GYNECOLOGY

Loop electrosurgical excision procedure with or without intraoperative colposcopy: a randomized trial

Ziad Hilal, MD; Günther A. Rezniczek, PhD; Ferizan Alici, MD; Anne Kumpernatz, MD; Askin Dogan, MD; Lale Alieva, MD; Clemens B. Tempfer, MD, MBA

BACKGROUND: Loop electrosurgical excision procedure is the standard surgical treatment for cervical dysplasia. Loop electrosurgical excision procedure is advised to be performed under colposcopic guidance to minimize adverse pregnancy outcomes. To date, there is no evidence from randomized trials for this recommendation.

OBJECTIVE: We sought to assess the benefits of performing loop electrosurgical excision procedure under colposcopic guidance in women with cervical dysplasia.

STUDY DESIGN: In a prospective, randomized trial, we compared loop electrosurgical excision procedure with loop electrosurgical excision procedure performed under direct colposcopic vision in a 1:1 ratio. The primary endpoint was resected cone mass; the secondary endpoints were margin status, fragmentation of the surgical specimen, procedure time, time to complete hemostasis, blood loss, and intraoperative and postoperative complications. A sample size of 87 per group (n = 174) was planned (with an assumed type I error of 0.05 and drop-out rate of 5%) to achieve 90% power to detect a 25% reduction in cone mass (with an assumed cone mass of 2.5 ± 1.6 g in the control group) using a nonparametric test (Mann-Whitney *U*).

RESULTS: From October 2016 through December 2017, we randomized 182 women: 93 in the loop electrosurgical excision procedure group and 89 in the loop electrosurgical excision procedure—direct colposcopic vision group. Women undergoing loop electrosurgical excision procedure—direct colposcopic vision had significantly smaller cone specimens than those undergoing loop electrosurgical excision procedure (weight: median 1.86 [interquartile range 1.20—2.72] vs median 2.37 [interquartile range 1.63—3.31] g, respectively, $P = .006$). Secondary outcome measures did not differ significantly between groups: resection margin status involved vs free margin: 12 (13%) vs 75 (82%) and 11 (12.4%) vs 75 (84.3%); fragmentation no vs yes: 85 (92.4%) vs 7 (7.6%) and 84 (94.4%) vs 5 (5.6%); procedure time: 190 (interquartile range 138—294) and 171 (interquartile range 133—290) seconds; time to complete hemostasis: 61 (interquartile range 31—108) and 51 (interquartile range 30—81) seconds; intraoperative blood loss (Δhemoglobin): 0.4 (interquartile range 0.2—1.0) and 0.5 (interquartile range 0.1—0.9); complication rate: 6 (6.5%) and 2 (2.2%). In a multivariate analysis, study group allocation ($P = .021$) and parity ($P = .028$), but not age, body mass index, type of transformation zone, and dysplasia degree independently influenced the amount of resected cone mass.

CONCLUSION: Loop electrosurgical excision procedure with intraoperative colposcopy leads to significantly smaller cone specimens without compromising margin status.

Key words: cervical dysplasia, colposcopy, conization, controlled trial, direct colposcopic vision, loop excision, randomized

Introduction

Loop electrosurgical excision procedure (LEEP) is the standard surgical treatment for eradicating cervical intraepithelial neoplasia (CIN).[1] This technique provides the most reliable specimens for histology with the least morbidity and is easy to learn.[2–4] This procedure, however, is not without harm, especially regarding future pregnancies and premature delivery. Specifically, the main long-term morbidity of cervical surgery is premature delivery due to a shortening of the cervical length. The risk of this pregnancy-related complication increases with the size and volume of the resected cone specimen.[5–8] Therefore, efforts have been undertaken to reduce the amount of cervical tissue resected during surgery, among them preoperative colposcopy for identifying the location and size of the CIN lesion, replacement of cold knife conization with LEEP, and the use of intraoperative colposcopy. The available data in the literature suggest that performing LEEP under intraoperative colposcopic guidance may lead to a reduction in the amount of cervical tissue resected and thus reduce the future risk of adverse pregnancy outcomes.[9–11] There are, however, no randomized trials to definitively prove whether or not intraoperative colposcopy has benefits in terms of cone volume reduction without compromising oncological safety, namely the resection margin status. To answer this clinically relevant question, we performed a randomized trial assessing the benefits of colposcopy-guided conization in women with cervical dysplasia undergoing LEEP, one of the most common surgical procedures in operative gynecology.[1]

