Radiosurgery in the Management of Cervical Intraepithelial Neoplasia

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OBJECTIVE: To evaluate the loop electrosurgical excision procedure (LEEP) and large loop excision of the transformation zone–conization (LLETZ-conization) in the management of cervical intraepithelial dysplasia using high-frequency, filtered waveform energy (radiosurgery).

STUDY DESIGN: Two hundred thirteen women attending the outpatient cervical colposcopy clinic with smears consistent with an epithelial abnormality, but macroscopically or colposcopically not consistent with invasive carcinoma, were included in the study. LEEP and LLETZ–conization were performed in 72 and 141 women, respectively. A matched pair group of patients undergoing cold knife conization was used for the comparison with LLETZ-conization. Using LEEP, in 83% a clear resection margin of the biopsy specimen was achieved. In this subset, diagnosis and therapy were achieved in a single visit. No complications, such as hemorrhage, occurred during the operation or postoperative period.

RESULTS: Comparison of LLETZ-conization with the matched-pair group undergoing cold knife conization showed a significantly shorter duration of surgery for LLETZ-conization (mean, 10.8 vs. 16.5 minutes, P < .001). We found no differences concerning posttreatment bleeding complications (2.8% vs. 3.3%) or clear resection margins (92% vs. 86%). Patients undergoing LLETZ-conization needed significantly less analgesic (P < .01).

CONCLUSION: Radiosurgical loop excision is a safe and cost-effective method in the diagnosis and treatment of cervical intraepithelial neoplasia. (J Reprod Med 1996;41:409–414)

In a high percentage of cases (83), LEEP offers the advantage (as compared to conventional punch biopsy) of diagnosing and treating premalignant lesions in a single visit.

Keywords: cervical intraepithelial neoplasia, cervix diseases.

Introduction

During the last decade, several factors, including the rising incidence of infections of the lower female genital tract and improvements in screening programs, resulted in an increasing number of cervical

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smears consistent with cervical intraepithelial neoplasia (CIN) and colposcopically suspect lesions. This increase is probably due to human papillomavirus infection and is found predominantly among women of reproductive age.[1] In order to find the most reliable and cost-effective treatment, surgical excision procedures on an outpatient basis were established. Electrosurgical procedures, known as the loop electrosurgical excision procedure (LEEP) and large loop excision of the transformation zone (LLETZ), became increasingly popular for removing suspect lesions.[2,3] The objective is to provide a diagnostic and therapeutic tool at the same time. Frequency and waveform of energy are important factors. With higher frequency and a filtered waveform, the relation of cutting effect to lateral heat spread (implicating tissue damage) is improved. In this study we performed surgery using radiofrequency, featuring a higher frequency (about 3.8 MHz) than electrosurgery, providing better cutting with less thermal damage to the resection margins.[4]

Radiosurgical loop excision combines the virtues of both excisional and destructive methods.

The standard method of colposcopically directed punch biopsy followed by excision or ablation of histologically proven cancer precursors requires at least two visits. Using LEEP, diagnosis and therapy can be achieved in most cases in a single visit on an outpatient basis.[5] In contrast to ablative methods, such as cautery, cryotherapy and laser ablation, radiosurgery techniques allow a histologic diagnosis, including evaluation of the excision margin, and therefore a radical operation. Locally destructive techniques possess the major disadvantage of inappropriate treatment of a microinvasive or frankly invasive lesion following inadequate sampling of a lesion.[6]

While LEEP represents an alternative to biopsy and subsequent ablative techniques, LLETZ-conization can be used instead of classic cold knife conization. Advantages of LLETZ-conization by radiosurgery are less mutilation of the cervix because a lower volume of cervical tissue is removed[7] and economic disadvantages because LLETZ-conization appears to be less time consuming.

In the present study we evaluated LEEP and LLETZ-conization in the management of CIN using high-frequency, filtered waveform energy (radiosurgery). A matched pair group of patients undergoing cold knife conization was used for comparison with LLETZ-conization.

