

Colposcopic assessment and outcome in low grade cervical intraepithelial neoplasia treated with loop electrosurgical excision procedure

Abstract

The aim of the research was to assess the outcome of persistent (\geq two years) low-grade cervical intraepithelial neoplasia (CIN 1) medicated with loop electrosurgical excision procedure (LEEP). An analysis of 38 topics with persistent biopsy-confirmed CIN 1 diagnosed after low-grade squamous intraepithelial lesion (LSIL) or atypical squamous cells of undetermined significance (ASC-US) on Pap test and treated using LEEP was performed. Post-LEEP follow-up were scheduled in 6 months, 1 year, and yearly thereafter: cytology, colposcopy, and plasma diagnostic examinations. There were 38 LSIL patients treated with LEEP conization. About 6 patients were excluded from the study due to subsequent hysterectomy and 2 patients never attended the follow-up schedule in the rest. The remaining 30 patients were retrospective studied for the incidence of recurrent rate. The mean age of the patient was 44 years. About 50% of patients were multiparity and nearly one - third used oral contraceptive pill. The results of this study suggest that the incidence of CIN 2+ lesions during follow-up of persistent biopsy-confirmed CIN 1 after ASC-US/LSIL treated by LEEP is very low.

Keywords: persistent CIN, loop electrosurgical excision procedure, HPV

Introduction

The actual incidence of cervical intraepithelial neoplasia (CIN) can only be estimated. From approximately 7% of Pap tests with epithelial abnormalities discovered annually, during screening, half is CIN. The incidence of CIN lesions varies among the studied populations as they correlate with the early onset of sexual life, socio-economic factors, and a variety of other risk-associated behaviors. In addition, clinical methods used in CIN diagnostics, mainly cytological screening and colposcopic examination, are devoid of sensitivity⁽¹⁾.

Pre-invasive lesions can spontaneously regress, remain stable for long periods, or progress to a greater degree of dysplasia. Although few CIN lesions have the potential to progress frankly towards invasive cancer, the neoplastic potential increases with CIN. It was observed progression to clinically isolated syndrome in 6% of "mild" histological dysplasia, 13% of dysplasia modeled and 29% of "marked" dysplasia. Regression of lesions to disappearance was observed in 62% of cases of mild dysplasia and in only 19% of cases of marked dysplasia⁽²⁾.

Recently, some authors have calculated that approximately 40% of CIN2 lesions are spontaneously regressing in 2 years⁽³⁾.

Identifiable risk factors for CIN, similar to those of invasive lesions, prove useful in the development of cervical cancer screening and prevention programs. The risk for cervical neoplasia is most associated with genital infection with human papillomavirus (HPV) and advanced age. Risk factors for cervical neoplasia have been proposed as behavioral and medical factors⁽⁴⁾.

The age average for diagnosing cancer is 48 years, approximately one decade more than CIN. HPV infection in older women is more likely a persistent than transient infection. Old age is associated with the accumulation of mutations that can lead to malignant cell transformation. In addition, the decrease in prenatal care and contraception needs a less frequent access of elderly women to cervical cancer prevention programs^(5,6).

For many years, epidemiological evidence has shown the link between cervical neoplasia and the following behaviors: early onset of sexual life, multiple sexual partners and promiscuous life of the sexual partner⁽⁷⁾.

The relationship between cervical cancer and smoking has been established. This is especially true for squamous cancers, the relationship between smoking and cervical adenocarcinoma and cervical adenosquamous carcinoma is less clear⁽⁸⁾. Smoking also increases the risk of pre-inva-

Ștefan Paitici¹,
Costin Berceanu²,
Cosmin Vasile Obleaga¹,
Elvira Brătîlă³,
Răzvan Ciorteș⁴,
Sabina Berceanu²,
Monica Mihaela Cîrstoiu³,
Roxana Elena Bohilțea³,
Sabina Berceanu²,
Claudia Mehedințu³

1. 2nd Surgery Clinic, Emergency County Hospital Craiova, Romania; PhD Studies School, University of Medicine and Pharmacy Craiova, Romania

