Interpretability of Excisional Biopsies of the Cervix: Cone Biopsy and Loop Excision

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■ **Abstract**

Objective. To compare the results of cold knife conization (CKC) and loop electrosurgical excision procedure (LEEP) for cervical intraepithelial neoplasia to determine if excisional method has effects on pathologic interpretation.

Methods. Retrospective review of the perioperative medical records of patients who had a CKC and electrosurgical loop excision of cervix. Patients selected had either primary treatment for cervical intraepithelial neoplasia, suspected invasion, glandular abnormalities or discordant cytology.

Results. Among the eligible patients, 61 had CKC and 96 had LEEP. Overall, CKC specimens had interpretable surgical margins more frequently than LEEP (95% vs 85%); however, it was not statistically significant (p = .1). Margins were less likely to be involved with neoplasia in CKC specimens (16% vs 38%; p = .005). Loop electrosurgical excision procedure specimens were less likely to yield a single intact specimen (1.1 vs 1.9; p = .000). Logistic regression showed a significant effect of specimen number (p = .04) on interpretability.

Conclusion. Current American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines for diagnostic excisional procedure used for glandular lesions suggest that the procedure provides "an intact specimen with interpretable margins." Loop electrosurgical excision procedure in the current study was associated with an increased number of specimens that limited interpretability and an increased number of positive margins. Cold knife conization is preferred in cases where margin status is critical, such as glandular lesions and suspected microinvasion. If LEEP is performed, clinicians should attempt to obtain a single surgical specimen maximizing the pathologic interpretation and disease-free margins. ■

Key Words: cervical intraepithelial neoplasia, cold knife conization, loop electrosurgical excision procedure

The loop electrosurgical excision procedure (LEEP) has become the more common technique for diagnosis and treatment of cervical intraepithelial neoplasia. Loop electrosurgical excision procedures have several advantages, including lower blood loss and shorter operative times, ease of use and low cost, and greater than 90% success rate [1]. Several randomized studies have proven that LEEP is a more rapid technique with favorable postoperative morbidity [2, 3].

The updated 2006 American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines allow for the use of LEEP for cervical adenocarcinoma and suspected invasion [4]. However, when comparing the 2 techniques, pathologic margins are often more frequently involved and more difficult to interpret with LEEP. Studies have demonstrated that positive margin involvement is a strong predictor for residual disease [5, 6].

We conducted the present study to compare the results of cold knife conization (CKC) and LEEP to determine if electrocautery will have a deleterious effect on pathologic interpretation and treatment recommendations.

MATERIALS AND METHODS

We performed a retrospective review of the charts and perioperative medical records of patients who underwent a CKC and electrosurgical loop excision of cervix

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uteri performed on Gynecologic Oncology Service at Main Line Health Hospitals from January 1, 2003, to October 1, 2007. The approval of study by the Lankenau Institute for Medical Research Institutional Review Board was obtained.

Patients selected had either primary treatment with CKC or electrosurgical loop excision for cervical intraepithelial neoplasia, suspected invasion, glandular abnormalities, or discordant cytology. We used routine pathology records containing pertinent information on interpretability and margin status of provided specimens. The review was performed by staff physicians of the pathology department in our institution. Patients with secondary procedures or incomplete medical records were excluded from the study.

Comparisons between groups were made for all predictor variables. For continuous data (age, parity, number of the specimen, and size of the specimen), a *t* test was used to compare the patients receiving the 2 procedures. For categorical data (smoking status, final diagnosis, margin involvement), procedures were compared using χ^2 analysis. In addition, margin involvement status was broken down into ectocervical and endocervical categories that were compared individually.

The effect of variables on interpretability was tested with a χ^2 test for categorical variables, and a logistic regression was performed for continuous predictor variables. Significant terms from the univariate comparisons were used to construct a simple logistic regression model. Variables used were the category of procedure, number of specimens, margin involvement, and the interaction between procedure and number of specimens. As margin involvement was shown to primarily driven by the "ectocervix" category, these results were used. The interaction between number of specimens and margin involvement was also considered but was removed from the model because it was nonsignificant ($p = .55$).

