The value of endocervical curettage after conization for cervical intraepithelial neoplasia

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Abstract: The objective of this study is to assess the value of postcone endocervical curettage, after conization of cervical intraepithelial neoplasia or carcinoma as a predictive tool for residual lesions. This is a retrospective observational study. All data were obtained by the University Hospital of Zurich, Department of Gynaecology. One hundred fifty patients underwent hysterectomy within 12 months after conization and endocervical curettage from 1993 to 2006. To analyze the sensitivity, specificity, and the positive predictive value (PPV) and negative predictive value (NPV) of the endocervical curettage after conization, we used the Fisher exact test and (2) test. The main outcome measures are the sensitivity and specificity as well as the PPV and NPV of the postconization endocervical curettage. The endocervical curettage exhibited a sensitivity of 0.38, a specificity of 0.85, a PPV of 0.56, and an NPV of 0.73. Comparing patients younger than 50 years to women 50 years or older, endocervical curettage had a sensitivity of 0.35 and 0.44, a specificity of 0.83 and 0.94, a PPV of 0.46 and 0.88, and an NPV of 0.76 and 0.63, respectively. The endocervical curettage after conization of cervical intraepithelial neoplasia does not generally improve the prediction of residual lesions. However, in women 50 years or older, a higher specificity and PPV, 0.94 and 0.88, respectively, was observed. Therefore, this subgroup of patients may benefit from an endocervical curettage.

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The value of endocervical curettage (ECC) following conization for cervical intraepithelial neoplasia (CIN)

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Abstract:

Objective: To assess the value of post-cone endocervical curettage, following conization of cervical intraepithelial neoplasia or carcinoma as a predictive tool for residual lesions.

Design: Retrospective observational study

Setting: All data were obtained by the University Hospital of Zurich, Department of Gynaecology

Population: 150 patients underwent hysterectomy within 12 months after conization and endocervical curettage from 1993 to 2006

Methods: To analyse the sensitivity, specificity, the positive and negative predictive values of the endocervical curettage following conization we used the Fisher's exact test and Chi2-Test.

Main outcome measures: The sensitivity and specificity as well as the positive and negative predictive values of the post-conization endocervical curettage.

Results: The endocervical curettage exhibited a sensitivity of 0.38, a specificity of 0.85, a positive predictive value of 0.56 and a negative predictive value of 0.73. Comparing patients <50 years to women ≥50 years, endocervical curettage had a sensitivity of 0.35 and 0.44, a specificity of 0.83 and 0.94, a positive predictive value of 0.46 and 0.88, a negative predictive value of 0.76 and 0.63, respectively.

Conclusion: The endocervical curettage following conization of cervical intraepithelial neoplasia does not generally improve the prediction of residual lesions. However, in women ≥50 years, a higher specificity and positive predictive value, 0.94 and 0.88, respectively, was observed. Therefore, this subgroup of patients may benefit from an endocervical curettage.

Keywords: ECC (= endocervical curettage), sensitivity, specificity, PPV (= positive predictive value), NPV (= negative predictive value)

Introduction:

There is controversy regarding the usefulness of performing an endocervical curettage (ECC) following excisional biopsy of cervical intraepithelial neoplasia (CIN). Especially the value for predicting residual lesions in the cervix above the excision site is controversial.
This retrospective observational study examined the value of post-cone ECC by analysis of the specificity and sensitivity as well as the positive and negative predictive values (PPV, NPV) of this procedure.

Materials and methods:
A retrospective case series was performed including 150 patients that were treated for cervical intraepithelial neoplasia between 1993. and 2006 at the University Hospital of Zurich, Department of Gynaecology. Treatment consisted of a conization and an ECC followed subsequently by a hysterectomy within 12 months after conization. The median age was 45.2 years (26-85 years).
The histological specimens were analysed by the Department of Pathology, University of Zurich. The conization samples were examined for the grade of CIN and/or carcinoma and the ECC for presence or absence of CIN. The margin status considered affected or lesion-free endo- and ectocervical margins. The subsequent hysterectomy specimens were analysed for residual/recurrent CIN or carcinomas. For the carcinomas, we did not differentiate between different stages, but summarized them all in one group.
The significance of the ECC following conization was examined with regard to its sensitivity, specificity as well as positive and negative predictive values. In addition, the relative frequencies were calculated. To analyse whether age has an influence on the significance of ECC, patients were divided into two groups: <50 years and ≥ 50 years. The 95%-confidence intervals (CI) were calculated according to Wilson. The statistical package StatView 5.0.1 was used. Statistical analysis was performed using Fisher's exact test and Chi2-Test. P-values <0.05 were considered to indicate statistical significance.

