SELECTIVE CERVICAL CONIZATION FOLLOWING COLPOSCOPY: A CRITICAL EVALUATION OF 107 CASES

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SYNOPSIS

We performed selective conization for diagnosis and therapy following colposcopy in 107 women with abnormal smears; all except 2 had cervical neoplasia confirmed which was cervical intraepithelial neoplasia (CIN) 96, microinvasion 6 and invasive cancer 3. One of 3 with cone margins involved and no further treatment had residual carcinoma-in-situ. Complications encountered with haemorrhage (2.8%), cervical stenosis (0.9%) but none in 3 who became pregnant. Follow-up was over 1 to 4 years with at least 2 post-conization smears in all patients and revealed persistent CIN in 2 patients but no case of invasive cancer. With selective conization cervical neoplasia is histologically verified in a very high proportion (98.1%), diagnostic conizations minimized, the procedure-associated morbidity low and the risk of undertreatment which exists with destructive methods is obviated.

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INTRODUCTION

Population screening with regular cervical smears reduces by one third both the incidence and mortality rate from cervical carcinoma (1). Cervical cytologic screening detects large numbers of asymptomatic women with abnormal smears from preclinical invasive cervical cancer, carcinoma-in-situ and dysplasias of varying severity (2). Cervical carcinoma-in-situ and invasive carcinoma are closely related, the in-situ lesion is often a precursor of invasive disease; invasive carcinoma may develop from severe and rarely even moderate dysplasia (3). The modern concept of cervical intraepithelial neoplasia (CIN) (4) developed from evidence derived from histology, cytogenetics, DNA content studies and the presence of aneuploidy; all intraepithelial lesions thought to be precursors are covered by the generic term CIN. In CIN nomenclature, mild dysplasia is termed CIN 1, moderate dysplasia CIN 2 and severe dysplasia/carcinoma-in-situ together as CIN 3; the latter two cannot be clearly or consistently differentiated, the diagnoses are not reproducible and diagnostic criteria are arbitrary and not clearly defined (5).

Until recently, treatment of carcinoma-in-situ has been by hysterectomy (6) with consequent loss of menstrual and reproductive functions. This is no longer acceptable in large numbers of young women; cone biopsy with lower morbidity is equally effective treatment (7) and allows fertility preservation. Currently, even less radical treatment by destruction with electrodiathermy (8), cryosurgery (9), the carbon dioxide laser (10) and most recently 'cold' coagulation (11) is being evaluated and may prove to be equally effective; longer follow-up data is however needed before destructive therapy can be considered as definitive treatment. Colposcopic expertise is an absolute necessity when destructive therapy is used to treat CIN. We employ cone biopsy for treatment of severe dysplasia/carcinoma-in-situ until more definitive long term follow-up data on the efficacy of the various destructive methods becomes available. In our department all patients with abnormal cervical smears have colposcopy and directed biopsy as indicated, followed by selective cone biopsy. We decided to critically evaluate our practice of selective cone biopsy, study histological findings in cone biopsies, the correlation of histology with cytology, assess the adequacy of cone excision and complications of the procedure.

Patient Characteristics

The patients ages ranged from 23 to 53 years with a mean of 35.5 years. Almost half (46%) were between 20 to 34 years of age and the others were almost equally divided into those aged between 35 to 39 years (26%) and 40 to 53 years (28%). Nearly all our patients were Chinese, 101 (94%) and there were only 4 (4%) Indians and 2 (2%) Malays. Ninety-eight (91%) patients were married, there were 3 patients each in the categories of those who were single, divorced or widowed. The ages at marriage ranged from 12 to 30 years with a mean of 21.3 years.

Fifty-eight (45%) patients had no history of induced abortion, while 31 (29%) and 10 (9%) had had 1 and 2 induced abortions respectively. A single 1 (1%) patient had had 4 induced abortions and in 3 this information was not recorded. Parity was defined as the number of births of more than 28 weeks gestation; 5 (5%) were nulliparous and 9 (8%) primiparas. There were 16 (15%) para 2 and 36 (34%) para 3, while the remaining 41 (38%) patients had parity ranging from 4 to 8.