Table 1. Comparison of Interpretability Predictor Variables Between 2 Groups

	CKC (n = 61)	LEEP (n = 96)	*p*
Interpretability, %	95	85	NS
Age (SD), y	43.3 (15)	34.9 (13)	.0004
Parity	1.54	0.99	.01
Smoking, %	23	24	NS
Size of specimen in cm^3 (mean)	2.9	2.0	.01
Number of specimens (mean)	1.1	1.9	.000
Margin involvement, %	16	38	.005
Endocervical	16	24	NS
Ectocervical	5	26	.001

CKC, cold knife conization; LEEP, electrosurgical excision; NS, nonsignificant value.

Table 2. The Results of Logistic Regression Model Constructed From Margin Involvements, Number of Surgical Specimen, and Type of Procedure to Analyze Negative Effect on Interpretability

	p
LEEP	NS
No. surgical specimens	.04
Involvement of surgical margins	.004
LEEP + No. surgical specimens	.056

LEEP, loop electrosurgical excision procedure; NS, nonsignificant value.

All statistical analyses were carried out using R statistical software version 2.6.0 (R Development Core Team 2007, Vienna, Austria) using the base statistical package, except for logistic regressions, which were carried out using the function *Irm* of the package Design version 2.1-1 (Harrel 2007, Nashville, TN).

RESULTS

A total of 162 women were identified. Three patients with secondary procedures and 2 patients with incomplete medical records were excluded from the study. Of the remaining 157 women, 61 had CKC and 96 had LEEP.

Comparison between the different predictor variables for effect on interpretability of the pathologic specimen revealed that several were substantially different among CKC and LEEP groups (Table 1). Overall, CKC specimens had interpretable surgical margins more frequently than LEEP (95% vs 85%), although it was not of statistical significance ($p = .1$). Significant differences were observed for age (43.3 vs 34.9; $p = .0004$), parity (1.54 vs 0.99; $p = .01$), size of the specimen obtained during procedure (2.9 cm^3 vs 2 cm^3; $p = .01$), number of the specimens collected (1.1 vs 1.9; $p = .000$), and involvement of surgical margins (16% vs 38%; $p = .005$). Of note, the difference in margin status was driven almost entirely by the involvement of ectocervix (5% vs 26%; $p = .001$), with the involvement of endocervical margins being nonsignificant ($p = .35$).

However, when logistic regression model was applied to the above predictor variables that differed among groups, only positive status of surgical margins ($p = .004$) and increasing number of specimens obtained ($p = .04$) had statistically significant negative effect on pathologic interpretability. The interaction between

LEEP and number of surgical specimens approached statistical significance (p = .056; Table 2).

DISCUSSION

Current ASCCP guidelines for diagnostic excisional procedure used for glandular lesions suggest that the procedure provides "an intact specimen with interpretable margins" [4].

Our data confirm that a single specimen will allow for better pathologic interpretation. In cases where a clinical treatment decision needs to be based on margin status and interpretability of the provided surgical specimen, it may still be prudent to perform a CKC. However, LEEP is an acceptable option, but the clinician should attempt to provide the pathologist with a single, intact specimen.

Although Bryson et al. [7] demonstrated that LEEP with negative margin status is an adequate treatment for adenocarcinoma in situ, the study of Widrich et al. [8] showed that margins are more frequently involved after LEEP compared with CKC. Some authors consider a CKC biopsy necessary if ACIS is diagnosed in a LEEP specimen [9]. In patients with cervical adenocarcinoma in situ pursuing fertility sparing treatment, CKC has been shown to be a superior technique for achieving negative margins [10].

In situations of early invasive squamous cell carcinoma, conservative management may be chosen if the lesion is completely excised and the specimen is interpretable for margin status and depth of invasion. To achieve that, CKC may be the optimal technique. Cases have been reported with LEEP in which margin status and depth of invasion are not interpretable may necessitate additional surgery [9, 11].

Our study is limited by its retrospective nature and the size of the sample. The size of the study might not be significantly powered to identify 10% difference. Post hoc power analysis showed that if we assume equal sample size, 133 samples in each category would have given us 80% power. The strength of the study is that all procedures were performed by 1 group of experienced gynecologic oncologists, and complete data were available in great majority of cases.

Although ASCCP guidelines allow for use of electrocautery, caution should be used in individual cases. Clinicians should still be familial with and able to perform CKC for selected individuals.

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