Outcomes of Patients Undergoing Loop Electrosurgical Excision Procedure for Persistent Low-grade Abnormal Cervical Smears: A Retrospective Observational Study

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Objective: To review the outcomes of patients undergoing loop electrosurgical excision procedure for persistent low-grade abnormal cervical smear results.
Methods: Data on patients undergoing loop electrosurgical excision procedure for persistent low-grade abnormal cervical smear results from January 2008 to December 2009 at Princess Margaret Hospital, Hong Kong were retrieved from the Hospital Authority Endoscopy Record System. Colposcopic findings, loop electrosurgical excision procedure histology, and patients' outcomes were reviewed through the Electronic Patient Record system, and the information was supplemented by follow-up telephone calls.
Results: A total of 123 patients were included in the study. The median follow-up duration was 3.6 years. In 87 (70.7%) patients, their follow-up cervical smears became normal after loop electrosurgical excision procedure, while the remaining 36 (29.3%) patients had persistent or recurrent abnormal cervical smear results. Patients aged ≥50 years were significantly more likely to have abnormal cervical smear results after loop electrosurgical excision procedure than those <50 years (50.0 vs. 21.3%, p=0.002). There was no correlation between prior colposcopic biopsy results, loop electrosurgical excision procedure histology, or margin status and recurrence of abnormal cervical smear results. In 13 (10.6%) patients, the final pathology was high-grade lesions (cervical intraepithelial neoplasia 2 or 3). The incidence of high-grade cervical intraepithelial neoplasia was similar in patients with prior colposcopic biopsy results of cervical intraepithelial neoplasia 1 or koilocytosis. The commonest complication was secondary haemorrhage, which occurred in 13 (10.6%) patients.
Conclusions: Loop electrosurgical excision procedure should be offered to women with persistent low-grade abnormal cervical smear results, whether the colposcopic cervical biopsy showed cervical intraepithelial neoplasia 1 or koilocytosis. Follow-up cervical smears after loop electrosurgical excision procedure in patients aged ≥50 years should be reinforced as they are more likely to have subsequent abnormal cervical smear results.
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Introduction

Cervical cancer is the tenth most common cancer in Hong Kong[1]. Early-stage cervical cancer can be asymptomatic. The Hong Kong SAR Government started the population cervical screening programme in 2004[2]. All eligible women aged between 25 and 65 years can be screened in Maternal Child Health Centres (MCHC). The screening aims to identify asymptomatic women with precancer (high-grade cervical intraepithelial neoplasia [CIN] 2-3) lesions and treat them to prevent progression to cervical cancer. The most widely accepted treatment modality is the loop electrosurgical excision procedure (LEEP). With improvement in cervical cancer screening and public awareness, detection and referral of patients with low-grade abnormal cervical smear results will increase.

For women with high-grade abnormal cervical smear results, 70-75% have high-grade lesions[3]. These women are usually treated with LEEP after confirmation by colposcopy and cervical biopsy. For women with low-grade abnormal cervical smear results, the risk of having a high-grade lesion in the cervix is lower. In women whose cervical smears show atypical squamous cells of undetermined significance (ASCUS), 5-17% have high-grade cervical lesions. If the cervical smear showed a low-grade squamous intraepithelial lesion (LGSIL), the risk of having a high-grade lesion is 15-30%[3].

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Most (around 80%)[4] low-grade lesions (koilocytosis, CIN 1) will regress spontaneously over 2 years, so immediate treatment may not be necessary. About 15% of these patients may progress to CIN 2 or 3 and require treatment later[5]. A specific group of patients with persistent low-grade abnormal cervical smear results and repeat colposcopy did not progress to high-grade lesions were recruited into the study. The reason for reviewing the outcomes of this group of patients is given below.

The Hong Kong College of Obstetricians and Gynaecologists (HKCOG) guidelines suggest that if a low-grade lesion is confirmed by colposcopy and biopsy, the patient can be followed up with cytology every 6 months. If LGSIL or ASCUS persists, colposcopy can be repeated after 12 to 18 months. Treatment is only indicated for patients with CIN lesions involving more than two quadrants of the cervix, or patients who are unable or unwilling to return for follow-up[3]. The American Society for Colposcopy and Cervical Pathology recommends that, in a patient with ASCUS or LGSIL cytology without CIN 2 or 3 identified by colposcopy, a follow-up cervical smear is recommended. If repeat cytology is reported as ASCUS or above, colposcopy is recommended. For women with CIN 1 persisting for at least 2 years, either continued follow-up or treatment is acceptable[6]. These guidelines do not advise on whether treatment is needed for patients with koilocytosis on colposcopic biopsy.