2. Department of Obstetrics and Gynecology, University of Medicine and Pharmacy Craiova Romania

3. Department of Obstetrics - Gynecology and Neonatology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

4. Department of Obstetrics and Gynecology, "Iuliu Hațieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

Correspondence:
Dr. Costin Berceanu
e-mail: dr_berceanu@yahoo.com

sive cervical lesions, and this relationship persists even after adjusting HPV positivity and low socioeconomic status. Current smoking, large packets per year, and smoking during menarche are all associated with cervical neoplasm. The biological verosimilitude of the linkage between smoking and cervical neoplasia is supported by: (i) the cervical mucus of the smoker contains carcinogens and it's mutagenic; (ii) genetic alterations in the cervical tissue of smokers are similar to those seen in smoking related neoplasms with other localizations; (iii) the risk is dose-dependent, increases with both the duration and the amount of cigarettes consumed; (4) risk decreases with smoking cessation^(8,9,10).

Although the data are inconclusive, the deficiency of certain vitamins such as A, C, E, beta carotene and folate may alter cellular resistance to HPV infection and thus persistent viral infection and cervical neoplasia⁽¹¹⁾.

Studies on the relationship between cervical neoplasia and exogenous hormones are contradictory and confusing, such as increased sexual activity and patient screening. In addition, cancerous epithelial cells are generally not influenced by hormonal factors⁽¹²⁾.

Methods

This study includes a group of 38 patients, recruited from among women attending our colposcopic service in the last 5 years from Emergency County Hospital Craiova, Romania. Eligibility criteria included the following:

1. a CIN 1 histopathological diagnosis was established at our institution after atypical squamous cells of undetermined significance/low-grade squamous intraepithelial lesion (ASC-US/LSIL) on Pap test;
2. persistence of a low-grade cervical lesion diagnosed either by cytology (LSIL, ASC-US) or histopathology (CIN 1) on at least 2 occasions during the subsequent 2 years of follow-up;
3. a satisfactory colposcopic examination;
4. a clinical decision for LEEP treatment for a persistent low-grade cervical lesion.

In these cases, we used a treatment protocol aiming for removal of the transformation zone when possible, according to the judgment of the colposcopist and the specific patient's requirements (e.g. age, desire for pregnancy, etc.).

All histopathological diagnoses, both at enrolment and during follow-up, were rendered by 2 independent expert gynecologists by consensus reading.

Follow-up cytologic, colposcopic, and molecular diagnostic examinations were scheduled at 6-month post-LEEP, 1 year, and yearly thereafter. All patients were treated according to an established protocol including HPV deoxyribonucleic acid detection and typing and colposcopy at each follow-up visit.

Results

Besides six patients which overdue the hysterectomy and 2 patients which do not attend the schedule and were excluded, 30 patients could be included in the follow-up program after the LEEP conization.

The mean age of the patients was 44 years. The multiparity presented about 50% of the patients and one-third used contraceptives in their past.

After 12 months of median follow up, 17 (56,6 %) patients showed a positive cytology aspect at 8-10 months after LEEP. All of them were negative for HPV testing.

From the total of the patients, only 3 (10%) patients followed two times LEEP. The curettage was achieved in 4 (13,3%) patients, in which 3 patients showed normal aspect and only 1 patient presented LSIL interpretation. Furthermore, the patients received another colposcopic examination.

Regarding the patients who presented ASC-US (n=5/16,6%) at cytology, showed in the end normal colposcopic findings (Figures 1 and 2).

In our series of cases, 13 (43,3 %) patients showed normal aspects without any other abnormal appearance after 6-45 months of follow-up (Figures 3 and 4). One patient presented high-grade squamous intraepithelial lesion (HSIL) aspect and at the colposcopic directed bi-



Figure 1. Low grade cervical lesion demonstrated at 10-12 o'clock. Magnification x 7.5. Pale acetowhite color and indistinct borders