Patients and Methods

The nomenclature for LEEP procedures is not uniform in different publications. For the purpose of this study, we defined LEEP as excision of colposcopically suspect lesions. LLETZ-conization was defined as excision of the complete transformation zone, including visible ectocervical lesions, combined with partial removal of the endocervical canal.[7]

Two hundred thirteen women attending the outpatient cervical colposcopy clinic with smears consistent with an epithelial abnormality, but macroscopically or colposcopically not consistent with invasive carcinoma, were included in the study. LEEP and LLETZ-conization were performed on 72 and 141 women, respectively. A control group matched in regard to indication for surgery, age, parity, histologic diagnosis and expertise of the surgeon consisted of 141 patients who underwent cold knife conization. This control group was selected for comparison with the LLETZ-conization group. All women underwent colposcopy, including acetic acid and Lugol's iodine solution test. Indications for LEEP were: (1) repeated cervical smears indicating low grade squamous intraepithelial lesion (LSIL) and a totally visible lesion, or (2) one smear indicating high grade SIL (HSIL) and a totally visible lesion on colposcopic examination. Indications for cold knife conization and LLETZ-conization were: (1) persisting LSIL without totally visible lesions (extending to the endocervix), (2) one smear indicating HSIL in cases of not totally visible lesions (extending to the endocervix), or (3) one cervical smear indicating invasive carcinoma without clinical evidence of malignant tissue.

LEEP was carried out in an outpatient setting under local anesthesia (using 2% lidocaine with epinephrine 1:100,000, 20 mg/mL lidocaine and 0.01 mg/mL epinephrine). Cold knife conizations and LLETZ-conizations were performed under general anesthesia.

Radiofrequency surgery was performed using a filtered wave at 3.8 MHz. A radiofrequency unit with a maximum power output of 140 W (position

9) (Ellman Surgitron FFPF, Hewlett, New York, U.S.A.) was used at position 5 for cutting and position 8 (spark gap, coagulation mode) for coagulation. The radiofrequency unit does not require a ground return pad. The unit uses an antenna that acts as a return electrode and is placed under the operative field. Different loop sizes ranging from 5 to 25 mm were used. For coagulation a ball electrode was used. LEEP and LLETZ-conization were carried out as previously described.[8,9] Single lesions were removed with a suitable loop according to their size. Loop sizes ranging from 15 to 25 mm were used for removal of the transformation zone. During LLETZ-conization we tried to remove the whole transformation zone with one large loop in order to obtain one histologic specimen and moved the loop from the anterior to the posterior or from the left to the right cervical area according to the lesion location. The resection margin was marked at 12:00. If removal of the transformation zone could not be achieved in one cut, it was done in two portions, and the topographic position of the two specimens was marked. LLETZ-conization included an additional step, using a small loop (10 mm) to remove an additional central tissue block of up to 10 mm in depth containing the endocervical canal portion positioned centrally. The resulting cervical wound had a "cowboy hat" configuration (Figure 1). All surgical procedures were performed with the use of a colposcope.

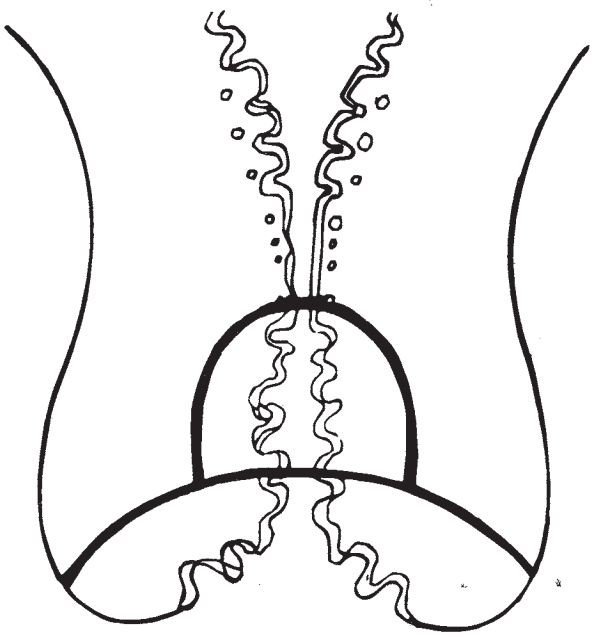

Figure 1 LLETZ-conization. Schematic sectional view of the cervix uteri. The resulting cervical wound has a "cowboy hat" configuration.

All histologic investigations were carried out by the same pathologist. LLETZ-conization specimens were also judged for the interpretability of the histopathologic specimen (heat destruction of the resection margins, orientation if multiple resections were necessary, endocervical and ectocervical resection margins).

