RESEARCH COMMUNICATION

Appropriate Interval for Repeat Excision in Women Undergoing Prior Loop Electrosurgical Excision Procedure for Cervical Neoplasia

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Abstract

The objective of the present study was to evaluate the impact of intervals on complications and pathological examination in women undergoing a repeat loop electrosurgical excision procedure (LEEP) for cervical neoplasia. During October 2004 and January 2007, 78 women who had undergone repeat LEEP at Chiang Mai University Hospital, were prospectively evaluated. The mean age was 47.5 years (range; 27-69 years). The mean duration of uncomplicated vaginal bleeding was 4.4 days (range; 1-20 days). The occurrence of persistent vaginal bleeding was noted in 9 women. Among 78 women, 2 (2.56%) and 7 (8.97%) experienced intraoperative and postoperative hemorrhage, respectively. Six (7.69%) had postoperative infection. These complications were not significantly different from those observed in women undergoing first LEEP in the same period (P=0.56). There was no significant difference in the incidence of perioperative complications and the incidence of non-evaluable cone margins among women who undergoing repeat LEEP within 4-6 weeks, between 6-8 weeks, and more than 8 weeks after first LEEP. In conclusion, repeat LEEP could be safely performed 4-12 weeks after the first procedure without any impact on pathological specimen examination.

Key Words: Loop electrosurgical excision procedure - margin involvement - complications - cervical neoplasia.

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Introduction

The loop electrosurgical excision procedure (LEEP), also known as large loop excision of the transformation zone (LLETZ) is the cervical conization technique using wire electrical loop. This procedure was initially introduced by Cartier in the early 1980 and was subsequently modified by Prendiville and co-workers in 1989 (Prendiville W, 1995). LEEP has been widely used for diagnosis and treatment of high-grade squamous intraepithelial lesion (HSIL) of the uterine cervix (Prendiville W, 1995). LEEP is simple, can be performed in outpatient department using only local anesthesia, has a high patient acceptability, and more importantly, provides specimens of the entire cervical lesions for definite histological diagnosis (Wright et al., 1992). However, the detection of incomplete excision after LEEP has been noted in some proportion of cases and may require repeat diagnostic LEEP to evaluate the residual disease and its severity before definite treatment planning (Kietpeerakool et al., 2005; Siriaree et al., 2006). The incidence of incomplete excision after LEEP depends on the individual risks of women including menopausal status, severity of preceding cervical cytology, LEEP histopathology, and depth of endocervical excision (Kietpeerakool et al., 2005). Although LEEP is a relatively complication-limited surgical procedure (Dunn et al., 2004; Kietpeerakool et al., 2006), we unaware of any study evaluated the possible complications of repeat LEEP and its appropriate interval. The present study was accordingly undertaken to evaluate the complications and effects on cervical specimen examination in women who had undergone repeat LEEP at various intervals.

Materials and Methods

After approval of the Research Ethics Committee, women who had undergone repeat LEEP at Chiang Mai University Hospital between October 2004 and January 2007 were prospectively evaluated for patient characteristics, size of LEEP specimens, bleeding symptoms, intraoperative and postoperative complications. Similar cohorts who had undergone first LEEP during the same period were recruited as

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Table 1. Characteristics of the 78 Women

Characteristics	Number (%)
Nulliparous	5 (6.4)
Postmenopausal status	25 (32.1)
Severity of Pap smear result	
HSIL	48 (61.5)
SCCA	14 (17.9)
ASC-H	6 (7.7)
LSIL	4 (5.1)
Others	6 (7.7)
Histology of first LEEP	
HSIL	67 (85.9)
SCCA	7 (9.0)
AIS	4 (5.1)
Indications for repeat LEEP	
HSIL positive endocervical margin[a]	44 (56.4)
HSIL positive ectocervical margin[a]	4 (5.1)
HSIL positive both margins[a]	19 (24.4)
SCCA positive endocervical margin[a]	7 (9.0)
AIS positive both margins[c]	4 (5.1)

HSIL, high-grade squamous intraepithelial lesion; SCCA, squamous cell carcinoma; ASC-H, atypical squamous cells cannot exclude HSIL; LSIL, low-grade squamous intraepithelial lesion; AIS, adenocarcinoma in situ; [a]all had HSIL at involved margin [b]5 and 2 women had HSIL and SCCA at the involved margin, respectively [c]all had AIS at involved margin

comparative group.