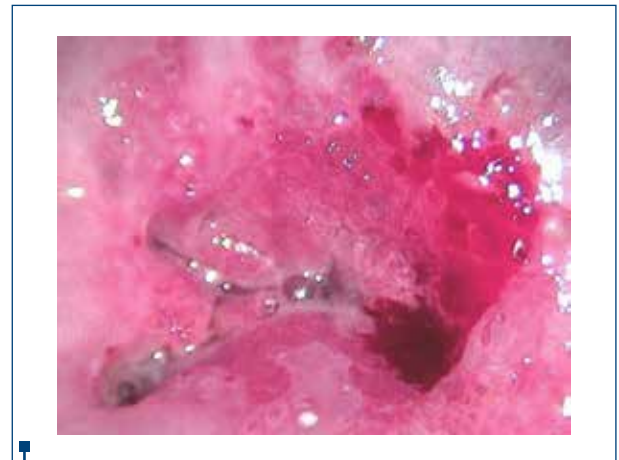


Figure 2. Low grade cervical lesion in the same patient. Magnification x 15. Repeated applications of dilute acetic acid in order to maintain visibility of the lesion

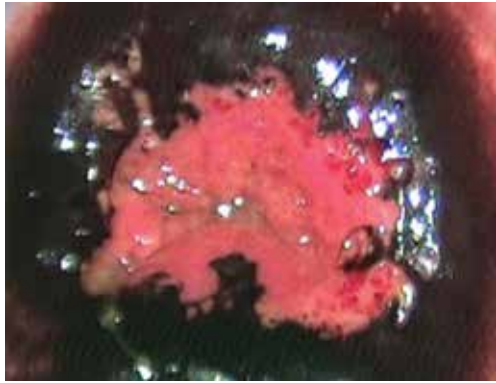


Figure 3. Low grade cervical lesion following application of Lugol's iodine solution. Magnification x 7.5. Colposcopy demonstrating a large flame-shaped lesion located predominantly on the anterior cervix

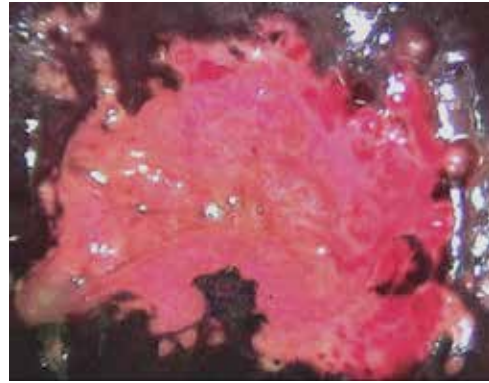


Figure 4. Low grade cervical lesion in the same patient. Magnification x 15. Colposcopy demonstrating a variegated iodine staining pattern



Figure 5. Colposcopic reassessment at 12 months after Loop Electrosurgical Excision Procedure (LEEP). Magnification x 7.5, demonstrating pink, stratified squamous epithelium of the cervix and clear mucus

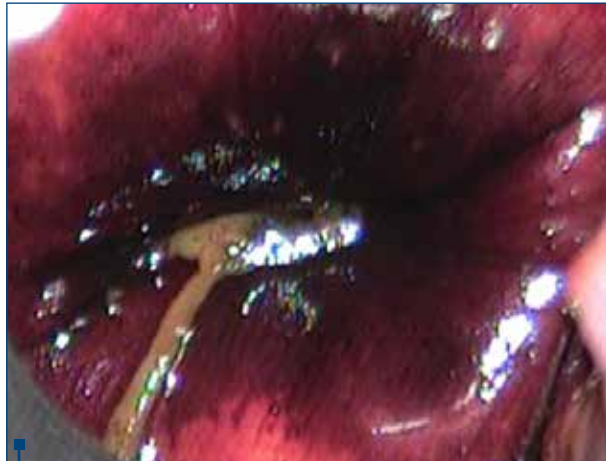


Figure 6. Colposcopic reassessment at 12 months after Loop Electrosurgical Excision Procedure (LEEP) following application of Lugol's iodine solution. Magnification x 7.5, demonstrating a rich mahogany brown color



Figure 7. Low grade cervical lesion. Colposcopy demonstrating an angular and geographic lesion in a moderately translucent acetowhite area predominantly on the anterior cervix. Note the dense acetowhite region at 9-10 o' clock

