RESEARCH COMMUNICATION

# High-Grade Squamous Intraepithelial Lesion with Endocervical Cone Margin Involvement after Cervical Loop Electrosurgical Excision: What Should a Clinician Do?

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## Abstract

**This study was undertaken to evaluate the incidence and severity of residual lesions in women featuring high-grade squamous intraepithelial lesion (HSIL) histology with endocervical cone margin involvement after the loop electrosurgical excision procedure (LEEP). The medical records of women undergoing LEEP at Chiang Mai University Hospital between October 2004 and February 2006 were retrospectively reviewed and 74 cases were identified. Nineteen women were excluded because of loss to follow-up. The remaining 4 were referred to other hospitals and 2 declined re-excision, leaving a study population of 55 women for analysis. Mean age ± SD of the patients was 48.5 ± 8.9 years. Residual lesions were noted in 26 (47.3%, 95%CI= 33.7 to 61.2). Four (7.3%) had unrecognized invasive cervical carcinoma in subsequent specimens. In conclusion, approximately half of women with positive endocervical cone margins after LEEP for HSIL histology have residual disease. Repeat diagnostic excision is recommended for evaluation of lesions and severity.**

**Key Words**: High-grade squamous intraepithelial lesion - loop electrosurgical excision procedure - endocervical involvement - residual lesion

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## Introduction

There is substantial evidence that well organized programs of cervical cancer prevention including both early detection and adequate treatment of preinvasive lesions reduce the incidence and mortality from cervical cancer (Sasieni et al. 1995; Austin et al., 1997). Achieving these favorable results is based on understanding of the natural history of preinvasive disease of the cervix, preinvasive cervical lesions being traditionally divided into low grade squamous intraepithelial lesion (LSIL) and high grade squamous intraepithelial lesion (HSIL). With LSIL, almost all regress spontaneously, particularly in young women, and only small proportion progress to more severe lesions. In contrast, with HSIL, if left untreated, progression to invasive cancer is striking (Mitchell et al., 1994). Thereby, the appropriate treatment of HSIL is mandatory.

Although there are various methods developed for treatment of cervical precancerous lesions, the loop electrosurgical excision procedure (LEEP) for the cervical transformation zone has become the preferred treatment in gynecological practice because of its high efficacy and low level of surgical complications (Wright et al., 1992; Kietpeerakool et al., 2006). However, incomplete excision of cervical neoplastic epithelium is noted in a considerably high proportion of cases, mainly at the endocervical margins (Kietpeerakool et al., 2005). Several studies have demonstrated incomplete excision at endocervical margins after LEEP to be a significant predictor for either persistence or recurrence of cervical dysplasia during follow-up (Felix et al., 1994; Das et al., 2005; Brockmeyer et al., 2005).

Generally, management of women with endocervical cone margin involvement after LEEP primarily depends on the risk of residual disease and its severity. However, the management of women with endocervical cone margin involvement following LEEP for HSIL is still inconclusive. The present study was, accordingly, undertaken to evaluate the incidence and severity of residual lesion in women with HSIL who had endocervical involvement after LEEP. These should provide important information, not only to physicians,

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but also to patients for counseling about the risk of observation versus further treatment.

## Materials and Methods

After approval of the Research Ethics Committee, the medical records of women undergoing LEEP at Chiang Mai University Hospital between October 2004 and February 2006 were retrospectively reviewed. To be eligible for this study, the patients had to have HSIL histology on LEEP specimens and had endocervical cone margin involvement with HSIL histology. The patients who had concurrent involvement of ectocervical and endocervical cone margin involvement were also recruited. Abstracted data included patient's characteristics, abnormal cervical cytology results, colposcopic findings, histology of LEEP specimens, and residual lesion after subsequent treatment.

LEEP was performed in an outpatient setting followed routinely by endocervical curettage. The electrical power for loop electrode was set to blended mode. In cases of LEEP margin involvement, repeat colposcopy was carried out at 6-8 weeks post-operatively. All subsequent surgical treatments were performed within 12 weeks of the first LEEP. We attempted to perform repeat loop excision as first choice of treatment after positive cone margin. Hysterectomy was carried out when loop excision was not possible. Cone margin involvement in the present study was defined as the presence of neoplastic epithelium consistent with HSIL at the margin by histological examination. Subjects with any type of histological abnormality after subsequent surgical treatment were classified as positive for residual disease.