The sensitivity of low-grade cervical cytology (ASCUS and LGSIL) for underlying CIN 2+ varies from 79% to 91%[7]. The commonly used 'gold standard' — colposcopically directed punch biopsy — has been reported to miss some CIN 2+ lesions (15-25% in different studies)[8-11]. This suggests limitations of cytology and colposcopy follow-up in patients with low-grade disease. Additionally, the problems of defaulting follow-up, patients annoyance and anxiety due to persistent abnormal cervical smear results, and overloading of colposcopy clinics raise the question of whether treatment should be offered to this group of patients.

LEEP can be performed as an outpatient procedure under local anaesthesia. Apart from its therapeutic value, LEEP has prognostic value by providing histological diagnosis and assessing margin status. Its use is widely accepted in the management of high-grade cervical dysplasia. However, the potential risks, including haemorrhage, pelvic infection and, more seriously, cervical stenosis or adverse obstetrical outcomes, cannot be ignored[12,13].

At the Department of Obstetrics and Gynaecology, Princess Margaret Hospital, Hong Kong, repeat colposcopy is done for patients with persistent low-grade abnormal cervical smear results. For this group of patients, the HKCOG guidelines advise LEEP if cervical biopsy result is CIN 1, but no recommendation if normal or koilocytosis. We discussed the options of conservative management (follow-up smears) versus LEEP with these patients, a number of them chose LEEP. The rationale of performing LEEP in patients with persistent low-grade abnormal cervical smear results is that treatment could remove the cervical dysplasia and follow-up cervical smears would become normal. The outcomes of these patients after LEEP were evaluated.

Methods

This study was approved by the Hospital Authority Kowloon West Cluster Ethics Committee. The patients underwent LEEP at the Department of Obstetrics and Gynaecology, Princess Margaret Hospital from January 2008 to December 2009, with the indication of persistent low-grade disease. This group of patients was defined as having more than two consecutive low-grade abnormal cervical smear or cervical punch biopsy results over the 18 months preceding the LEEP.

All LEEPs were performed under colposcopic vision after iodine application. Loops of the appropriate size for each patient were used. Ball electrode diathermy was used for haemostasis. Histology reports of LEEP were reviewed. CIN was graded according to the classification system of the World Health Organization classification of tumours of the breast and female genital organs[14].

Patients who were <65 years and without malignant lesions were referred to MCHC or family clinic for follow-up cervical smears after LEEP. Colposcopic diagnosis, LEEP histology, and follow-up intervals were stated in the referral letters. The intervals for follow-up cervical smears were the same as suggested by the HKCOG. Patients with low-grade lesions were advised to have cervical smears every 6 months for 3 times, and if the results were normal, they could return to the usual 3-yearly screening schedule until they reached the age of 65 years. Patients with high-grade lesions with three normal cervical smear results done every 6 months were advised to have 10 annual cervical smears followed by 3-yearly cervical smears for the rest of their lives. Conditions requiring referral back to the colposcopy clinic were also included in the letter. Patients with low-grade lesions would be referred back if the results showed ASCUS twice or LGSIL once at 18 months or more

after colposcopy or LEEP. Patients with high-grade lesions would be referred back to the colposcopy clinic if the results showed ASCUS twice or LGSIL once at 12 months or more after LEEP.

The target patients of this study were identified from the Hospital Authority Endoscopy Record System. The principal investigator then identified two groups of patients, the first group were those who had follow-up in public hospitals whereas the second group were those having follow-up in MCHC. Follow-up smear results of the former group were retrieved from the Electronic Patient Record system. Before the study, applications were made for collaboration with the MCHC and the Department of Health in order to review patients' cervical smear results through the Cervical Screening Programme database, which were refused, so the patients in the second group were contacted to ascertain their cervical smear results. The interview was conducted either by telephone or face to face if the patients agreed to come to the clinic. Informed consent was obtained from all patients. A total of 78 patients were interviewed successfully in this group and 75 were recruited into the study; three were excluded as they did not have regular follow-up cervical smears. The main clinical outcome was abnormal cervical smear results after LEEP, defined as ASCUS or above. The abnormal cervical smear results were categorised according to the time interval of occurrence and cytology results.