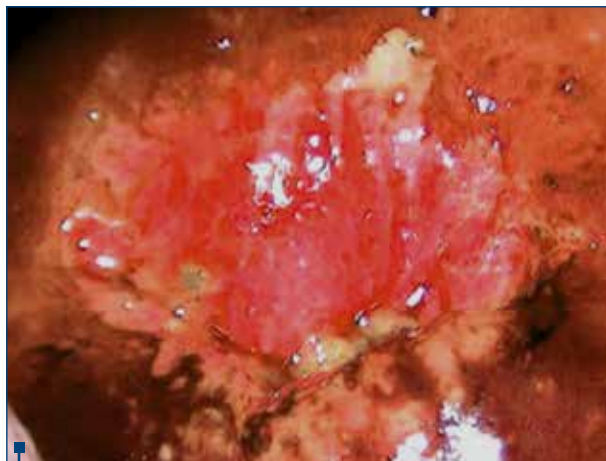


Figure 8. Low grade cervical lesion following application of Lugol's iodine solution. Magnification x 7.5. Colposcopy demonstrating the geographic lesion border and irregular margins



Figure 9. Colposcopic reassessment at 12 months after Loop Electrosurgical Excision Procedure (LEEP). Magnification x 7.5 demonstrating the surgically cured cervix

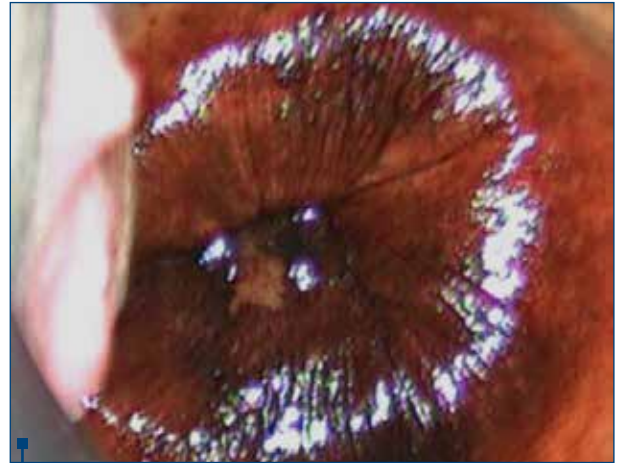


Figure 10. Colposcopic reassessment at 12 months after Loop Electrosurgical Excision Procedure (LEEP) following application of Lugol's iodine solution. Magnification x 7.5, demonstrating the iodine-homogenous uterine cervix

opsy, it was present only the squamous epithelium. After 1 year follow-up, her cervical smear was normal. Another 2 patients showed LSIL interpretation with satisfactory colposcopic features (Figures 5,6, 7 and 8). Moreover, colposcopically directed biopsy, demonstrated the existence of HSIL in a patient and LSIL at another. The patient who presented HSIL showed at 11-12 o'clock free surgical margins (Figures 9 and 10). After 2 years of follow-up, her smears remain negative.

Therefore, only 2 patients who presented high ASC-H revealed unsatisfactory colposcopic features, being negative for the next 12 and 19 months of follow-up.

Discussion

The results of this study suggest that among women with persistent LSIL treated by LEEP, the subsequent incidence of high-grade cervical lesions during follow-up is low and is associated with the persistence/incidence of hrHPV infection. On the other hand, the

10% annual rate of low-grade cervical lesions during follow-up suggests that this group of subjects remains at a significant risk of persistence of low-grade lesions even after LEEP^(13,14).

The number of subjects treated and the protocol used (HPV typing, colposcopic follow-up, and colposcopies performed before the results of HPV typing were known) is the main strengths of this study. Given the 9% to 11% annual rate of subjects lost to follow-up, we cannot exclude a potential selection bias.

Conclusions

The results of this study suggest that the incidence of CIN 2+ lesions during follow-up of persistent biopsy-confirmed CIN 1 after ASC-US or LSIL treated by LEEP is very low.