Results:

The conization specimens (n=150) showed CIN 1 and 2 in 13 (8.7%), CIN 3 in 87 (58%) and cervical carcinoma in 50 (33.3%) cases, respectively. The subsequent ECC revealed neoplastic lesions in 34 (22.7%) patients.
Table 1 shows the correlation between the pathological ECCs and the affected endo- and ectocervical margins of the cone. Seven (10.8%) of the conization specimens with clean margins exhibited intraepithelial neoplastic changes in the subsequent ECC.
Twenty-six (34.7%) of the patients with affected endocervical margins showed a pathological ECC. Lesion-free margins in the conization specimen correlated in 58 cases (89%) with a normal ECC.
The correlation between the histological findings in the hysterectomy specimen, the conization specimen and the ECC are shown in table 2.
Fifty (33.3%) hysterectomy specimens revealed intraepithelial lesions whereas 100 cases (66.7%) were without pathologies. Patients with pathological findings in the hysterectomy specimen had significantly more often pathological ECCs as compared to the group without intraepithelial lesions at time of hysterectomy, 38% versus 15%, respectively ($p= 0.0001$).
Patients with a lesion-free hysterectomy specimen (n=100) had a negative ECC in 85 cases (85%) and an ECC with neoplastic lesions in 15 cases (15%).

Patients with pathological findings in the hysterectomy specimen had a significantly higher rate of affected endocervical cone margins compared to non-pathological histology at time of hysterectomy. Affected endocervical margin status in the cone (n=75) correlated significantly with neoplastic findings in the subsequent hysterectomy: 76% with pathological histology in the hysterectomy specimen versus 37% without pathological findings ($p< 0.0001$).
In 26 patients, ECC and endocervical margins were positive. Of these, 16 (61.5%) hysterectomies showed pathological findings. On the other hand, when both were negative (n=67), the hysterectomies showed neoplastic lesions in 9 cases (13.4%). This revealed a high statistical correlation ($p< 0.0001$).
The influence of patient's age on the significance of the ECC following conization was evaluated in table 3. In the 32 older patients (≥50 years), the ECC status correlated significantly with the hysterectomy status: Of 16 patients with a positive finding at hysterectomy, seven (43.8%) showed pathological findings in the ECC whereas of the 16 patients with normal findings at hysterectomy, fifteen also had physiological findings in the preceding ECC ($p= 0.0373$).
In the younger group (<50 years, n=118 patients), of the 34 cases with pathological histology at time of hysterectomy, twelve had a positive ECC. In contrast, of 84 younger patients without neoplastic findings in the hysterectomy specimen, seventy patients also had a normal ECC ($p=0.0476$).
The distribution of the different CIN grades with positive margin status in the cone and the CIN grades in the subsequently performed hysterectomies is shown in table 4. Interestingly, high CIN grades and cervical carcinomas in the conization were found to show a lower grade of pathology in the hysterectomy specimens. Three out of four conizations with CIN 2 had no further pathologies in the hysterectomies. Similar findings were detected for CIN 3 in the conization: 23 patients had no more neoplastic findings in the hysterectomies. Furthermore, eleven women with cervical carcinoma in the conization had physiological findings in the subsequent hysterectomies.
In table 5, the significance of ECC and endocervical margin status as predictive tools for residual disease is evaluated. Table 5 shows the sensitivity, specificity, the 95%-confidence intervals and the positive and negative predictive values of ECC and endocervical margin status stratified by the age of the women.
For the ECC, we found better values for women aged ≥50 years a sensitivity of 0.44, a specificity of 0.94, a PPV of 0.88 and a NPV of 0.63. For the whole study group, we found a sensitivity of 0.38, a specificity of 0.85, a PPV of 0.56 and a NPV of 0.73.
For the endocervical margin, the study group comprising the younger patients showed better values. We found a sensitivity of 0.79, a specificity of 0.64, a PPV of 0.47 and a NPV of 0.89. For all 150 patients, the values were as followed: a sensitivity of 0.76, a specificity of 0.63, a PPV of 0.51 and a NPV of 0.84.