Materials and Methods

This prospective randomized trial was carried out at the Department of Obstetrics and Gynecology, Ruhr-Universität Bochum, Bochum, Germany, in a population of women referred to our institution for the treatment of cervical dysplasia. The study was not blinded due to the study design. The study protocol was approved by the local ethics committee (registration number 5832-16) and the trial was registered with ClinicalTrials.gov (NCT02910388). All women who participated in this trial gave written informed consent. We

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AJOG at a Glance

Why was this study conducted?

To clarify whether intraoperative colposcopy during conization reduces cone mass without affecting margin status, operation time, and procedure-associated complications.

Key findings

Intraoperative colposcopy leads to significantly smaller cone specimens without compromising margin status.

What does this add to what is known?

This study provides high-level evidence that intraoperative colposcopy during conization is useful for reducing cone mass and potentially reduces the risk of subsequent preterm delivery.

included women with a biopsy-proven, persistent, low-grade squamous intraepithelial lesion (LSIL) or high-grade squamous intraepithelial lesion (HSIL) who underwent LEEP. In addition, we included women undergoing diagnostic LEEP in case of an abnormal Pap smear result. Colposcopy and colposcopically guided cervical biopsy were performed prior to LEEP in all patients to confirm the presence of cervical dysplasia. Exclusion criteria included pregnancy, a personal history of conization, a significant language barrier, concomitant oncological disease, a known hematologic disorder, and the use of a blood-thinning medication.

LEEP was performed under general anesthesia in an outpatient setting, ie, in a hospital from which patients were discharged the same day. Local anesthetics or vasoconstrictive agents were not used. In women assigned to group 1 (LEEP—direct colposcopic vision [DCV]), LEEP was carried out with a binocular colposcope (KSK 150 FC-Kolposkop; Zeiss, Oberkochen, Germany) with 3 magnifications (×7.5, ×15, and ×30) as follows. After visualization of the cervix and the squamocolumnar junction, the transformation zone (TZ) was assessed in its native condition (type 1: TZ fully visible; type 2: TZ partly visible; type 3: TZ not visible). We then applied acetic acid 3% to identify the cervical abnormalities. Once the resection zone was determined, we used an electrical loop with a size according to the dimensions of the cervix. Then, the electrosurgical unit (Vio 300D; Erbe, Tübingen, Germany) was set at 120 W on blend 3, and the high-cut mode was set (effect 4, 180 W). We performed LEEP by carefully passing the loop around the TZ from top (12 o'clock) to bottom (6 o'clock). After the TZ was removed, a Hegar dilator was used to explore the length of the cervical canal. Additional tissue was excised from the ectocervix if the visible lesion was not fully excised or if preoperative colposcopy suggested the presence of an endocervical lesion. This was an optional step performed at the surgeon's discretion. Endocervical curettage was not performed. Hemostasis was exclusively obtained with a ball electrode using the spray or forced coagulation modes. In all procedural steps, the colposcope was used. In women assigned to group 2 (LEEP), the surgeons underwent the same procedural steps without the use of a colposcope. Four surgeons performed the LEEPs.