Table 1. Histology results from loop electrosurgical excision procedure (n=123)

Histology	No. (%) of patients
Normal	3 (2.4)
Cervicitis	3 (2.4)
Koilocytosis	59 (48.0)
CIN 1	45 (36.6)
CIN 2 or 3	13 (10.6)

Abbreviation: CIN = cervical intraepithelial neoplasia

The data were analysed using the Statistical Package for the Social Sciences (Windows version 17.0; SPSS Inc., Chicago [IL], US). The rate of subsequent abnormal cervical smear results, risk factors for recurrence of abnormal cervical smear results, and complication rates were determined. Chi-square test, Student's *t* test, and Fisher's exact test were used when appropriate. A p value of <0.05 was considered as statistically significant.

Results

A total of 410 patients had LEEP performed from January 2008 to December 2009. In all, 255 patients were excluded as LEEP was performed for high-grade lesions (n=253) or there was presence of vaginal dysplasia (n=2). Twenty-eight patients were unable to be contacted, three patients did not have regular follow-up cervical smears, and one patient died of unrelated causes. None of the contacted patients refused to disclose their follow-up cervical smear results. The results of 123 patients were analysed, including both groups of patients under public hospital and MCHC follow-ups. Their median follow-up duration was 3.6 (range, 2.1-4.8) years.

For the LEEP histology results, most showed koilocytosis and CIN 1 (Table 1). There were 13 (10.6%) patients whose final pathologies were high-grade lesions (CIN 2 or 3), among whom one had an unsatisfactory colposcopy due to receded transformation zone. Four patients were immediately treated after colposcopy. The median interval between colposcopy and LEEP was 1.1 (range, 0-17.6) months. Some patients opted for follow-up cervical smears initially, but then changed their minds after one or more persistent abnormal cervical smear results.

Subgroup analysis of the biopsy results found that there was no significant difference in the risk of high-grade cervical lesions in patients with cervical biopsies with or without CIN 1 (p=0.49; Table 2).

A total of 87 (70.7%) patients had successful

Table 2. Subgroup analysis of cervical biopsy results and rate of high-grade lesions on final loop electrosurgical excision procedure (LEEP) histology (n=92)*

Cervical biopsy	No. (%) of patients		p Value
	Normal / human papilloma virus / low-grade LEEP histology	High-grade LEEP histology	
Koilocytosis or cervicitis (n=63)	58 (92.1)	5 (7.9)	0.49
Cervical intraepithelial neoplasia 1 (n=29)	26 (89.7)	3 (10.3)	

* Those with normal or inadequate cervical biopsy results before the LEEP were excluded from analysis

treatment and their cervical smear results became normal. The times of recurrence of abnormal cervical smear results and their distributions are shown in Tables 3 and 4. For the eight patients with abnormal cervical smear results recurring within 6 months, only one patient had unsatisfactory colposcopy before LEEP due to receded transformation zone. All of these eight patients had low-grade lesions on LEEP specimens. Moreover, four of them were postmenopausal and five of them had unclear or unknown margin status, which might explain the treatment failure.

Table 3. Rate and time of recurrence of abnormal cervical smear results after loop electrosurgical excision procedure (n=123)

Item	No. (%) of patients
Normal cervical smear results	87 (70.7)
Subsequent abnormal cervical smear results	36 (29.3)
Occurred at or <6 months	8 (6.5)
Occurred 6 months to 1 year	7 (5.7)
Occurred >1 year to 2 years	15 (12.2)
Occurred >2 years	6 (4.9)

Table 4. Distribution pattern of abnormal cervical smear results after loop electrosurgical excision procedure (n=36)

Item	No. (%) of patients
ASCUS	11 (30.6)
LGSIL	23 (63.9)
HGSIL	1 (2.8)
AGC	1 (2.8)

Abbreviations: ASCUS = atypical squamous cells of undetermined significance; LGSIL = low-grade squamous intraepithelial lesion; HGSIL = high-grade squamous intraepithelial lesion; AGC = atypical glandular cell

Different biopsy results and the associated risk of recurrence of abnormal cervical smear results were analysed. There was no correlation between the biopsy results and recurrence. Histology and margin status of LEEP also did not affect risk of recurrence (Table 5).

The patients were divided into two groups to analyse the effects of age (Table 6). The rate of subsequent abnormal cervical smear results was significantly higher in the age-group of ≥50 years (p=0.002). There were no significant differences in the rate of high-grade lesions, unclear margins, or complication rates between the two groups.