Discussion:

The aim of this observational retrospective study was the evaluation of the predictive value of post-cone endocervical curettage for residual cervical intraepithelial neoplasia or cervical carcinoma. Therefore, data of patients were analysed who underwent hysterectomy 6 to 12 months after conisation and ECC for CIN.
In our study group (n=150), residual disease in the hysterectomy was found in 33.3% (50 patients). 41 of these patients (82%) had positive ECC and/or positive endocervical margins. However, nine patients (18%) with a residual/recurrent disease had neither a positive ECC nor a positive endocervical margin. The literature regarding the incidence of residual disease after conization varies from 23.3%- 91.1% (1-10). Also, the rates of positive ECC and positive

endocervical margins vary widely, from 12.2 %- 41% (2, 4-5, 8-9, 11) and from 14.1%-67.5% (1-3, 5, 7-12), respectively.

In the study group, 22.7% of ECC were positive for CIN. Interestingly, when the margins of the cone were not affected (n=65), 10% of the patients still showed a pathological ECC. When the endocervical margin was affected histologically (n=75), only 34.7% also had a pathological ECC (5, 7, 11). The discrepancy could be explained by the fact that an ECC delivers only fragments of uterine/cervical tissue and often the samples are admixed with blood. Lin et al. (7) reported that also the technique of the curettage could have an influence of the positivity of the ECC. They performed a circumferential scraping method and also the tissue that remained at the jaws of the instrument was fixed and sent to pathology for histological examination. Applying this procedure, they reported 33 (24.8%) positive ECC from 133 patients which is consistent with our results.

Hysterectomy specimens with pathological histology (n=50) presented CIN or cervical carcinoma in only 38% of the preceding ECC, but 76% showed an affected endocervical margin status of the cone. Endocervical margin and ECC were positive in 32% of the hysterectomy specimens with pathological histology, similar to the pathological ECC alone (38%). Lu et al. (9) found pathological hysterectomy specimens in 64.6% (31 patients) when the preceding ECC was positive and pathological findings in the hysterectomy in 46.9% (38 patients) when the endocervical margin was involved. When the ECC and the endocervical margins were involved, they found an incidence of residual disease in 71.4%. However, the likelihood of finding residual disease when the ECC is pathological varies in the literature from 32.2% to 88%. Also, the rate of residual lesions in the hysterectomy specimen after positive endocervical margins in the cone biopsy ranges from 23.3%- 67% (1-9, 11). These results are similar to our findings.

Interestingly, we found lower grades of pathology in the hysterectomy (Table 4) especially for higher CIN grades and cervical carcinoma after conization. A hypothesis could be that the conization and the ECC activate and stimulate local immune reactions, which help to eliminate and repair pathological tissue finally resulting in a lower grade of pathology in the hysterectomies. . However, data to support this theory are lacking. Another reason could be, that the high gade lesions were completely removed upon conization and that the lower grade lesions found at hysterectomy represent accompanying residual disease.

When the two defined age groups were compared, the correlation of histologically positive ECC and pathological findings in the hysterectomy specimen was similar: 35.3% and 43.8%, respectively. Normal ECC and normal hysterectomy specimens were found in 83.3% of the younger patients and 93.7% of the older patients (≥50 years). These findings are similar to those reported in the literature (4, 7-9). Lu et al. (9) found incidences for residual disease in 56.5% of patients over 50 years and in 29.3% of patients younger than fifty years. An explanation for the results could be the fact that the transformation zone in older women is retracted into the endocervical canal (deep inversion) and that a progressive atrophy of the genital tract occurs in elder women (4, 7-10).

The sensitivity of ECC for residual CIN and/or carcinoma is low in both age groups,, 0.35 and 0.44, respectively, whereas sensitivity of a positive endocervical margin status of the cone is higher in both groups, 0.79 and 0.69, respectively.

The specificity of ECC is high in both groups, younger women 0.83 and older patients 0.94, whereas the positive endocervical margin showed low specificity in both groups, 0.64 and 0.56.

These findings concerning the sensitivity and specificity of ECC and endocervical margin status are similar to that reported by Lu et al. (8). The sensitivity of ECC was 0.581 versus 0.655 for the endocervical margin, while the specificity of ECC was 0.943 versus 0.836 for the endocervical margin. The authors did not differentiate between the age of the women.