The primary endpoint of the study was the resected cone mass measured in grams (by weighing the removed tissue with a precision scale located in the operating room). Cone mass (as a proxy for cone volume) was chosen as the primary endpoint because the means to accurately weigh the specimens in the operating room setting were easier to set up and the measurement process less demanding (both, in time and skill) than methods for volume determination such as submersion volumetry or measuring linear dimensions with a ruler. Secondary endpoints included the resection margin status of the surgical specimen (involved margin [R1] vs free margin [R0]) judged by a board-certified pathologist who was unaware of the study assignment. The resection margin was judged as R0 if abnormal cells were not found at the margin of the cone specimen or R1 if abnormal cells were identified at the margin of the cone specimen. Other endpoints of this study were intraoperative blood loss (measured as Δhemoglobin between the day before conization and 4—5 hours after conization); operation time measured from the start of the excision until all hemostatic interventions ended; and time to complete hemostasis (TCH) measured using a stopwatch following the surgeon's commands "start" and "stop" that marked the beginning of the coagulation, defined as pressing the coagulation button on the hand-held device attached to the coagulation electrode and the moment when the surgeon stopped all coagulation efforts. Further secondary endpoints were cone fragmentation, the number of additional resections (ie, additional passes of the electrode during surgery), and the dimensions (width, length, height, and calculate volume, approximated as a pyramid) of the cone specimen. Intraoperative and postoperative complications were noted if they occurred within 14 days after conization (eg, postoperative bleeding, local cervical or uterine or urinary infection). Satisfaction of the surgeon with the procedure and handling of the surgical instruments were assessed by all surgeons after each surgery using an 11-step scale ranging from 0 (worst) to 10 (best). The surgeons were not made aware of a patient's wish for future pregnancy as per study protocol. However, the patient's reproductive history and attitude toward future pregnancies was noted in the patient chart, which was available in the operating room.

Statistical analyses were performed using the Mann-Whitney U test for all continuous data failing the Shapiro-Wilk normality test or using χ^2 test or Fisher exact test (for small counts) to compare frequencies. All P values are 2-tailed and a value $<.05$ was considered statistically significant. Where appropriate, values

are given as medians with interquartile ranges in parentheses. We performed multivariate linear and logistic regression analyses with resected cone mass, resection margin status, and cone fragmentation as the dependent variables and age, body mass index, parity, type of TZ, prescription drug use, concomitant/past diseases, allergies, smoking, degree of cervical dysplasia, and study group assignment (LEEP-DCV vs LEEP) as the independent variables.

The sample size was calculated based on the study hypothesis that LEEP-DCV would produce significantly smaller cone specimens. The assumption of a reduction of 25% of the cone mass in women undergoing LEEP-DCV was based on previous studies demonstrating a mean reduction in volume of 30%.[10] Based on our own previous results, we assumed a LEEP cone mass of (2.5 ± 1.6) g (mean ± SD), with the data not following a normal distribution (median of 2.1 g).[12] Thus, with an effect size of 0.47, an α of 0.05 (type I error), and an assumed drop-out rate of 5%, 87 patients (total of 174; 1:1 randomization, 1-tailed) needed to be recruited for each group to achieve a power of at least 90% to confirm the superiority of LEEP-DCV regarding the primary endpoint. We used the statistics software package SigmaPlot 12.5 (Systat Software Inc, San Jose, CA) and G*Power 3.1.9.2 (University of Duesseldorf, Duesseldorf, Germany) to perform the calculations.

Randomization was performed using a computer-generated list with a block size of 2. Study group assignment was sealed in sequentially numbered opaque envelopes. Women were enrolled by 2 authors (Z.H., C.B.T.). The envelopes were opened in the operating room before the start of LEEP. Women were unaware of the study group allocation.

TABLE 1
Group-specific characteristics of study participants in groups 1 and 2

Patient characteristic	Group 1 LEEP-DCV	Group 2 LEEP, without colposcope
No. of patients	92	89
Age, y[a]	35.1 (28.6–41.6)	38.0 (30.8–44.6)
Body mass index, kg/m^2	23.3 (21.3–27.0)	23.9 (21.2–27.3)
Parity	1 (0–2)	1 (0–1)
Allergies, yes/no	41 (44.6%)/49 (53.3%) [2]	33 (37.1%)/51 (57.3%) [5]
Smoking, yes/no	44 (47.8%)/46 (50.0%) [2]	44 (49.4%)/39 (43.8%) [6]
Alcohol abuse, yes/no	0 (0.0%)/90 (97.8%) [2]	1 (1.1%)/82 (92.1%) [6]
Drug abuse, yes/no	0 (0.0%)/90 (97.8%) [2]	1 (1.1%)/82 (92.1%) [6]
Prescription drug use, yes/no	49 (53.3%)%/41 (44.6%) [2]	37 (41.6%)/47 (52.8%) [5]
Concomitant disease, yes/no	37 (40.2%)/53 (57.6%) [2]	32 (36.0%)/52 (58.4%) [5]
Type of transformation zone		
○ 1	73 (79.3%)	73 (82.0%)
○ 2	5 (5.5%)	8 (9.0%)
○ 3	14 (15.2%)	8 (9.0%)
Indication for conization		
○ HSIL	73 (79.3%)	77 (86.5%)
○ LSIL	4 (4.4%)	4 (4.5%)
○ Abnormal Pap smear, inconclusive colposcopy	15 (16.3%)	8 (9.0%)
Histological results		
○ Negative for dysplasia	5 (5.4%)	2 (2.3%)
○ LSIL	18 (19.6%)	9 (10.1%)
○ HSIL	66 (71.7%)	74 (83.1%)
○ Carcinoma	3 (3.3%)	4 (4.5%)