One hundred and two patients (95%) were still having regular menstruation while 3 (3%) had secondary amenorrhoea not due to pregnancy and 2 (2%) were post-menopausal. Twenty-eight (26.1%) patients did not use contraception; of the others 13 (12.1%) used the condom, 9 (8.4%) oral contraceptive pills, 21 (19.6%) the IUCD and 28 (26.2%) had been ligated. In 8 (7.5%) the method of contraception was not know.

Cone biopsy procedure

Cone biopsy was done following staining of the cervix with Lugol's iodine to outline the area of unstained cervical epithelium and the ectocervical incision included the entire non-stained area together with an adequate margin of iodine-stained epithelium. The depth of the cone biopsy was generally determined by prior colposcopic findings and removed a significant portion of the cervical canal when the abnormal transformation zone receeded into the cervical canal; the cone biopsy was shallow in those without endocervical extension. To secure hemostasis 2 lateral stitches of absorbable suture were placed at 3 and 9 o'clock positions of the cervix and additional Sturmdorf sutures placed on the anterior and posterior cervical lips only if bleeding continued after the lateral stitches. No vaginal packing or retention bladder catheterisation was used. The

patients were discharged home 48 hours after operation and reviewed 4 to 6 weeks later. Further follow-up involved cervical smears twice at 3 monthly intervals, 3 times at 6 monthly intervals and then annually.

PATIENT AND METHODS

Patient selection

Over 4 years between March 1979 and February 1983 colposcopy was performed in 427 patients of whom 372 (87.1%) had abnormal cervical smears (doubtful, suspicious or positive), 32 (7.5%) a clinically suspicious appearing cervix and 23 (5.4%) other indications. The techniques and criteria used for colposcopic abnormalities were those of Coppleson (12) and Kalstad and Stafl (13). Colposcopically directed biopsies were obtained from any abnormal areas identified. Cone biopsy was performed in 107 (25%) of 427 patients who had colposcopy. Diagnostic cone biopsies were performed in 45 (42.1%) when the entire transformation zone could not be visualized (unsatisfactory colposcopy), when no colposcopic abnormality could be identified in those with persistent suspicious or positive cervical smears or microinvasion found in directed biopsy. Therapeutic cone biopsies were performed in 62 (57.9%) when colposcopy was satisfactory and directed biopsy histology severe dysplasia/carcinoma-in-situ.

RESULTS

Cytologic-histologic correlation

All patients had a cervical smear before colposcopy and selective conization. The most advanced histologic diagnosis in cervical cone biopsy was correlated with the cervical smear report (Table 1). Cone biopsy histology revealed CIN in 1 (33.3%) of 3 with normal smears and in 23 (95.8%) of 24 patients with doubtful smears. In 62 patients with suspicious smears, CIN was found in 55 (88.7%) and of 18 with positive smears 17 (94.4%) had CIN present in the cone biopsy.

When the most advanced histologic diagnosis made by either directed or cone biopsy was considered (Table 1), there were 2 (66.7%) of 3 with normal smears who had severe dysplasia/carcinoma-in-situ and 1 (33.3% had microinvasion. Out of 24 with doubtful smears there was mild dysplasia in 1 (4.2%), moderate dysplasia in 5 (20.8%), severe dysplasia/carcinoma-in-situ in 16 (70.8%) and possible microinvasion in 1 (4.2%). In 62 with suspicious smears, there was mild dysplasia in 2 (3.2%), moderate dysplasia in 3 (4.8%), severe dysplasia/carcinoma-in-situ in 52 (83.8%), microinvasion in 1 (1.6%), invasive carcinoma in 2 (3.2%) and no abnormality in 2 (3.2%) patients. In 18 with positive smears, mild dysplasia was present in 1 (5.5%), severe dysplasia/carcinoma-in-situ in 16 (88.9%) and invasive carcinoma in 1 (5.5%). The reasons for diagnostic conization in 3 patients found to have invasive cancer are given in footnotes d and e in Table 1.