Interestingly, the positive predictive value (PPV) of ECC was much higher in older patients compared to younger women, 0.88 and 0.46, respectively. Whereas the negative predictive value (NPV) was moderate and similar in both, 0.63 and 0.76, respectively. The value concerning the NPV for ECC varies in the literature from 0.92- 0.99. However, there is no differentiation between younger and older women which could be a partial explanation for the difference between our findings and the results in the literature.
For the whole study group, the highest NPV of 0.84 was found for the endocervical margin status. Lea et al. (5) reported a NPV for the endocervical margin of 0.57 and Lu et al. (8) had a NPV for the endocervical margin status of 0.94. The findings are consistent with our data. In addition, Lea et al. examined the risk factors for residual adenocarcinoma in situ and Lu et al. evaluated patients with CIN 3. This could be one reason for the differences of the results.
Finally, in the whole study group, specificity was 85% for ECC. This is similar to results by Vierhout et al. (13), who found a specificity for the ECC of 0.95. Also, Lu et al. (8) reported a high specificity of 0.943 for ECC. As mentioned above, they only included patients with CIN 3 in their study. That is in contrast to our study group that consisted of patients with every CIN grade and cervical carcinomas.

Conclusion:

In our study, the risk of having residual disease in the hysterectomy specimen was 33.3% (50 patients). Most of these patients (n=41, 82%) had positive ECC and/or positive endocervical margins. However, 18% (9 patients) with a residual/recurrent disease had neither a positive ECC nor a positive endocervical margin.
ECC following conization of cervical intraepithelial neoplasia does not generally improve the prediction of residual lesions. However, the subgroup of women ≥50 years showed a high specificity and PPV, 0.94 and 0.88, respectively. Therefore, these patients may benefit from ECC post conization.

References:

1. Bretelle F, Cravello L, Yang L, et al. Conization with positive margins: what strategy should be adopted? Ann Chir. 2000; 125: 444-9.
2. Denehy TR, Gregori CA, Breen JL. Endocervical curettage, cone margins, and residual adenocarcinoma in situ of the cervix. Obstet Gynecol. 1997; 90: 1-6.
3. Fine BA, Feinstein GI, Sabella V. The pre- and postoperative value of endocervical curettage in the detection of cervical intraepithelial neoplasia and invasive cervical cancer. Gynecol Oncol. 1998; 71: 46-9.
4. Kobak WH, Roman LD, Felix JC, et al. The role of endocervical curettage at cervical conization for high-grade dysplasia. Obstet Gynecol. 1995; 85: 197-201.
5. Lea JS, Shin CH, Sheets EE, et al. Endocervical curettage at conization to predict residual cervical adenocarcinoma in situ. Gynecol Oncol. 2002; 87: 129-32.
6. Lee SE, Kim JW, Kang SB. Marginal involvement after large loop excision of transformation zone in patients with cervical cancerous lesion. Int J Gynaecol Obstet. 2005; 89: 53-4.
7. Lin H, Chang HY, Huang CC, et al. Prediction of disease persistence after conization for microinvasive cervical carcinoma and cervical intraepithelial neoplasia grade 3. Int J Gynecol Cancer. 2004; 14: 311-6.
8. Lu CH, Liu FS, Kuo CJ, et al. Prediction of persistence or recurrence after conization for cervical intraepithelial neoplasia III. Obstet Gynecol. 2006; 107: 830-5.
9. Lu CH, Liu FS, Tseng JJ, et al. Predictive factors for residual disease in subsequent hysterectomy following conization for CIN III. Gynecol Oncol. 2000; 79: 284-8.
10. Temkin SM, Hellmann M, Lee YC, et al. Dysplastic endocervical curettings: a predictor of cervical squamous cell carcinoma. Am J Obstet Gynecol. 2007; 196: 469 e1-4.
11. Roman LD, Felix JC, Muderspach LI, et al. Risk of residual invasive disease in women with microinvasive squamous cancer in a conization specimen. Obstet Gynecol. 1997; 90: 759-64.
12. Narducci F, Occelli B, Boman F, et al. Positive margins after conization and risk of persistent lesion. Gynecol Oncol. 2000; 76: 311-4.
13. Vierhout ME, de Planque PM. Concomitant endocervical curettage and cervical conization. Acta Obstet Gynecol Scand. 1991; 70: 359-61.

Figures and table legends:

Table 1: Margin status of the conization specimen (affected / not affected) and histology of the ECC (pathological / normal).

