

A retrospective study of exfoliative cytologic evaluation, colposcopy, and conization followed by hysterectomy for various stages of intraepithelial neoplasia of the cervix

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The efficacy of cold-knife conization as a cure for dysplasia of the cervix has been demonstrated repeatedly and is supported by a retrospective study of 43 women who underwent hysterectomy out of a population of patients who had undergone exfoliative cytologic study, colposcopy-directed biopsy, and cold-knife conization. In all 43 the procedures had shown intraepithelial neoplasia of varying degrees in the cervix. Neither the patient's age nor the stage of neoplasia was as important in determining the outcome as the degree of the lesion. Patients with clear cone margins rarely showed residual dysplasia at hysterectomy.

Cervical intraepithelial neoplasia (CIN) is of major concern to the gynecologist because of its precancerous potential. Since the disease is part of a continuum and may well lead to invasive cancer, it is the obligation of the gynecologist to diagnose, treat, and closely follow patients with CIN. There are several methods of doing this, each with its advantages and disadvantages.

Cryosurgery

Cryosurgery is a method by which the cervix is "frozen" by a single- or double-freezing technique. Several authors¹⁻⁵ have emphasized the requirement that the lesion be visualized in its entirety. Townsend¹ reported that in his study of 775 patients the failure rate of the procedure increased

with the increase in grade of CIN as well as in lesion size. He concluded that the size of the lesion is of greater importance than the grade of CIN. His overall primary failure rate was 12 percent. Kaufman and Irwin⁴ reported a failure rate of 11 percent and stated that when endocervical curettage (ECC) gave a positive result, the failure rate was 20.8 percent. They emphasized the importance of visualizing the total lesion. Ostergard² and Popkin and associates³ reported similar results. Sevin and colleagues⁵ reported 8 cases of invasive carcinoma detected after cryosurgery, but their evaluations were incomplete since 7 had not had ECC, and only 3 had had colposcopy.

It may be stated that cryosurgery is a safe method for the treatment of all stages of dysplasia if the pretreatment evaluation is thorough.

Laser therapy

A relatively new method of treating CIN employs a carbon dioxide laser beam. Like cryosurgery, this modality requires strict pretreatment evaluation. Jordan⁶ listed as requirements for its use that the entire lesion be visualized by the colposcopist, that it be assessed by an expert colposcopist, that invasive carcinoma be excluded by selective punch biopsy, and cytologic and colposcopic follow-up be adequate. A 95 percent cure rate has been reported,⁶ and advantages include precise tissue destruction, performance without anesthesia, decrease in blood loss, infrequency of late hemorrhage, and preservation of the squamocolumnar junction.⁷⁻¹⁰ Disadvantages include equipment cost and lack of long-term follow-up.

Electrocoagulation diathermy

A less studied method is electrocoagulation diathermy. According to Chanen,¹¹ the four prerequisites listed by Jordan⁶ apply as well. In addition, Chanen recommended ECC in all cases and concurred in the observation that the anatomic extent of the lesion is more important than the grade of

CIN. If the basic guidelines are fulfilled, a cure rate of 95 percent after a 2-year follow-up can be expected.

Colposcopically directed biopsy

It is possible to remove an entire lesion from the cervix at biopsy if the lesion can be clearly visualized and no endocervical involvement is present. When this is possible, a simple biopsy will take the place of full conization.^{12,13}

Conization of the cervix

Conization is considered a more definitive procedure than biopsy for the removal of dysplastic tissue and is required if the colposcopic examination is inadequate and the ECC shows CIN. Kolstad¹⁴ stated that conization is the method of choice for carcinoma in situ. He reported 97 percent cures, with progression to invasive carcinoma in 1 percent of cases and recurrent carcinoma in situ in 2 percent. Caglar and Delgado¹⁵ studied the accuracy of cervical conization. They performed conization on thirty-three patients and immediately followed the procedure with vaginal hysterectomy. They found residual disease of the same type in 9 percent of uterine specimens after conization. Jones and Buller¹⁶ found recurrence rates from 3.8 to 9.4 percent in a review of several studies between 1970 and 1976. They did not find an increase in abortions or a decrease in term pregnancies, although abortion and premature delivery often are listed in the literature as complications of conization. Ostergard¹⁷ recently found that 16 percent of patients with clear cone margins and 34 percent with unclear margins had residual CIN. He concluded that recurrence cannot be predicted on the basis of a clear margin and that the failure rate approaches 16 percent in skilled hands. The question then arises whether conization is really as good as a definitive therapy as it originally was perceived to be.