Cone biopsy histology and final histologic diagnosis

In the 107 patients cone biopsy histology (Table 2) showed CIN I, II, and III in 96 (89.7%) microinvasion in 2 (1.8%) and invasive cancer in 3 (2.7%). In 6 (5.6%) patients the cone biopsy showed no abnormality. The details of these 6 cases are given in Table 1 in footnotes a, b, and c. When directed or cone biopsy findings are considered together to formulate the most advanced final histologic diagnosis in each case (Table 3), it was found to be CIN in 96 (89.7%), microinvasion in 6 (5.6%) and invasive cancer in 3 (2.8%). There were 2 (1.8%), cases without abnormality (details given in footnote c of Table 1) and were the only instances of false positive

TABLE I

CORRELATION OF CERVICAL SMEAR AND CONE BIOPSY HISTOLOGY

CERVICAL SMEARS			CONE BIOPSY HISTOLOGY					
Category	Class	n	No Abnormality	Mild Dysplasia (CIN1)	Moderate Dysplasia (CIN2)	Severe Dysplasia/ Carcinoma-in-situ (CIN3)	Microinvasion	Invasive Carcinoma
Normal	(II)	3	1[a]	0	0	1	1	0
Doubtful	(IIR)	24	1[b]	1	5	17	0	0
Suspicious	(III)	62	4[c]	2	3	50	1	2[d]
Positive	(IV/V)	18	0	1	0	16	0	1[e]
Total		107	6	4	8	84	2	3

Footnote:

a Colposcopic features of severe dysplasia/carcinoma-in-situ with carcinoma-in-situ in directed biopsy.

b Colposcopic features of severe dysplasia/carcinoma-in-situ, directed biopsy showed adenocarcinoma-in-situ with possible microinvasion and severe and moderate squamous epithelial dysplasia. Subsequent hysterectomy showed no evidence of disease.

c In 2 patients with colposcopic features of severe dysplasia/carcinoma-in-situ, there was carcinoma-in-situ in directed biopsy. In one with colposcopic microinvasion and in another with no colposcopic abnormality, no directed biopsies were done.

d In one, only the edge of an endocervical tumor seen and no directed biopsy was done; in the other with colposcopically suspect invasive carcinoma the directed biopsy showed only carcinoma-in-situ with microinvasion.

e Colposcopic features of microinvasion but directed biopsy showed only carcinoma-in-situ.

TABLE II

CORRELATION OF DIRECTED BIOPSY AND CONE BIOPSY HISTOLOGY

DIRECTED BIOPSY HISTOLOGY	CONE BIOPSY HISTOLOGY					
	No Abnormality	Mild Dysplasia (CIN1)	Moderate Dysplasia (CIN2)	Severe Dysplasia/ Carcinoma-in-situ (CIN3)	Microinvasion	Invasive Carcinoma
No biopsy	2	0	0	9	0	1
Cervicitis	0	1	0	0	0	0
Mild Dysplasia	0	1	0	3	0	0
Moderate Dysplasia	0	0	1	9	0	0
Severe Dysplasia/ Carcinoma-in-situ	3	2	6	61	1	1
Microinvasion	1	0	1	2	1	1
Total	6	4	8	84	2	3

TABLE III

DIRECTED AND CONE BIOPSY HISTOLOGIC DIAGNOSIS AND FINAL HISTOLOGIC DIAGNOSIS

Type of Biopsy	HISTOLOGIC DIAGNOSIS			
	No Abnormality	CIN[1]	Microinvasion	Invasive Carcinoma
Directed Biopsy[2]	1[a]	88	6	0
Cone Biopsy	6[b]	96	2	3[c]
Final Histologic Diagnosis[3]	2	96	6	3

1 Cervical intraepithelial neoplasia all grades

2 In 12 patients no directed biopsy done

3 Most advanced histologic diagnosis by directed or cone biopsy

a Mild dysplasia found in cone biopsy specimen

b In 3 patients directed biopsy showed CIN and in another adenocarcinoma-in-situ with possible microinvasion. In 2 patients no directed biopsies were done prior to conization. (Details given in Table 1 and accompanying footnotes a, b, and c).

c See table 1 footnotes d and e for details

cervical cytology, both having had suspicious (Class III) cervical smears and no directed biopsies preceeding conization.