Values are counts (percentage proportions) or medians (interquartile ranges). No. in brackets indicates missing values.

DCV, direct colposcopic vision; *HSIL*, high-grade squamous intraepithelial lesions; *LEEP*, loop electrosurgical excision procedure; *LSIL*, low-grade squamous intraepithelial lesions.

[a] $P = .013$ (Mann-Whitney *U* test).

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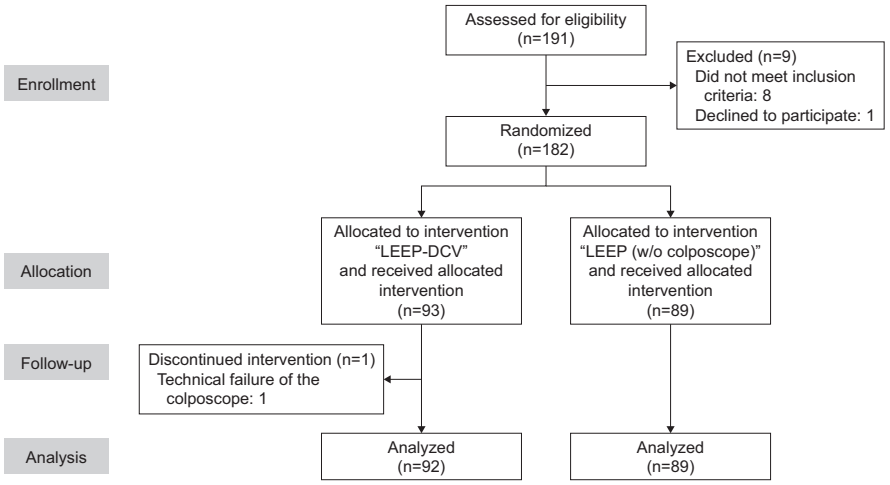
Results

From October 2016 through December 2017, 191 patients were screened for this study. Eight patients did not meet the inclusion criteria and were therefore not included in the study (screening failures). One patient declined to participate before randomization. Thus, 182 patients were included in the study. Patient characteristics according to study allocation are shown in Table 1 and were comparable between the 2 treatment groups. In all, 93 patients were randomized to arm 1 (LEEP-DCV) and 89 patients were randomized to arm 2 (LEEP). In 1 patient, allocated to group 1, the colposcope failed during the procedure and the patient was excluded from analysis. The primary as well as the secondary outcome parameters were measured in 181 participants in a per-protocol analysis. A flow diagram depicting the patients' flow through the study is shown in the Figure. Twelve different surgeons performed the procedures. As shown in Table 1, the histopathologic results of the surgical specimens were as follows: 27 patients had LSIL, 140 patients had HSIL, 7 patients had a microinvasive cervical cancer (pT1a1), and 7 patients had no CIN in the specimen.

Table 2 shows a comparison of the primary and secondary outcomes in women assigned to both study groups. Specifically, we compared resected cone mass, resection margin status, cone dimensions (length, width, height, and

FIGURE
Study flow diagram showing the patients' flow through the study



Study flow diagram.

DCV, direct colposcopic vision; *LEEP*, loop electrosurgical excision procedure.