In our institute, a repeat LEEP was routinely carried out at least 4 weeks after first LEEP. Colposcopy was carried out in all women to determine the feasibility of repeat excision. LEEP was performed at the outpatient department using 1% lidocaine with 1:100,000 epinephrine intracervical injection for local anesthesia. The choice of loop size was based on the extent of disease and volume of residual cervix evaluated by colposcopy. The electrical power for loop electrode was set in blended mode. Prophylactic antibiotics were not routinely prescribed. The first follow-up visit was scheduled at 2 weeks postoperatively. All women were called 24 hours and 4 weeks following the procedure to inquire about any possible complications. Uncomplicated vaginal bleeding was defined as a bleeding that did not require treatment.

Table 2. Operative Outcomes and Complications following First (N = 472) **and Repeat LEEP** (N = 78)

Variable	First	Repeat	P-value
Operative time (min)	8.15 ± 4.90	7.67 ± 3.05	0.39
Cone base (mm)	22.2 ± 7.19	18.8 ± 5.05	< 0.001
Cone length (mm)	9.33 ± 2.93	9.45 ± 2.81	0.73
Application of Monsel's solution	260 (55.08)	34 (43.59)	0.07
Invasive lesions	88 (18.64)	6 (7.69)	0.01
Uncomplicated vaginal bleeding* (days)	3.71 ± 3.97	4.41 ± 4.74	0.16
Persistent vaginal bleeding*	27/401 (6.73)	9/63 (14.28)	0.07
Complications (hemorrhage)			
Intraoperative	23 (4.87)	2 (2.56)	0.56
Early postoperative	2 (0.42)	0 (0)	
Late postoperative	25 (5.29)	7 (8.97)	
Infections	21 (4.45)	6 (7.69)	

* Excluding women who experienced any complications. Data are presented as number (percentage) or mean ± standard deviation.

Persistent bleeding was defined as a prolong bleeding more than 2 weeks postoperatively that did not require treatment. Intraoperative hemorrhage was considered a complication when adequate hemostasis took longer than 30 minutes to achieve, or necessitated cervical suturing, vaginal packing or hysterectomy. Early and late postoperative hemorrhage were defined as bleeding occurring within 24 hours or later, respectively, and require hemostatic interventions. Postoperative infection was defined as purulent vaginal discharge, cervicitis, and/ or pelvic inflammatory disease. We did not attempt to estimate the amount of blood loss during either intraoperative or postoperative periods because the majority of post-LEEP cervical wounds generally did not bleed excessively.

Descriptive statistics with number and percentage, mean standard deviation (SD) were described. Chi-square, Fisher's exact test, Student's t test, and Mann-Whitney U test, one way ANOVA, Kruskal-Wallis tests, were used whenever appropriate to compare between the groups. Value of P less than 0.05 was considered statistically significant. All statistical tests were two sided significance.

Results

During the study period, 78 women undergoing repeat LEEP were examined. The mean age was 47.5 years (range; 27-69 years). The clinical characteristics of all women are summarized in Table 1. The mean cone base and length of repeat LEEP specimens were 18.8 mm (range; 5-30 mm) and 9.5 mm (range; 4-15 mm), respectively. All 7 women whose first LEEP specimens revealing invasive squamous cell carcinoma had tumor depth and width less than 3 mm and 7 mm, respectively.

Seventy (89.7%) women experienced some degree of vaginal bleeding after LEEP. The mean duration of uncomplicated vaginal bleeding after repeat LEEP was 4.4 days (range; 1-20 days). The occurrence of persistent vaginal bleeding was noted in 9 (14.28%) women. Intraoperative hemorrhage was observed in 2 (2.6%) women requiring cervical suturing and vaginal packing for hemostasis. Seven (9.0%) women experienced late postoperative hemorrhage and were treated by electrical cauterization with an application of Monsel's solution at bleeding site (6) and cervical suturing (1). Postoperative infection occurred in 6 (7.7%) women. All were diagnosed with cervicitis and could be successfully treated by oral antibiotic at an outpatient setting. None had early postoperative hemorrhage.

Table 2 shows the results of the cone specimen dimensions, mean operative time, perioperative symptoms and complications stratified by the first and repeat LEEP setting. Specimens obtained from first LEEP had significant larger cone base and higher incidence of invasive lesion than those from repeat LEEP. There was no significant difference in cone length, operative time, duration of uncomplicated vaginal bleeding, incidence of persistent vaginal bleeding and perioperative complications between first and repeat LEEP.