Present study

The present study was undertaken in the hope of shedding light on the predictive value of cone clearance with regard to residual CIN. It was our aim to determine: (1) the correlation of patients' age to the severity of CIN on Papanicolaou smear; (2) the relation between the severity shown by Pap smear and by conization; (3) the relation between severity shown by Pap smear and by directed biopsy; (4) the relation between the severity shown by directed biopsy and by conization; (5) the pathologic observations at conization; (6) the cone margins; (7) pathologic evidence of residual CIN at hysterectomy; and, (8) the concurrent gynecologic patho-

logic changes at the time of hysterectomy.

Methods and materials

A retrospective study was made of all patients who underwent Pap smear, colposcopy, directed biopsy, and conization for CIN from January 1975 to July 1980 and subsequently had hysterectomy. There were forty-three such patients, three of whom had moderate dysplasia and forty of whom had severe dysplasia or carcinoma in situ, observed on either Pap smear, directed biopsy, ECC, or conization. Six patients requested sterilization.

Three patients underwent hysterectomy immediately after conization, and one had the operation after almost 2 years. For the others the average interval between conization and hysterectomy was 7 weeks, with a range from 3 to 26 weeks.

The reports on the conization as well as on hysterectomy of the forty-three study patients were retrieved. Records for 1975 and 1976 had been retired, but the admission history and physical examination, discharge summaries, and pathologic reports were available. The charts from 1977 to July 1980 were intact.

The charts were scrutinized for the aforementioned criteria to determine whether the results of conization supported those reported by most authors or those of Ostergard.¹⁷ An average of 13 slides for conization specimens and 12 slides for hysterectomy specimens were available. In pathologic reports prior to 1978, clearance of cone margins was not stated routinely. Twenty-two of the study patients (51.1 percent) were treated in this period. All cone slides in the study were examined for margin clearance by us and a member of the Department of Pathology of Tripler Army Medical Center. Cone specimens then were matched with the corresponding hysterectomy specimens to determine the efficacy of conization in the treatment of CIN.

Results

Table 1 shows that CIN may be seen on Pap smears of patients of all ages. Of the forty-three patients in the study, thirty-four were less than 40 years old, and twenty-six of these had severe CIN. The table also shows that the progressive return of CIN may be observed at any age.

A total of forty-one of the forty-three patients had a satisfactorily documented Pap smear and conization (Table 2). The conization showed exactly the same result as the Pap smear for eighteen patients (43.9 percent), a lower degree of dysplasia than the Pap smear for six patients (14.6 percent), and a higher degree for seventeen patients (41.5 percent). However, all forty-one patients who

TABLE 1. STAGE OF NEOPLASIA SHOWN BY PAP SMEAR IN RELATION TO AGE OF PATIENT.

Patients (No.)	Age	Severity of neoplasia			
		Mild (No.)	Moderate (No.)	Severe (No.)	Negative (No.)
6	25-9	2	1	3	
16*	30-4	2		13	
12*	35-9	2	5	4	
5	40-4	1		3	1
4	45+	1		3	

*No data on 1 patient

showed dysplasia on the Pap smear also showed dysplasia on conization.

Table 3 shows that when the Pap smear was compared with a colposcopically directed biopsy, in fifteen patients (34.8 percent) the biopsy gave the same result as the Pap smear; in eight patients (18.6 percent) the biopsy showed a lower grade of dysplasia than the Pap smear, and in twelve patients (27.9 percent) the biopsy showed a higher grade. Eight patients (18.6 percent) were not included here because the Pap smears were not documented or no directed biopsy was done. When only patients with both Pap smears and directed biopsy were evaluated, the overall correlation between a positive Pap smear and a positive directed biopsy was 100 percent.

The correlation of results of directed biopsy and of conization also was studied (Table 4). Again, of the number of patients that had both colposcopically directed biopsy and conization (100 percent) showed dysplasia in both tissue samples. However, here the severity of dysplasia shown at biopsy and at conization was the same in 57.1 percent and conization showed the same or a degree greater than the biopsy in 77.1 percent.