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volume), fragmentation of the surgical specimens, number of additional resections, procedure time, TCH, intraoperative blood loss, and intraoperative as well as postoperative complications. In the intention-to-treat analysis, a significant difference in the primary outcome, resected cone mass, was observed between LEEP-DCV and LEEP (resected cone mass 1.86 [1.20−2.72] vs 2.37 [1.63−3.31] g, respectively, P = .006). All other secondary outcomes did not differ between groups: resection margin status R1 vs R0: 12 (13%) vs 75 (82%) and 11 (12.4%) vs 75 (84.3%), respectively, P = .98; fragmentation no vs yes: 85 (92.4%) vs 7 (7.6%) and 84 (94.4%) vs 5 (5.6%), respectively, P = .81; procedure time in seconds: 190 (138−294) and 171 (133−290), respectively, P = .64; TCH in seconds: 61 (31−108) and 51 (30−81), respectively, P = .23; and intraoperative blood loss (Δhemoglobin): 0.4 (0.2−1.0) and 0.5 (0.1−0.9), respectively, P = .99.

There were 8 intraoperative complications and 12 postoperative complications. The rate of complications was not significantly different between the 2 study groups (intraoperative complications: 6 [6.5%] and 2 [2.2%], respectively, P = .30; postoperative complications: 8 [8.7%] and 4 [4.5%], respectively, P = .40). In detail, in the LEEP-DCV group 5 women had prolonged intraoperative bleeding: 2 of them needed vaginal tamponade and 1 needed vaginal tamponade and inpatient observation. Three women had postoperative bleeding up to 5 hours after conization and 1 of them needed vaginal tamponade. Two women reported nausea and in 1 woman an injury of the labia minora occurred during coagulation. One woman reported strong pain after LEEP; 1 woman had a loss of consciousness after discharge, was readmitted, but did not require further treatment; and 1 woman experienced an allergic reaction to dipyrone. In the LEEP group, 1 woman had prolonged intraoperative bleeding and 3 women had postoperative bleeding after 6, 10, and 14 days, respectively, and were readmitted. One woman reported strong pain after LEEP and 1 woman had a vaginal laceration with opening of the cul-de-sac and underwent laparoscopic repair. Table 3 shows a multivariate analysis with resected cone mass, resection margin status, and cone fragmentation as the dependent variables and age, body mass index, parity, type of TZ, degree of cervical dysplasia, and study group assignment (LEEP-DCV vs LEEP) as the independent variables. This analysis demonstrates that study group allocation (odds ratio, 0.47; [0.24−0.89]; P = .021) and parity (odds ratio, 1.47 [1.04−2.07]; P = .028), but not age, body mass index, type of TZ, and dysplasia degree independently influenced the resected cone mass, whereas resection margin status and cone fragmentation were not influenced by the assessed parameters.

In addition, we performed a subgroup analysis excluding 40 patients with a type 3 TZ, LSIL, or inconclusive colposcopy (Table 1), because in this case the benefit of LEEP-DCV is doubtful. However, the results did not change, ie, LEEP-DCV (n = 70) vs not using a colposcope (n = 71) was still associated with a significantly lower resected cone mass while the resection margin status did not differ between groups (data on file). In addition, the technique of excision and the sizes of the loops were not significantly different in both groups (data not shown).

With a mean follow-up of 13.0 ± 5.3 months, we recorded 9 recurrences. Of these, 4 were LSIL, 5 were HSIL, and 0 were invasive carcinomas (LEEP-DCV: 1/3/0; LEEP: 3/2/0).

Comment

Preterm delivery due to short cervix is the most important long-term sequela of LEEP, which is one of the most common surgical procedures in gynecology.[5−7] Performing LEEP under colposcopic guidance (LEEP-DCV) may be a way to reduce the resected cone volume and thus preserve more healthy cervical tissue. To date, there is no high-quality evidence to reliably assess the benefits of LEEP-DCV. In this randomized trial, we demonstrated that LEEP-DCV leads to significantly smaller cone specimens without compromising margin status.