Resection of the complete lesion and subsequent histopathologic evaluation, the major advantages of all excisional techniques, can be achieved with loop excision.

For LEEP we evaluated excision margin status and intraoperative and postoperative complications. In patients undergoing LLETZ and cold knife conization we compared excision margin status, duration of operation, intraopertive and postoperative complications (hemorrhage, perforation), and length of hospitalization. For postoperative analgesia, patients were offered analgesic suppositories (50 mg Diclofenac-Natrium) according to the level of pain, up to a maximum of one suppository every four hours. Severity of pain was indirectly measured by the number of analgesic suppositories used.

For statistical analysis Student's t test was used. Probability $< .05$ was considered significant.

Results

LEEP

Table I demonstrates the histologic diagnoses of the biopsy specimens obtained by LEEP. Cytology showed HSIL in 14 of 17 cases, with histology showing CIN 2 or 3 (HSIL), while the remaining two cases were underdiagnosed as LSIL by cytology. In 54 patients (83%) a clear resection margin of the biopsy specimen was diagnosed. In this subset diagnosis and therapy were achieved in a single visit. In 11 patients the margins were not clear: 1 condyloma, 4 CIN 1, 4 CIN 2 and 2 CIN 3. In cases of condyloma or CIN 1, patients were followed at three-month intervals for at least one year without evidence of persistent or recurrent disease. In cases

Table I *Results of LEEP*

Result	No.	%
Histology		
Negative	7	9
Condyloma	21	29
CIN 1	27	38
CIN 2	12	17
CIN 3	5	7
Resection margins[a]		
Clear	54	83
Not clear	11	17
Intraoperative complications	0	0
Postoperative complications	0	0

[a]Only cases with condyloma or CIN.
Total cases, 72.

of CIN 2 or 3, conization was performed. No residual disease was found except in one case of CIN 3. In this case the whole lesion was removed by the conization procedure.

No complications, such as hemorrhage, occurred during the LEEP operation or during the postoperative period.

LLETZ-Conization

Of the LLETZ-conization specimens, 96% were adequate for histologic examination. In 3% the heat destruction zone did not allow a proper evaluation of the resection margins. The depth of the heat destruction zone depended mainly on adequate movement of the electrode and ranged from a 0.2-mm coagulation zone to a 0.55-mm destruction zone. In 1% the anatomic positioning of the resection margins could not be reconstructed properly in the pathology department because of insufficiently marked tissue samples.

Table II gives the comparison of LLETZ-conization with the matched control group of cold knife conization in regard to resection margin status, postoperative complications, duration of operation and length of hospitalization.

Resection margins were not clear after LLETZ-conization in 11 cases and after cold knife conization in 20. In cases of condyloma or CIN 1, patients were followed at three-month intervals for at least one year without evidence of persistent or recurrent disease. In cases of CIN 2 or 3, reconization was performed. There was no difference in the rate of residual disease in the reconization specimen between the LLETZ-conization group (27%) and cold knife conization group (30%). All patients with microinvasive carcinoma had disease-free resection margins.

Four of 141 patients (2.8%) treated with LLETZ-conization had posttreatment bleeding complications during the first three postoperative days. Three cases were managed by either recauterization or packing of the cervix. In one case ligation of the bleeding vessel was necessary.

Patients undergoing LLETZ-conization used significantly less analgesia (number of analgesic suppositories used, mean 4.1 ± 1.8 SD) compared with the cold knife conization group (number of analgesic suppositories used, mean 8.2 ± 3.8 SD, Student's t test $P < .01$).

Discussion

Management of lower grade CIN is open to a variety of treatment modalities, comprising excisional and destructive techniques. Due to a significant increase in premalignant cervical lesions in the last decade,[1] diagnosis and treatment become more important. Judgment must also be exercised about the cost-effectiveness of diagnosis and treatment modalities. LEEP is supposed to replace colposcopically guided punch biopsy and subsequent treatment. In our series we found clear resection mar-