## Results

During the study period, 74 women who had HSIL histology with endocervical cone margin involvement after LEEP were identified. Nineteen women were excluded because of loss to follow-up. The remaining 4 were referred to other hospitals and 2 declined re-excision, leaving a study population of 55 women for final analysis. Mean age ± SD was 48.5 ± 8.9 years (median 49, range 27-78). Almost all of the women (96.4%) were multiparous and 24 (43.6%) were postmenopausal. Three (5.5%) were anti-HIV positive. The majority of women (83.6%) had unsatisfactory colposcopy before LEEP. Mean cone length and maximum cone base were 8.6 mm (median 8.0, range 4-15) and 20.5 mm (median 20.0, range 11-35), respectively. In repeat colposcopy after LEEP, only 8 (14.6%) had abnormal colposcopy. The remaining 46 (83.6%) and 1 (1.8%) had unsatisfactory and normal colposcopy, respectively. The subsequent treatment after LEEP included repeat LEEP (30), total abdominal hysterectomy (for 22), total laparoscopic hysterectomy (2), and vaginal hysterectomy (1). Residual lesions were noted in 26 (47.3%, 95%CI= 33.7 to 61.2) women. Four women had unrecognized invasive cervical carcinoma in subsequent excision specimens. The distributions of Pap smear results, site of margin involvement, extent of HSIL at endocervical cone margin, and result of endocervical curettage after LEEP are displayed in Table 1.

**Table 1. Characteristics of the 47 Patients**

| Characteristics | Number (percentage) |
|---|---|
| Severity of abnormal Pap smear findings | |
| HGSIL | 35 (63.6) |
| SCCA | 12 (21.8) |
| Others | 8 (14.6) |
| Site of cone margin involvement | |
| Endocervical only | 41 (74.5) |
| Endocervical and ectocervical | 14 (25.5) |
| Endocervical curettage | |
| Abnormal | 23 (41.8) |
| Normal | 21 (38.2) |
| Inadequate | 11 (20.0) |
| Extent of endocervical involvement | |
| 1-2 quadrants | 39 (70.9) |
| 3-4 quadrants | 16 (29.1) |
| Residual lesion | |
| Absent | 29 (52.7) |
| HGSIL | 22 (40.0) |
| SCCA | 4 (7.3) |

Abbreviations: HGSIL, high-grade squamous intraepithelial lesions; SCCA, squamous cell carcinoma

**Table 2. Characteristics of the 4 Women who had Residual Cervical Carcinomas after LEEP**

| Characteristics | No 1 | No 2 | No 3 | No 4 |
|---|---|---|---|---|
| Age (years) | 35 | 64 | 45 | 56 |
| Pap result | HSIL | SCCA | SCCA | SCCA |
| Cone length (mm) | 7 | 5 | 10 | 7 |
| Margin involvement | Endo | Endo | Endo/Ecto | Endo/Ecto |
| Extent (quadrants)† | 4 | 3 | 1 | 1 |
| ECC | Abn | Abn | Inad | Abn |
| Second operation | TAH | TAH | TAH | LEEP |
| Depth, width‡ (mm) | 7.1,10 | <1,<1 | 1.6,3.5 | 2.1,2.0 |

Abbreviations: LEEP, loop electrosurgical excision procedure; HGSIL, high-grade squamous intraepithelial lesion; SCCA, squamous cell carcinoma; ECC, endocervical curettage; TAH, total abdominal hysterectomy; Abn. abnormal; Inad, inadequate

*Concurrent endocervical and ectocervical cone margin involvement, †Extent of endocervical cone margin involvement with HSIL histology, ‡Depth of stromal invasion and width of superficial extension

Unrecognized invasive cervical carcinomas were observed in 4 women who underwent repeat LEEP (1) or total abdominal hysterectomy because re-excision was technically not possible (3). The detailed characteristics of these women are shown in Table 2. One undergoing total abdominal hysterectomy was found to have invasive lesions consistent with the presumed FIGO stage IB1. After counseling for management options, the patient decided to be treated with postoperative radiation.