Subjects were divided into three groups according to the interval between the first and repeat LEEPs to determine the impact of time interval on the incidence of

Table 3. Surgical Outcomes and Complications Following Repeat LEEP Stratified by the Time Interval from the First Operation

Variables	Group 1 (N=31)	Group 2 (N=29)	Group 3 (N=18)	P-value
Interval (days)	38.2 ± 5.96	52.9 ± 4.19	74.7 ± 13.4	< 0.001
Cone base (mm)	18.7 ± 5.04	19.1 ± 5.07	18.5 ± 5.31	0.93
Cone length (mm)	8.94 ± 2.86	10.1 ± 3.11	9.28 ± 2.02	0.27
Operative time (min)	7.10 ± 2.95	8.55 ± 3.68	7.22 ± 1.52	0.21
Nonevaluable margin	0 (0)	1 (3.45)	1 (5.56)	0.76
Uncomplicated vaginal bleeding* (days)	4.16 ± 4.73	4.31 ± 4.55	5.00 ± 5.27	0.88
Persistent vaginal bleeding*	4/26 (15.4)	3/22 (13.6)	2/15 (13.3)	0.94
Complications				
Intraoperative hemorrhage	1 (3.23)	1 (3.45)	0 (0)	0.55
Late postoperative hemorrhage	1 (3.23)	3 (10.34)	3 (16.67)	
Infections	3 (9.68)	3 (10.34)	0 (0)	

* Excluding women who experienced any complications.Data are presented as number (percentage) or mean ± standard deviation.Group 1, within 4-6 weeks; Group 2, between 6-8 weeks; Group 3, more than 8 weeks, after first LEEP

perioperative complications and the incidence of non-evaluable cone margins following repeat LEEP: group 1 (repeat LEEP performed within 4-6 weeks), group 2 (between 6-8 weeks), and group 3 (more than 8 weeks). Of the 78 women, 31, 29, and 18 were in group 1, 2, and 3, respectively. The mean age of these three groups was 49.5, 46.9, and 44.9 years, respectively. The cone dimensions, the incidence of non-evaluable cone margins, and the operative time of repeat LEEP were comparable among the 3 groups. There were no significant different in the mean duration of uncomplicated vaginal bleeding, the occurrence of persistent vaginal bleeding, the incidence of postoperative complications and the incidence of non-evaluable cone margins among these three groups (Table 3).

Discussion

Numerous studies have demonstrated the safety of outpatient LEEP for managing cervical neoplasia. However, it should be noted that the complications following LEEP reported from these studies were mainly evaluated in the first LEEP setting (Wright et al., 1992; Dunn et al., 2004; Kietpeerakool et al., 2006). Because repeat LEEP is strongly recommended as the first option for women whose previous LEEP margins are involved (Spitzer et al., 2006), the information about the safety of repeat LEEP is therefore needed for appropriate patient counseling before the operation.

In the present study, the mean duration of uncomplicated vaginal bleeding was 4.41 days that did not significantly differ from those undergoing first LEEP (3.71 days, P=0.16). The incidences of persistent vaginal bleeding following the first and repeat LEEPs were 14.28% and 6.73 %, respectively. This difference was not statistically significant (P=0.07). Additionally, the incidence of perioperative complications following repeat LEEP was not significantly different from those of women undergoing first LEEP in the same period (P=0.56). Our findings demonstrated that repeat LEEP in appropriately selected women is safe with an acceptable and manageable surgical morbidities. Moreover, either bleeding symptoms or perioperative complications following repeat LEEP in such women did not significantly differ from those observed in first LEEP setting

In this study, the incidence of invasive cancer on first LEEP specimens was significantly higher than that in repeat LEEP (18.64% versus 7.69%, P=0.01). This may raise the concern of its impact on either bleeding symptoms or perioperative complications after LEEP. Nevertheless, we recently reported that the presence of invasive lesion on LEEP specimens did not pose any significant impact on symptoms and perioperative complications after LEEP (Kietpeerakool and Srisomboon, 2006).

To reduce the perioperative complications and the incidence of non-evaluable LEEP margins, the determination of an appropriate time for repeat LEEP is utmost required. However, such time interval is quite different among the hospital guidelines in Thailand ranging from 4 weeks to 12 weeks. In this study, there was no significant difference in the incidence of non-evaluable LEEP margins, the duration of uncomplicated vaginal bleeding, the incidence of persistent vaginal bleeding and the perioperative complications when repeat LEEP was performed within 4-6 weeks, between 6-8 weeks, and more than 8 weeks after first LEEP, respectively. Based on these findings, repeat LEEP could be conducted at any of such three time intervals. However, since the women frequently have significant psychological morbidities during the long waiting period prior to LEEP (Le et al., 2006), we therefore recommend that the repeat LEEP be performed 4-6 weeks after initial LEEP to reduce such burdens.

The limitations of the present study were the small sample size and the non-randomization of women undergoing repeat LEEP. A large randomized study on the impact of intervals on the complications and pathological specimen evaluation should be carried out to confirm such findings.

In conclusion, repeat LEEP in appropriately selected women is safe and could be carried out as 4-12 weeks after the first operation without any significant impact on histopathological specimen evaluation.

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