Table 5 demonstrates that in all age groups both clear and unclear cone specimens were seen. The number of patients with clear cone margins was twenty-four (55.8 percent). However, fifteen (34.8 percent) had unclear endocervical margins and four (9.3 percent) had unclear ectocervical margins. It should be noted that patients with the highest frequency of unclear conization were between 25 and 29 years old (83.3 percent).

Table 6 demonstrates that twenty-two of the twenty-four patients (91.7 percent) who had clear conization margins were still free of disease at the time of hysterectomy. This table also demonstrates that two of the twenty-four patients who had clear conization margins were found to have residual disease at the time of hysterectomy. One of these patients had mild dysplasia and the other had severe dysplasia or carcinoma in situ. This represents 8.3 percent of the study group and is not

TABLE 2. COMPARISON OF RESULTS OF PAP SMEAR AND CONIZATION.

Results	Patients	
	(No.)	(Percent)
Same	18	43.9
Pap more severe	6	14.6
Cone more severe	17	41.5

TABLE 3. COMPARISON OF RESULTS OF PAP SMEAR AND DIRECTED BIOPSY.

Results	Patients*	
	(No.)	(Percent)
Same	15	34.8
Pap more severe	8	18.6
Biopsy more severe	12	27.9

*Data not complete for 7 patients

TABLE 4. COMPARISON OF RESULTS OF DIRECTED BIOPSY AND CONIZATION.

Results	Patients	
	(No.)	(Percent)
Same	20	57.1
Biopsy more severe	8	22.8
Cone more severe	7	20

similar to Ostergard's 16 percent rate of residual dysplasia.

Table 7 shows that twelve of the nineteen patients (63.1 percent) who had unclear margins at conization had no residual dysplasia at hysterectomy. It also demonstrates that seven of the nineteen patients (36.8 percent) who had unclear margins at the time of conization continued to have residual dysplasia at the time of hysterectomy. One patient had mild dysplasia, one had moderate disease, and five had severe disease. The 36.8 percent rate is close to Ostergard's 34 percent rate for residual dysplasia.

Table 8 demonstrates that nine of forty-three patients who had conization for dysplasia (20.9 percent) had residual dysplasia at hysterectomy.

Table 9 shows that seventeen of forty-three patients (39.5 percent) had an incidental concurrent gynecologic pathologic condition. An additional six elected hysterectomy for sterilization.

Comment

The data reviewed here showed that dysplasia is a

TABLE 5. PATIENTS' AGE IN RELATION TO STATE OF CONE MARGIN.

Patients (No.)	Age	Clear Margin (No.)	Unclear endocervical margin (No.)	Unclear ectocervical margin (No.)	Unclear margin (percent)
6	25-9	1	4	1	83.3
16	30-4	11	3	2	31.2
12	35-9	6	5	1	50
5	40-4	5			0
4	45+	1	3		75

TABLE 6. RELATION OF AGE TO PRESENCE OF RESIDUAL DYSPLASIA IN PATIENTS WITH CLEAR CONE MARGINS.

Age of patients	No. without residual dysplasia	No. with residual dysplasia
25-9	1	
30-4	9	2
35-9	6	
40-4	4	
45+	2	

TABLE 7. RELATION OF AGE TO PRESENCE OF RESIDUAL DYSPLASIA IN 19 PATIENTS WITH UNCLEAR CONE MARGINS.

Age of patients	No. without residual dysplasia	No. with residual dysplasia
25-9	5	
30-4	4	1
35-9	2	4
40-4		
45+	1	2

TABLE 8. RELATION OF AGE TO PRESENCE OF DYSPLASIA IN HYSTERECTOMY SPECIMENS FROM 43 PATIENTS.

Age of patients	No. without residual dysplasia	No. with residual dysplasia
25-9	6	
30-4	13	3
35-9	8	4
40-4	4	
45+	3	2

TABLE 9. CONCURRENT GYNECOLOGIC DISEASE AMONG 43 PATIENTS UNDERGOING HYSTERECTOMY FOR DYSPLASIA.

No. patients	Condition
8	Leiomyoma
2	Adenomyosis
1	Leiomyoma and adenomyosis
1	Endocervical polyp
1	Benign cystic teratoma
2	Endometriosis
1	Chronic pelvic inflammatory disease
1	Urinary stress incontinence

disease of all ages, and that severity of dysplasia is not necessarily related to age. The Pap smear, colposcopic examination with directed biopsy, and conization showed a high degree of correlation for dysplasia. Although at times the degree of dysplasia may vary according to its site, the frequency of positive results was relatively constant. This illustrates the need for colposcopic examination when the Pap smear gives a positive result.