Table 2: Correlation of the histological findings in the hysterectomy specimen, the conization specimen and the ECC.

Table 3: Association between pathological ECC, pathological histology in the hysterectomy, and the age of the patients; ECC= endocervical curettage, younger < 50 years, older ≥50 years

Table 4: Correlation between CIN grades and cervical carcinoma with positive endocervical margins and the histological findings in the hysterectomy specimens.

Table 5: Sensitivity and specificity as well as PPV and NPV of ECC and endocervical margin status in pre- and postmenopausal women and the whole study group. PPV= positive predictive value, NPV= negative predictive value. ECC= endocervical curettage, younger women: patients younger than fifty years, older women:≥ 50 years.

Table 1:

	margins not affected in conization (n= 65)	endocervical margin affected in conization (n= 75)	ectocervical margin affected in conization (n= 10)
pathological ECC n= 34 (22.7%)	7 (10.8%)	26 (34.7%)	1 (10%)
normal ECC n= 116 (77.3%)	58 (89.2%)	49 (65.3%)	9 (90%)

Table 2:

hysterectomy specimen			
	with pathological histology n= 50 (33.3%)	without pathological histology n= 100 (66.7%)	p-value
pathological ECC (n= 34)	19 (38%)	15 (15%)	p =0.0001
normal ECC (n= 116)	31 (62%)	85 (85%)	
endocervical margin status of the cone			
affected (n= 75)	38 (76%)	37 (37%)	p < 0.0001
clean (n= 75)	12 (24%)	63 (63%)	
endocervical margin (EM) and ECC			
EM and ECC positive (n= 26)	16 (32%)	10 (10%)	p < 0.0001
EM positive and ECC negative (n= 49)	22 (44%)	27 (27%)	
EM negative and ECC positive (n= 8)	3 (6%)	5 (5%)	
EM and ECC negative (n= 67)	9 (18%)	58 (58%)	

Table 3:

	Younger patients (118) with / without pathological findings in hysterecomy			Older patients (32) with / without pathological findings in hysterecomy		
	With (n= 34)	without (n= 84)	p- value	with (n= 16)	without (n= 16)	p- value
pathological ECC (n= 34)	12 (35.3%)	14 (16.7%)	p = 0.0476	7 (43.8%)	1 (6.3%)	p = 0.0373
normal ECC (n= 116)	22 (64.7%)	70 (83.3%)		9 (56.2%)	15 (93.7%)	

Table 4:

	Conization specimens with positive endocervical margin CIN ≥ 2 incl. carcinoma (n= 75)
No pathologies in hysterectomy (n= 37)	37
CIN 1 in hysterectomy (n= 3)	3
CIN 2 in hysterectomy (n= 8)	8
CIN 3 in hysterectomy (n= 17)	17
Cervical carcinoma in hysterectomy (n= 10)	10

Table 5:

ECC:	Younger women (n=118)	Older women (n=32)	Total (n=150)
Sensitivity	0.35 CI 95% (0.21, 0.52)	0.44 CI 95% (0.23, 0.67)	0.38 CI 95% (0.25, 0.52)
Specificity	0.83 CI 95% (0.74, 0.9)	0.94 CI 95% (0.72, 0.99)	0.85 CI 95% (0.76, 0.91)
PPV	0.46 CI 95% (0.29, 0.65)	0.88 CI 95% (0.53, 0.98)	0.56 CI 95% (0.39, 0.71)
NPV	0.76 CI 95% (0.66, 0.84)	0.63 CI 95% (0.43, 0.79)	0.73 CI 95% (0.64, 0.8)
endocervical margin:	Younger women (n=118)	Older women (n=32)	Total (n=150)
Sensitivity	0.79 CI 95% (0.63, 0.9)	0.69 CI 95% (0.44, 0.86)	0.76 CI 95% (0.63, 0.86)
Specificity	0.64 CI 95% (0.54, 0.74)	0.56 CI 95% (0.33, 0.77)	0.63 CI 95% (0.53, 0.72)
PPV	0.47 CI 95% (0.35, 0.6)	0.61 CI 95% (0.39, 0.8)	0.51 CI 95% (0.4, 0.62)
NPV	0.89 CI 95% (0.78, 0.94)	0.64 CI 95% (0.39, 0.84)	0.84 CI 95% (0.74, 0.91)