There are only limited data available in the literature comparing LEEP and LEEP-DCV, all of them coming from retrospective, uncontrolled studies or prospective observational studies. Based on a PubMed literature search (search date: January-26-2018; search terms: LLETZ[All Fields] AND ("colposcopy"[MeSH Terms] OR "colposcopy"[All Fields]), we identified 169 articles, 4 of them describing the results of LEEP-DCV.[9−11,13] Three of them were

TABLE 2
Primary and secondary outcome measures

	Group 1 LEEP-DCV	Group 2 LEEP, without colposcope	*P*
N	92	89	
Primary outcome measure			
Resected cone mass, g	1.86 (1.20–2.72) [1]	2.37 (1.63–3.31)	.006[b]
Secondary outcome measures			
Resection margin status	[5]	[3]	
R1 vs R0	12 (13%) vs 75 (82%)	11 (12.4%) vs 75 (84.3%)	.98
Cone dimensions	[1]	[1]	
Base length, mm	23 (20–27)	25 (21–28)	.12
Base width, mm	8 (6–13)	11 (9–15)	<.001[b]
Height, mm	20 (16–23)	20 (17–23)	.45
Volume,[a] cm^3	1.38 (0.67–2.30)	1.76 (1.18–2.56)	.005[b]
No. of fragments			
1 vs >1	85 (92.4%) vs 7 (7.6%)	84 (94.4%) vs 5 (5.6%)	.81
No. of additional resections	2 (1–2.75)	1 (1–2)	.13
Procedure time, s	190 (138–294) [3]	171 (133–290) [3]	.64
TCH, s	61 (31–108) [8]	51 (30–81) [8]	.23
Intraoperative blood loss, ⊿hemoglobin	0.4 (0.2–1.0) [8]	0.5 (0.1–0.9) [14]	.99
Complications			
Intraoperative	6 (6.5%)	2 (2.2%)	.30
Postoperative	8 (8.7%)	4 (4.5%)	.40

Values are counts (percentage proportions) or medians (interquartile ranges); no. in brackets indicates missing values. *P* values were calculated using Mann-Whitney *U* test for nonnormally distributed data and Fisher exact test for proportions.

DCV, direct colposcopic vision; *LEEP*, loop electrosurgical excision procedure; *R0*, free margin; *R1*, involved margin; *TCH*, time to complete hemostasis.

[a] Cone volume was calculated as length × width × height ÷ 3 (pyramid); [b] Statistically significant.

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retrospective cohort studies[9,11,13] and 1 was a prospective observational study.[10] In this trial, Preaubert et al[10] compared 216 women who underwent LEEP with prior colposcopy, LEEP without prior colposcopy, and LEEP-DCV. They observed a significant decrease in all dimensions of the surgery specimens obtained by LEEP-DCV, while margin status was not different between groups. Specifically, the mean cone volume was significantly lower in the LEEP-DCV group (adjusted mean difference, −0.66 mL; 95% confidence interval, −1.17 to −0.14). Of note, the probability that negative margins would be achieved together with a volume <5 cm^3 and a thickness <10 mm was highest in the LEEP-DCV group. Carcopino et al[9] retrospectively analyzed 436 women undergoing LEEP. In this study, LEEP-DCV compared to LEEP immediately after or long after colposcopy led to a significantly higher rate of clear margins: 33 (52.4%) vs 104 (68.0%) vs 142 (84.5%), respectively ($P < .001$). LEEP-DCV also allowed for a higher probability of achieving both negative margins and a depth of the cone specimen <10 mm: 10 (15.9%) cases, 47 (30.7%) cases, and 125 (74.4%) cases, respectively ($P < .001$). In a multivariate analysis, LEEP-DCV was associated with negative resection margins and the combination of negative resection margin and a specimen depth <75th percentile. This trial confirmed the results of a prior study with partly overlapping patients.[13] The same group also analyzed recurrence rates after LEEP and LEEP-DCV.[11] Compared to LEEP performed without any use of colposcopy, LEEP-DCV was not found to have a significant impact on the risk of recurrence (hazard ratio, 0.58; 95% confidence interval, 0.16–2.13, $P = .4$), suggesting that LEEP-DCV is oncologically safe despite the smaller amount of healthy tissue surrounding the excised CIN. In summary, these previously published data strongly suggested that LEEP-DCV should be tested in a randomized trial. LEEP-DCV might be beneficial for women in the sense that it may preserve healthy tissue and avoid unnecessary shortening of the cervix in young women with future pregnancy plans. The results of our randomized trial confirm that LEEP-DCV is a suitable method for reducing the cone mass without increasing the risk of