## Discussion

Several studies have demonstrated an increased risk of harboring residual lesions in women who had endocervical margin involvement after cervical cone biopsy

(Husseinzadeh et al., 1989; Lapaquette et al., 1993; Natee et al., 2005). Women undergoing cold-knife cervical conization for HSIL in whom the endocervical cone margin is involved, have approximately 50% risk of residual lesion on subsequent evaluation (Husseinzadeh et al., 1989; Lapaquette et al., 1993), in line with the present study (47.3%).

In the literature, several studies have reported the incidence of undiagnosed invasive cervical cancer in the post-cone hysterectomy specimens that ranged from 0.9% to 9.6% (Husseinzadeh et al., 1989; Whiteley et al., 1990; Huang et al., 1999; Natee et al., 2005). In the aforementioned series, majority of histological diagnosis on cone specimens were HSIL after either cold knife cervical conization or LEEP. In the present study which included only women who had HSIL histology on LEEP specimens, the unrecognized invasive cervical cancer rate was 7.3%. Although specific characteristics of women who were found to have unrecognized invasive lesion after first loop cervical excision for HGSIL could not be strongly addressed in the present study due to small study size, the authors believe that this is important information which should be taken into account during counseling on subsequent management after first LEEP.

Ectocervical margin involvement after cervical cone excision is generally disregarded as a strong predictor for residual or recurrent disease (Lopes et al., 1993; Moore et al., 1995; Mohamed-Noor et al., 1997). In the present study, there was no significant difference in the incidence of residual lesion after LEEP in women who had only endocervical cone margin involvement compared to those with concurrent endocervical and ectocervical cone margin involvement. Explanations for this finding have been proposed including the thermal destruction of the remaining ectocervical lesion during the electrical fulguration, chemical destruction after application of some topical hemostatic agent, i.e. Monsel's solution, and immunological response triggered by local inflammatory reaction after LEEP.

There have been conflicting reports regarding the accuracy of ECC for prediction of residual disease with post-cone hysterectomy specimens. Felix et al (1994) and Kalogirou et al (1997) pointed out that post-LEEP ECC could predict residual lesions on subsequent treatment. On the other hand, Vierhout and de Plangue (1991) and Natee et al (2005) reported that ECC did not provide significant value in predicting residual lesions. In the present study, ECC was not a significant independent predictor for residual disease from multivariate analysis. The heterogeneity of these results might be partially explained by differences in surgical technique and experience of surgeons.

The management of women featuring HSIL with endocervical cone margin involvement is still debatable. The American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines recommend a repeat diagnostic excision procedure as the first option. When repeat excision is not feasible, hysterectomy is acceptable (Wright et al., 2003). However, based on this guideline, the argument has been raised that hysterectomy is unnecessary in some proportion of cases and could be avoided with better identification of women at risk of harboring residual lesion. There are several reports demonstrated that the use of a human papillomavirus (HPV) test could predict the persistent or recurrent disease after cervical cone biopsy. Women with negative tests are unlikely to have dysplastic lesions and then could be assigned to yearly cytological surveillance (Houfflin Debarge et al., 2003; Costa et al., 2003; Sarion et al., 2004). However, in resource-limited settings, for example in Thailand, access to laboratories for routine HPV testing is currently not available in all institutions. Therefore, this management strategy might not be appropriate in our situation.

Post-treatment surveillance with cytology may be an alternative after LEEP for HGSIL with endocervical cone margin involvement in women who need no hysterectomy and, especially while other method, i.e. HPV test is not available. Skinner et al (2004) followed women who underwent LEEP for HGSIL to determine the time interval from treatment to the diagnosis of persistent/recurrent HGSIL. In our series the probability of persistent/recurrent HGSIL was greatest in the first 6 months after treatment, less during months 7 to 21, and interestingly, increased again during months 22-24, pointing to the need for long-term follow up.

In conclusion, women undergoing LEEP for HSIL histology with endocervical margin involvement carry a high risk of having residual HSIL and unrecognized invasive cancer. Based on these findings, a repeat diagnostic excision is recommended to evaluate the residual disease and its severity, consequently, the definite treatment could be given confidently. However, when a repeat excision is clinically not feasible, hysterectomy or long-term cytological surveillance are alternatives. The decision depends on the desire for fertility preservation, cancerphobia, and follow-up compliance of individual patients and should be made after adequate counseling regarding risk of having either residual HSIL or unrecognized invasive lesions.

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