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

Cite this article as: Hilal Z, Rezniczek GA, Alici F, et al. Loop electrosurgical excision procedure with or without intraoperative colposcopy: a randomized trial. Am J Obstet Gynecol 2018;219:377.e1-7.

0002-9378/$36.00

https://doi.org/10.1016/j.ajog.2018.07.023

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