Cold-knife conization has been reported by many clinical investigators to be highly successful as definitive therapy for all degrees of CIN. Ostergard's study,¹⁷ however, showed 34 percent residual neoplasia for uncleared cones, and, more significantly, a 16 percent residual disease rate for cleared cones.

In our study group all degrees of CIN were represented. The high number of patients, nineteen (44.1 percent) whose cone specimens had unclear margins is disturbing. Although no residual disease was found at the time of hysterectomy in twelve of the nineteen patients with unclear cone margins, the clinician cannot depend on necrosis of the surgical margin to finish the intended surgical task. The overall rate of residual disease of 20.9 percent is also high, and improvement might be obtained by improved technique. However, the review by Jones and Buller¹⁶ showed that at conization there was residual disease in from 3.8 to 9.4 percent of cases, and our study showed a rate of 8.3 percent. Of interest was the number of patients in our study (seventeen of forty-three) who had a concurrent gynecologic pathologic condition at the time of hysterectomy.

We believe that an accurate diagnosis of the severity of dysplasia may be made if the standard set forth by Jordan⁶ is followed. The most important criterion is that the examination must be performed by an expert in colposcopy.

The present study was limited by the small number of patients. However, the patients represented a population represented by computer files. A larger number of specimen sections would have been valuable, but these were not available because of the retrospective nature of the study. Finally, we believe that cold-knife conization, although an acceptable procedure, is not necessarily the best procedure for all stages of CIN.

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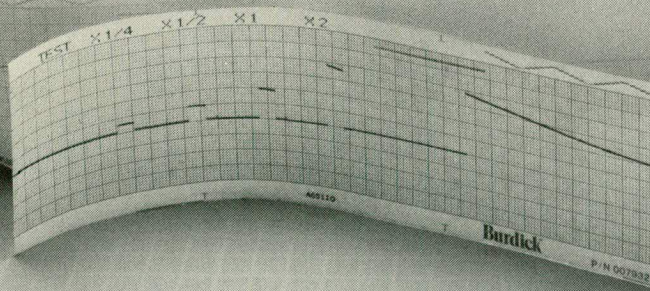
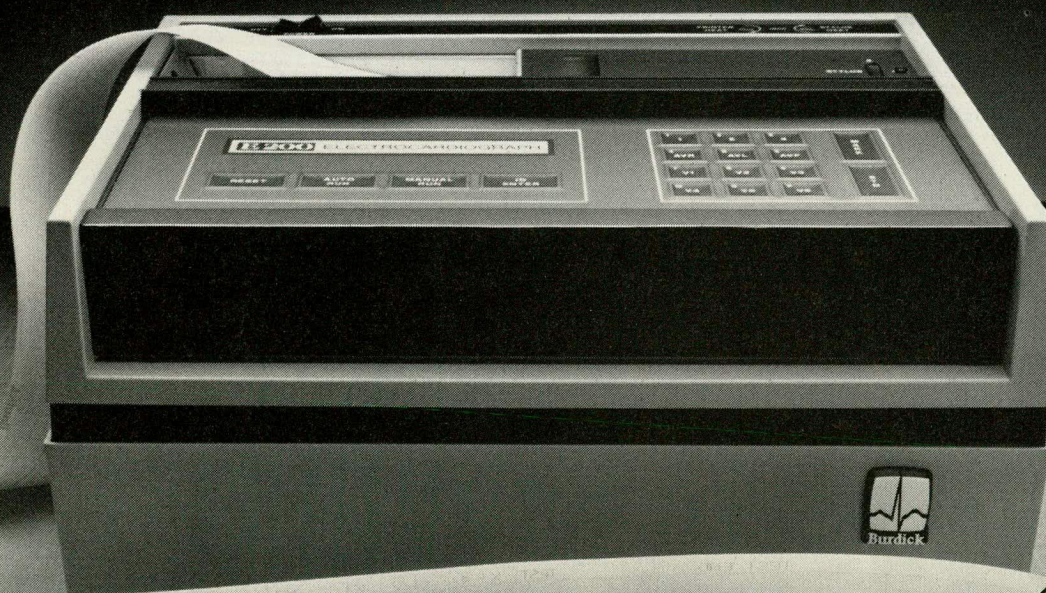
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