The most common complication was secondary haemorrhage, which occurred in 13 (10.6%) patients (Table 7). All of these patients were treated in outpatient clinics or in the examination room of a gynaecology ward, without the need for blood transfusion or re-operation for haemostasis. Only one patient had vaginal discharge. Only two patients underwent LEEP under general anaesthesia for reasons of technical difficulties due to a displaced or flushed cervix.

Discussion

This study showed that LEEP is an effective management for most patients with persistent low-grade abnormal cervical smear results. Subsequent cervical

Table 5. Correlation of biopsy results, histology of treatment, and margin status with recurrence status

Parameter	No. (%) of abnormal cervical smear results	p Value
Cervical biopsy		0.25
Koilocytosis or cervicitis (n=63)	19 (30.2)	
CIN 1 (n=29)	6 (20.7)	
Histology of LEEP		0.71
Koilocytosis / normal / cervicitis (n=65)	18 (27.7)	
CIN 1 (n=45)	15 (33.3)	
CIN 2 and 3 (n=13)	3 (23.1)	
Margin		0.55
Not clear / unknown (n=53)	17 (32.1)	
Clear (n=70)	19 (27.1)	

Abbreviations: CIN = cervical intraepithelial neoplasia; LEEP = loop electrosurgical excision procedure

Table 6. Comparison of risk of recurrence, margin status, rate of high-grade lesions, and complications by age

Item	No. (%)		p Value
	<50 years (n=89)	≥50 years (n=34)	
Subsequent abnormal cervical smear results	19 (21.3)	17 (50.0)	0.002
High-grade lesion on loop electrosurgical excision procedure	9 (10.1)	4 (11.8)	0.51
Margin not clear / unknown	40 (44.9)	13 (38.2)	0.32
Complication rate	9 (10.1)	6 (17.6)	0.20

Table 7. Complications of loop electrosurgical excision procedure (n=123)

Complication	No. (%) of patients
No complication	108 (87.8)
Secondary haemorrhage	13 (10.6)
Pelvic inflammatory disease	1 (0.8)
Others (vaginal discharge)	1 (0.8)

smear results were normal in 70.7% of the studied patients. LEEP is an outpatient procedure that can be performed under local analgesia and has an acceptable safety profile.

This study only included patients with persistent low-grade abnormal cervical smear results for whom no high-grade lesions had been found on colposcopy. However, 10.6% of patients had high-grade lesions on LEEP histology. Previous studies[8-11] have shown similar rates of high-grade lesions in this group of patients (15-25%). This result highlights the limitations of cervical smears and colposcopic biopsies. Prior colposcopic biopsy results were not predictive of the final high-grade histology on LEEP. In patients with biopsy histology of CIN 1, the rate of high-grade lesions was 10.3% which was not significantly different from those whose biopsies showed koilocytosis or cervicitis (7.9%, p=0.49). There were also no significant differences in the rates of subsequent abnormal cervical smear results between the two groups of patients. These findings suggest that LEEP should be offered to patients with persistent low-grade cervical smear results and colposcopic biopsies of less than CIN 1.

In some previous studies, the recurrence rate of CIN after LEEP varied between 8% and 14%[15,16], although most of the analysed patients had high-grade lesions. In this study, 29.3% of patients had subsequent abnormal cervical smear results. However, cervical smears are only used for screening and abnormalities may not reflect the true recurrence of CIN. Recurrence should be confirmed by histology. The primary outcome of this study — recurrence of subsequent abnormal cervical smear results — did not equal to recurrence of CIN. There were no correlations between prior colposcopic biopsy results, LEEP histology, or margin status and recurrence. Patients aged ≥50 years were significantly more likely to have recurrence of abnormal cervical smear results after LEEP than those <50 years (50.0% vs. 21.3%, p=0.002). This might be because in postmenopausal women, the transformation zone tends to recede into the endocervical canal. Their smaller cervices might also require use of a smaller diathermy loop for the LEEP procedure, resulting in a smaller and shallower excision. The rate of high-grade lesions on LEEP was comparable between the two groups.