Table II *Comparison of LLETZ-Conization and Cold Knife Conization*

	LLETZ		Cold knife	
	No.	%	No.	%
Histology[a]				
Condyloma	3	2	3	2
CIN 1	28	20	28	20
CIN 2	36	26	36	26
CIN 3	72	51	72	51
Microinvasive carcinoma	2	1	2	1
Resection margins clear	130	92	121	86
Resection margins not clear				
Endocervically	7	5	13	9
Ectocervically	4	3	7	5
Intraoperative complications	0	0	0	0
Postoperative complications	4	2.8	4	3.3
Duration of operation (min)	10.8*		16.5*	
Length of hospitalization (d)	3.5**		4.9**	

[a]The two groups were matched by histologic diagnosis.
*$P < .001$ (Student's t test).
**$P < .01$ (Student's t test).

gins in 83%; in these patients we could achieve diagnosis and treatment in a single visit. Nine percent of women treated with LEEP showed histologically no condyloma or dysplastic lesion in the resected tissue. The colposcopically identified lesions were cervicitis or metaplastic changes. There were no dysplastic lesions missed in these cases because follow-up smears showed no pathology. Because LEEP is of comparable invasiveness and has the same complication rate as punch biopsy, the 9% of women treated with no condyloma or dysplasia present seems justified. The advantage of LEEP lies in outpatient treatment and the combination of diagnosis and treatment at a single visit in a high percentage of patients (83). These facts reduce visits and save health care resources. For our health care system we calculated a cost-savings of approximately US $210 if the lesion was diagnosed and removed by LEEP in one session as compared to colposcopically guided punch biopsy and treatment in a separate visit.

LLETZ-conization as an alternative to conventional cold knife conization or laser conization was carried out for diagnostic and therapeutic purposes. In a comparison with our matched pair sample undergoing cold knife conization, we found comparable results concerning disease-free resection margins. According to our experience, LLETZ-conization is very practical, especially for the resection of lesions located in the endocervical canal, because resection of the endocervical specimen can be performed very accurately. Intraoperative and postoperative complications were the same as for the conventional conization procedure. The coagulation features of the radiofrequency energy used were good, and additional intraoperative coagulation with a ball electrode achieved sufficient hemostasis in all cases.

As compared to other studies, in ours surgery in both groups[10] lasted longer because our calculations included the presurgical Lugol's iodine solution test, setup of the equipment and hemostasis. An additional advantage of LLETZ-conization as compared to cold knife conization lies in the optimal cutting features combined with good hemostasis, especially when surgery was performed at high radiofrequency. In our study this resulted in a significantly shorter operation time in the LLETZ-conization group (Table II): the result, again, was a more economical treatment modality. Also, the length of hospitalization was significantly shorter in the LLETZ-conization group. LLETZ-conization is a less invasive procedure than conventional conization, with less tissue volume removed.[7] Patients in the LLETZ-conization group needed significantly fewer analgesic drugs in the postoperative period.

We used radiosurgery at a frequency of 3.8 MHz. As compared to conventional electrosurgery, performed at much lower frequencies (about 0.3 MHz), there was less lateral heat spread during the cutting procedure, with a thinner thermal damage zone in the cervical wound as well as in the specimen. In our series only 3% of the specimens were insufficient for a reliable diagnosis because of thermal damage at the resection margin. The thickness of the thermal damage zone correlated with the power used and the speed of electrode movement. Experienced surgeons moving the electrode constantly and as fast as possible without stopping during the cutting procedure produce tissue specimens that are comparable to samples obtained by laser conization, with resection margins with a minimal, thin thermal damage zone.

Keijser et al[5] recommend LEEP, especially in young women, because it preserves the function of the cervix.[5] It remains a disturbing fact that papers on the long-term effects of LEEP still report contradictory results.[5,11] Most of the patients who are treated for CIN are of reproductive age. Long-term studies to assess the effect of LEEP on cervical function (e.g., cervical competence) in general and on fertility in particular are required.

In a high percentage of cases (83), LEEP offers the advantage (as compared to conventional punch biopsy) of diagnosing and treating premalignant lesions in a single visit. This should increase the compliance of women with cervical dysplasia and reduce the risk that patients will be lost to follow-up before treatment. The reduced number of visits is a useful contribution to reducing health care costs. Radiosurgical loop excision combines the virtues of both excisional and destructive methods. Resection of the complete lesion and subsequent histopathologic evaluation, the major advantages of all excisional techniques, can be achieved with loop excision. It is a cost-effective method, which, like the destructive techniques, can be performed on an outpatient basis.

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