TABLE 3
Multivariate analysis: influence of clinicopathologic parameters on resected cone mass, resection margin status, and cone fragmentation

	Dependent variables						
	Resected cone mass			Resection margin status		Cone Fragmentation	
Independent variables	OR (CI)	*P* (logistic)	*P* (linear)	OR (CI)	*P* (logistic)	OR (CI)	*P* (logistic)
Study group, DCV use	0.47 (0.24–0.89)	.021[a]	.004[a]	1.06 (0.42–2.67)	.89	1.63 (0.47–5.70)	.44
Age	1.01 (0.97–1.06)	.58	.79	0.96 (0.90–1.03)	.24	1.06 (0.99–1.14)	.099
Body mass index	1.01 (0.94–1.09)	.74	.27	1.08 (0.98–1.18)	.11	0.98 (0.86–1.13)	.81
Parity	1.47 (1.04–2.07)	.028[a]	.002[a]	0.97 (0.58–1.63)	.92	0.91 (0.49–1.70)	.77
Type of transformation zone	0.80 (0.45–1.41)	.43	.79	2.04 (0.84–4.97)	.11	0.49 (0.15–1.58)	.23
Dysplasia degree	0.93 (0.50–1.72)	.81	.56	2.98 (0.85–10.45)	.089	0.79 (0.28–2.21)	.65

Multiple linear and logistic regression analyses with resected cone mass (linear, after box-Cox transformation; and $<$ or $\geq$ median, respectively), resection margin status (free or involved margin), and cone fragmentation (1 or >1 fragments) as dependent variables, respectively, and study group, age, body mass index, parity, type of transformation zone, and degree of dysplasia (0, negative; 1, low-grade squamous intraepithelial lesions; 2, high-grade squamous intraepithelial lesions; 3, carcinoma) as independent variables. Values are or OR (5–95% CI) and *P* values from linear and/or logistic models, respectively.

CI, confidence interval; *DCV*, direct colposcopic vision; *OR*, odds ratio.

[a] Statistically significant.

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resection R1. Our data may aide clinicians in the decision whether to implement intraoperative colposcopy, which is associated with significant equipment costs.

Our study has limitations. For example, women were selected for this trial based on specific inclusion and exclusion criteria. Thus, our study population may not be comparable to the general population of women undergoing LEEP. Therefore, this study has a considerable potential for selection bias that will compromise generalizability of findings, which is true for any single-center, hospital-based study. In addition, we only assessed short-term outcomes and are therefore unable to comment on possible differences in long-term outcomes such as premature delivery in the 2 study arms. Furthermore, it is questionable if the use of a colposcope during LEEP has an advantage on postmenopausal women or women who have completed childbearing. In addition, subjective measurements performed by investigators who were not blinded to the group allocation, such as TCH, are subject to bias. Furthermore, since all surgeons were aware of the study hypothesis, this could have impacted their performance of the procedure and the resulting conization size. All of these limitations must be acknowledged when interpreting the results of our study.

We found that LEEP under colposcopic guidance resulted in smaller cones. Whether the magnification of the scope, a better visibility of the acetowhite lesion(s), or both were responsible for this effect is a matter of speculation. It is also possible that using a scope forces the surgeon to concentrate more and longer on the lesion by using more time adjusting the scope.

