and invasive cancer on LEEP pathology (Kietpeerakool et al., 2005). It might due to the more severe the disease, the larger the lesion, though there was not significant in multivariable analysis. The possibility would be that the percentage of invasive cancer on cytology was only 4% while other study was 10% (Kietpeerakool et al., 2005). Also, patients with carcinoma in situ and invasive cancer on pathology were only 15.2% compared to other study that invasive cancer on pathology was 20.9% (Kietpeerakool et al., 2005). In our study, multiparity, size and glandular involvement of LEEP specimen did not present as risk factors.

The limitation of this study was loss of some essential information due to retrospective study nature and lacking of the pathological review. Suggestions for further study are investigation for new risk factors, multicenter study,

prospective cohort study and proper research design to follow up the recurrence in case of incomplete-complete excision which will reflect clinical significant of the incomplete excision. Moreover, detail data during LEEP such as extent of lesion finding, iodine unstained size, excision design, analyzing the size of LEEP specimen in 3 dimensions and volume analysis of the specimen are interesting factors to study in the future.

In conclusion, multiple pieces of specimen from LEEP were 1.3 times more risk for incomplete excision of the procedure. Alternative methods such as cold knife conization (CKC), needle excision of the transformation zone (NETZ) or contoured loop excision of the transformation zone (C-LETZ) should be justified when all lesions could not be operated at by single sweep.

Funding Statement

None.

Statement conflict of Interest

The authors declare no conflicts of interest.

Acknowledgements

We would like to thank Professor Jayanton Patumanond MD, PhD. for providing insight and expertise that greatly assist the research.

References

- Ayhan A, Tuncer HA, Reyhan NH, Kuscü E, Dursun P (2016). Risk factors for residual disease after cervical conization in patients with cervical intraepithelial neoplasia grades 2 and 3 and positive surgical margins. *Eur J Obstet Gynecol Reprod Biol*, **201**, 1-6.
- Boonlikit S, Thitisagulwong S (2012). C-LETZ versus large loop excision of the transformation zone for the treatment of cervical intraepithelial neoplasia: a randomized controlled trial. *Arch Gynecol Obstet*, **286**, 1173-9.
- Bruni L, Barrionuevo-Rosas L, Albero G, et al (2017). ICO Information centre on HPV and cancer (HPV information centre). Human papillomavirus and related diseases in Thailand. Summary Report 30 June 2017.
- Chaijindaratana S, Lomdee T (2013). Prevalence and risk factor of incomplete cervical excision in Chonburi hospital. *Thai J Obstet Gynaecol*, **21**, 41-8.
- Chen Y, Lu H, Wan X, Lv W, Xie X (2009). Factors associated with positive margins in patients with cervical intraepithelial neoplasia grade 3 and postconization management. *Int J Gynecol Obstet*, **107**, 107-10.
- Costa S, de Nuzzo M, Terzano P, et al (2000). Factors associated with cone margin involvement in CIN patients undergoing conization-equivalent electrosurgical procedure. *Acta Obstet Gynecol Scand*, **79**, 586-92.
- Ferlay J, Soerjomataram I, Ervik M, et al (2013). GLOBOCAN 2012 v1.0: Cancer incidence and mortality worldwide. Version 1.0. IARC cancer base No. 11. Lyon. IARC Press.
- Fogle RH, Spann CO, Easley KA, Basil JB (2004). Predictors of cervical dysplasia after the loop electrosurgical excision procedure in an inner-city population. *J Reprod Med*, **49**, 481-6.
- Geneva: World Health Organization (2014). WHO guidelines for treatment of cervical intraepithelial neoplasia 2-3 and adenocarcinoma in situ: cryotherapy, large loop excision of

- the transformation zone, and cold knife conization. WHO Press, Geneva, pp 1-34.
- Ghaem-Maghani S, Sagi S, Majeed G, Soutter WP (2007). Incomplete excision of cervical intraepithelial neoplasia and risk of treatment failure: a meta-analysis. *Lancet Oncol*, **8**, 985-93.
- Gonzalez DI Jr, Zahn CM, Retzliff MG, et al (2001). Recurrence of dysplasia after loop electrosurgical excision procedures with long-term follow-up. *Am J Obstet Gynecol*, **184**, 315-21.
- Kanjanasirirut P, Pataradool K, Manusirivithaya S, Phaloprakarn C, Chavanisakun C (2015). Prevalence and risk factors of positive surgical margin after loop electrosurgical excision procedure (LEEP) in patients with high grade squamous intraepithelial lesion. *Thai J Obstet Gynaecol*, **23**, 240-5.
- Kietpeerakool C, Srisomboon J, Ratchusiri K (2005). Clinicopathologic predictors of incomplete excision after loop electrosurgical excision for cervical preneoplasia. *Asian Pac J Cancer Prev*, **6**, 481-4.
- Massad LS, Einstein MH, Huh WK, et al (2013). 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. *J Low Genit Tract Dis*, **17**, 1-27.
- Panoskaltis T, Ind TE, Perryman K, et al (2004). Needle versus loop diathermy excision of the transformation zone for the treatment of cervical intraepithelial neoplasia: a randomised controlled trial. *BJOG*, **111**, 748-53.
- Panna S, Luanratanakorn S (2009). Positive margin prevalence and risk factors with cervical specimens obtained from loop electrosurgical excision procedures and cold knife conization. *Asian Pac J Cancer Prev*, **10**, 637-40.
- Sadek AL (2000). Needle excision of the transformation zone: A new method for treatment of cervical intraepithelial neoplasia. *Am J Obstet Gynaecol*, **182**, 866-71.
- Serati M, Siesto G, Carollo S, et al (2012). Risk factors for cervical intraepithelial neoplasia recurrence after conization: a 10-year study. *Eur J Obstet Gynecol Reprod Biol*, **165**, 86-90.
- Zaitoun AM, McKee G, Coppen MJ, Thomas SM, Wilson PO (2000). Completeness of excision and follow up cytology in patients treated with loop excision biopsy. *J Clin Pathol*, **53**, 191-6.
- Zeng SY, Liang MR, Li LY, Wu YY (2012). Comparison of the efficacy and complications of different surgical methods for cervical intraepithelial neoplasia. *Eur J Gynaecol Oncol*, **33**, 257-60.