However, the rates of low-grade cervical abnormalities in our group were still high during a median follow-up period of 25 months. ■

References

- Spinillo A, Gardella B, Iacobone AD, Dominoni M, Cesari S, Alberizzi P. Outcome of persistent low-grade cervical intraepithelial neoplasia treated with loop electrosurgical excision procedure. *J Low Genit Tract Dis* 2016, 4, 307-11.
- Msyamboza KP, Phiri T, Sichali W, Kwenda W, Kachale F. Cervical cancer screening uptake and challenges in Malawi from 2011 to 2015: retrospective cohort study. *BMC Public Health* 2016, 16(1), 806.
- Jeronimo J, Castle PE, Temin S, Denny L, Gupta V, Kim JJ, Luciani S, Murokora D, Ngoma T, Qiao Y, Quinn M, Sankaranarayanan R, Sasieni P, Schmeler KM, Shastri SS. Secondary prevention of cervical cancer: ASCO resource-stratified clinical practice guideline. *J Glob Oncol* 2016, 3(5), 635-57.
- Du R, Meng W, Chen ZF, Zhang Y, Chen SY, Ding Y. Post-treatment human papillomavirus status and recurrence rates in patients treated with loop electrosurgical excision procedure conization for cervical intraepithelial neoplasia. *Eur J Gynaecol Oncol* 2013, 34(6), 548-51.
- Houfflin Debarge V, Collinet P, Vinatier D, Ego A, Dewilde A, Boman F, Leroy JL. Value of human papillomavirus testing after conization by loop electrosurgical excision for high-grade squamous intraepithelial lesions. *Gynecol Oncol* 2003, 90(3), 587-92.
- Senkomago V, Royalty J, Miller JW, Buenconsejo-Lum LE, Benard VB, Saraiya M. Cervical cancer screening in the National Breast and Cervical Cancer Early Detection Program (NBCCEDP) in four US-Affiliated Pacific Islands between 2007 and 2015. *Cancer Epidemiol* 2017, 50(Pt B), 260-7.
- Kuroki LM, Bergeron LM, Gao F, Thaker PH, Massad LS. See-and-treat loop electrosurgical excision procedure for high-grade cervical cytology: are we overtreating? *J Low Genit Tract Dis* 2016, 20(3), 247-51.
- Noothong S, Inthasorn P, Wannissorn M. Pathological discrepancy between colposcopic directed cervical biopsy and Loop Electrosurgical-Excision Procedures (LEEPs) in patients with biopsies proven high grade cervical intraepithelial neoplasia. *Taiwan J Obstet Gynecol* 2017, 56(5), 628-63.
- Li K, Yin R, Li Q, Wang D. Analysis of HPV distribution in patients with cervical precancerous lesions in Western China. *Medicine (Baltimore)* 2017, 96(29), e7304.
- Liu Y, Alqatari M, Sultan K, Ye F, Gao D, Sigel K, Zhang D, Kalir T. Using p16 immunohistochemistry to classify morphologic cervical intraepithelial neoplasia 2: correlation of ambiguous staining patterns with HPV subtypes and clinical outcome. *Hum Pathol* 2017, 66, 144-51.
- Zeitay AG, Gungör ES, İlhan G, Çetin O, Dane C, Furtuna C, Atmaca FFV, Tuna M. Cervical Conization and the risk of preterm birth: A population-based multicentric trial of Turkish cohort. *J Clin Diagn Res* 2017, 11(3), QC21-QC24.
- Kietpeerakool C, Srisomboon J. Safety of the loop electrosurgical excision procedure in women with early invasive cervical carcinoma. *Int J Gynaecol Obstet* 2006, 95(1), 54-5.
- Kim HS, Kwon JE, Kim JH, Kim A, Lee NR, Kim M, Lee M, Suh DH, Kim YB. Efficacy of loop electrosurgical excision procedure with cold coagulation for treating cervical intraepithelial neoplasia: A two center cohort study. *Obstet Gynecol Sci* 2017, 60(2), 200-6.
- Guo HJ, Guo RX, Liu YL. Effects of loop electrosurgical excision procedure or cold knife conization on pregnancy outcomes. *Eur J Gynaecol Oncol* 2013, 34(1), 79-82.

Received:
November 12, 2017
Revised:
November 30, 2017
Accepted:
December 07, 2017