After LEEP, 10.6% of patients had easily controlled secondary haemorrhage. Primary haemorrhage was uncommon and did not occur in any of these patients. All patients with secondary haemorrhage were treated with ferric subsulfate paste (Monsel's paste), with or without vaginal packing, either in outpatient clinics or in a gynaecology ward. Antibiotics (usually Augmentin; GSK) were given to cover potential infection of the LEEP wound. None of the patients required re-operation for haemostasis. The reported incidence of bleeding in this study was higher than that in some previous reports[11,17,18], which ranged from 2.6-5.4%. This might be due to the small sample size analysed. Future audit on the incidence of secondary haemorrhage should be performed in the unit.

LEEP is regarded as an acceptable treatment because it resulted in normalisation of cervical smear results in most of the patients in this study; some of whom had high-grade lesions in the cervix. The decision to perform LEEP in patients with persistent low-grade abnormal cervical smear results should be made after individual assessment, which should include patients' preferences, feasibility of regular follow-up, fertility wishes, and age. For young patients who wish to retain their fertility, the possible risk of preterm delivery after LEEP is a concern.

Limitations

Limitations of this retrospective study include some incomplete data (e.g. complications) and loss of contact with some patients. The follow-up cervical smear results were partly based on patients' verbal report, so there was a potential problem of accuracy. However, since most of the patients with abnormal cervical smear results were referred back to a public hospital for treatment, the abnormal results could be traced from the electronic patient records. Those patients having regular follow-up in MCHC without being referred back the outpatient clinic were likely to have normal cervical smear results. To facilitate management and follow-up of patients with abnormal cervical smear results, a common electronic platform could be set up to link the information in a cervical screening programme between the Hospital Authority and the Department of Health. In this study, only 2-year data were studied due to limited resources. Further larger-scale study should be performed in future. Long-term complications were not evaluated in this study as the follow-up time was insufficient.

Recommendations

Testing for high-risk human papillomavirus (HPV) was not performed in the patients in this study, but testing patients with mild cervical dysplasia would improve the prediction of high-grade lesions and reduce overtreatment. Triaging women with borderline or mildly abnormal cytology results has been recommended by the American Society for Colposcopy and Cervical Pathology guidelines[6]. The high-risk HPV DNA test using Hybrid Capture 2 technology (Digene Corporation, Gaithersburg [MD], US) is an in-vitro nucleic acid hybridisation assay for the qualitative detection of 13 high-risk types of HPV DNA in cervical specimens. This test can be performed in liquid-based cytology specimens. Women who have persistent HPV DNA positivity have been found to have a higher incidence of CIN 2 or higher lesions despite normal colposcopy[19]. Using the HPV DNA test for triaging patients with ASCUS or LGSIL for LEEP was shown to have a high sensitivity (84.0-96.4%)[7,20] for high-grade lesions. However, Walker et al[8] showed the absolute risk (which equates to positive predictive value) for HPV-positive women developing CIN 3 within 2 years was 12%, while for those who were HPV-negative, the risk was 2%. The HPV test is useful for reassuring patients with negative results. For patients with a positive HPV test, management should still be individualised.

Conclusions

LEEP is an acceptable treatment for patients with persistent low-grade disease, as most treated patients will have normal cervical smear results after treatment. With the limitations of monitoring by follow-up cervical smears and colposcopy, LEEP should be offered as one of the management options but the decision should be made after individual assessments.

In this study, whether the cervical biopsies showed CIN 1 or koilocytosis did not predict reliably the possibilities of high-grade disease and subsequent abnormal cervical smear results. Therefore, treating both groups of patients should be considered. Future research should be conducted to further evaluate this key decision-making step. HPV tests can be performed to triage these patients. Older women tend to have more recurrences. Keeping the follow-up of these patients in the colposcopy unit should be considered and the importance of compliance with follow-up must be reinforced.

This study aimed to increase discussion on this topic in the hope that more research on managing patients with persistent low-grade disease will be done in future.

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References

1. Hospital Authority, Hong Kong SAR. Hong Kong Cancer Registry, 2010. Available from: http://www3.ha.org.hk/cancereg/statistics.html#topten. Accessed Feb 2013.
2. Department of Health, Hong Kong SAR. Cervical Screening Programme website: http://www.cervicalscreening.gov.hk/english/about/abt_objectives.html. Accessed Feb 2013.
3. HKCOG Guidelines on the management of abnormal cervical cytology (revised). Hong Kong College of Obstetricians and Gynaecologists, November 2008. Available from: http://hkcog.obg.cuhk.edu.hk/public/guidelines.asp. Accessed Feb 2013.
4. Lee SS, Collins RJ, Pun TC, Cheng DK, Ngan HY. Conservative treatment of low grade squamous intraepithelial lesions (LSIL) of the cervix. *Int J Gynaecol Obstet* 1998;