Preterm delivery is a serious complication of pregnancy and a prior LEEP increases the risk of preterm delivery, depending on the number of procedures as well as the size of the cone specimen(s).[2,3,5,6] Therefore, attempts to reduce the risk of preterm delivery in women who need to undergo LEEP are valuable. Our study provides high-level evidence that intraoperative colposcopy during conization is useful for reducing cone mass and may potentially reduce the risk of subsequent preterm delivery. Clearly, our study looked at a short-term outcome, ie, cone mass, which might or might not be a good proxy for the truly interesting endpoint, namely preterm delivery. On the other hand, if colposcopically guided LEEP would not have been shown to reduce the size of the cones, then a long-term study would probably not make sense. The differences in cone mass, base width, and volume were statistically significantly different. Whether or not these differences also translate into a reduced rate of preterm delivery is a matter of speculation. However, the functional integrity of the cervix can be expected to be a continuous phenomenon rather than a threshold issue. Thus, it is reasonable to speculate that any reduction of unnecessary removal of healthy cervical tissue is valuable. To clarify the clinical impact of colposcopically guided LEEP, a long-term study is necessary.

In summary, we found that the 2 investigated surgical techniques, LEEP-DCV and LEEP, are both suitable for treating cervical dysplasia. However, LEEP-DCV has a significant advantage in terms of a lower resected cone mass and thus reduces the amount of healthy tissue lost due to surgery. The primary outcome parameter of this study, resected cone mass, was significantly smaller in the LEEP-DCV group, while all other outcome parameters, especially the rate of resection R1, were comparable between the 2 study groups. Therefore, based on the results of this trial, we recommend LEEP-DCV as the preferred surgical method to treat cervical dysplasia. ■

References

1. Martin-Hirsch PPL, Paraskevaidis E, Bryant A, Dickinson HO. Surgery for cervical intraepithelial neoplasia. Cochrane Database Syst Rev 2013;12:CD001318.

2. Massad LS, Einstein MH, Huh WK, et al. 2012 Updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. Obstet Gynecol 2013;121:829–46.

3. WHO. Guidelines for treatment of cervical intraepithelial neoplasia 2-3 and adenocarcinoma in situ: cryotherapy, large loop excision of the transformation zone, and cold knife conization. Geneva: World Health Organization; 2014.

4. Rezniczek GA, Severin S, Hilal Z, et al. Surgical performance of large loop excision of the transformation zone in a training model: a prospective cohort study. Medicine (Baltimore) 2017;96:e7026.

5. Kyrgiou M, Athanasiou A, Paraskevaidi M, et al. Adverse obstetric outcomes after local treatment for cervical preinvasive and early invasive disease according to cone depth: a systematic review and meta-analysis. BMJ 2016;354:i3633.

6. Arbyn M, Kyrgiou M, Simoens C, et al. Perinatal mortality and other severe adverse pregnancy outcomes associated with treatment of cervical intraepithelial neoplasia: meta-analysis. BMJ 2008;337:a1284.

7. Khalid S, Dimitriou E, Conroy R, et al. The thickness and volume of LLETZ specimens can predict the relative risk of pregnancy-related morbidity. BJOG 2012;119:685–91.

8. Jiang Y-M, Chen C-X, Li L. Meta-analysis of cold-knife conization versus loop electrosurgical excision procedure for cervical intraepithelial neoplasia. Onco Targets Ther 2016;9:3907–15.

9. Carcopino X, Mancini J, Charpin C, et al. Direct colposcopic vision used with the LLETZ procedure for optimal treatment of CIN: results of joint cohort studies. Arch Gynecol Obstet 2013;288:1087–94.

10. Preaubert L, Gondry J, Mancini J, et al. Benefits of direct colposcopic vision for optimal LLETZ procedure: a prospective multicenter study. J Low Genit Tract Dis 2016;20:15–21.

11. Heineman M, Mancini J, Villeret J, et al. Treatment failure following excision therapy of CIN: the impact of direct colposcopic vision during procedure. Arch Gynecol Obstet 2016;293:825–31.

12. Hilal Z, Rezniczek GA, El-Fizazi N, Tempfer CB. Large loop excision of the transformation zone versus true cone biopsy electrode excision: a randomized trial. J Low Genit Tract Dis 2017;21:272–8.

13. Grisot C, Mancini J, Giusiano S, et al. How to optimize excisional procedures for the treatment of CIN? The role of colposcopy. Arch Gynecol Obstet 2012;285:1383–90.

Author and article information

From the Department of Obstetrics and Gynecology, Ruhr-Universität Bochum, Bochum, Germany.

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Corresponding author: Ziad Hilal, MD. z.hilal@zydolab.de