60:35-40.
5. Wright TC Jr, Cox JT, Massad LS, Twiggs LB, Wilkinson EJ; 2001 ASCCP-sponsored Consensus Conference. Consensus guidelines for the management of women with cervical cytological abnormalities. *JAMA* 2002; 287:2120-31.
6. Wright TC Jr, Massad LS, Dunton CJ, Spitzer M, Wilkinson EJ, Solomon D. 2006 Consensus guidelines for the management of women with cervical intraepithelial neoplasia or adenocarcinoma in situ. For the 2006 American Society for Colposcopy and Cervical Pathology–sponsored Consensus Conference. *Am J Obstet Gynecol* 2007; 197:340-5.
7. Arbyn M, Bergeron C, Klinkhamer P, Martin-Hirsch P, Siebers AG, Bulten J. Liquid compared with conventional cervical cytology: a systematic review and meta-analysis. *Obstet Gynecol* 2008; 111:167-77.
8. Walker JL, Wang SS, Schiffman M, Solomon D; ASCUS LSIL Triage Study Group. Predicting absolute risk of CIN3 during post-colposcopic follow-up: results from the ASCUS-LSIL Triage Study (ALTS). *Am J Obstet Gynecol* 2006; 195:341-8.
9. Kyrgiou M, Tsoumpou I, Vrekoussis T, et al. The up-to-date evidence on colposcopy practice and treatment of cervical intraepithelial neoplasia: the Cochrane Colposcopy & Cervical Cytopathology Collaborative Group (C5 group) approach. *Cancer Treat Rev* 2006; 32:516-23.
10. Ihonor AO, Cheung WY, Freites ON. A comparative study of the assessment of cervical intraepithelial neoplasia in women having large loop excision of the transformation zone. *J Obstet Gynaecol* 1999; 19:169-71.
11. Duesing N, Schwarz J, Choschzick M, et al. Assessment of cervical intraepithelial neoplasia (CIN) with colposcopic biopsy and efficacy of loop electrosurgical excision procedure (LEEP). *Arch Gynecol Obstet* 2012; 286:1549-54.
12. Boonlikit S, Asavapiriyanont S, Junghuttakarnsatit P, Tuipae S, Supakarapongkul W. Correlation between colposcopically directed biopsy and large loop excision of the transformation zone and influence of age on the outcome. *J Med Assoc Thai* 2006; 89:299-305.
13. Martin-Hirsch PP, Paraskevaidis E, Bryant A, Dickinson HO. Surgery for cervical intraepithelial neoplasia. *Cochrane Database Syst Rev* 2000; (2):CD001318.
14. *World Health Organization classification of tumors. Pathology and genetics of tumours of the breast and female genital organs*. Tavassoli FA, Deville P, editors. Lyon: IARC Press; 2003.
15. Kyrgiou M, Koliopoulos G, Martin-Hirsch P, Arbyn M, Prendiville W, Paraskevaidis E. Obstetric outcomes after conservative treatment for intraepithelial or early invasive cervical lesions: systematic review and meta-analysis. *Lancet* 2006; 367:489-98.
16. Lima MI, Tafuri A, Araújo AC, de Miranda Lima L, Melo VH. Cervical intraepithelial neoplasia recurrence after conization in HIV-positive and HIV-negative women. Int J Gynaecol Obstet 2009; 104:100-4.
17. Lubrano A, Medina N, Benito V, et al. Follow-up after LLETZ: a study of 682 cases of CIN 2-CIN 3 in a single institution. *Eur J Obstet Gynecol Reprod Biol* 2012; 161:71-4.
18. Cecchini S, Visioli CB, Zappa M, Ciatto S. Recurrence after treatment by loop electrosurgical excision procedure (LEEP) of high-grade cervical intraepithelial neoplasia. *Tumori* 2002; 88:478-80.
19. Sutthichon P, Kietpeerakool C. Perioperative complications of an outpatient loop electrosurgical excision procedure: a review of 857 consecutive cases. *Asian Pac J Cancer Prev* 2009; 10:351-4.
20. Kietpeerakool C, Srisomboon J, Khobjai A, Chandacham A, Tucksinsook U. Complications of loop electrosurgical excision procedure for cervical neoplasia: a prospective study. *J Med Assoc Thai* 2006; 89:583-7.