In 96 patients the cone biopsy revealed CIN of all grades and of these, the resection margins were free of disease in 90 (93.4%) but were involved by CIN in 6 (6.6%). Of the latter 6 patients with CIN involving cone biopsy margins, 3 patients subsequently had hysterectomy (abdominal 1, vaginal 2) and residual foci of carcinoma-in-situ found in 2 but no disease in the third; of the remaining three, 2 have both been followed up for 3 years without any evidence of recurrence and the other has a small residual focus of carcinoma-in-situ and is awaiting further treatment (vide infra). Of 2 patients with microinvasion in the cone biopsy, the margins were free of any pathology in the first but the endocervical resection margin involved by severe dysplasia in the second. A hysterectomy was done in the first with uninvolved margins and no residual disease found, the other has been followed up for 2 years following the conization without any evidence of recurrence. Of the remaining 9 patients who had conization there was no abnormality in 6 but invasive cancer in 3 and the criterion of disease-free resection margins of no relevance. Of 3 with invasive cancer, 2 had radical hysterectomy with pelvic lymphadenectomy and both had invasive cancer in the surgical specimen but all lymph nodes were negative; the other was treated by radiotherapy.

Complications and pregnancies following cone biopsy

Primary haemorrhage occured in 3 (2.8%) following cone biopsy and required surgical measures for haemostasis. Both cryosurgery and Sturmdorf sutures were used in one and only Sturmdorf sutures in the second; the last settled with firm vaginal packing and blood transfusion. A single (0.9%) case which developed cervical stenosis needed only probing of the cervical os and gentle dilatation as an outpatient without further problems. Three patients became pregnant

and none developed any complications during the antenatal, intrapartum or postpartum periods; all had normal spontaneous vaginal deliveries.

Follow-up after cone biopsy

Follow-up over a period of 1 to 4 years was achieved in 73 (68.2%) patients, while the other 34 (31.8%) have been followed up for less than 1 year but have had at least 2 cervical smears following conization. There were 2 patients who were discovered to have abnormal smears following conization. In one with a doubtful smear, cone margins were involved by carcinoma-in-situ due to an intentional cut through of a very extensive lesion extending to the vaginal fornices and the planned definitive hysterectomy confirmed extensive residual carcinoma-in-situ. The other had a positive smear after cone biopsy in which only the ectocervical margin was involved by carcinoma-in-situ and a small focus of carcinoma-in-situ was identified colposcopically and confirmed by directed biopsy; she is scheduled for electrodiathermy treatment because further pregnancies are desired.

DISCUSSION

The treatment of choice for carcinoma-in-situ of the cervix is still a debated issue. Therapy varies from conservative locally destructive methods (14) to conization (15) and hysterectomy (16) including removal of a vaginal cuff. An increasing number of young women have cervical neoplasia detected by cytologic screening, with a peak incidence of carcinoma-in-situ at 25 to 29 years (17); less severe grades of CIN are diagnosed at even younger ages. In our patients most of whom are young, adequate follow-up after treatment of CIN cannot always be guaranteed and we therefore, prefer to treat severe dysplasia/carcinoma-in-situ (CIN3) by cone biopsy, a proven effective modality (18,19) rather than destructive therapy. Cone biopsy provides an adequate tissue

specimen for full histologic evaluation which obviates any possible risk of undertreating an early invasive cancer; destructive procedures have the advantage of lower cost because of outpatient treatment and probably lower long-term morbidity but have the disadvantage that there is no opportunity for thorough histologic evaluation.

Colposcopy and directed biopsy prior to conization results in only 25% of our colposcopy clinic population needing conization for diagnosis and treatment of cervical neoplasia. Doubtful smears may be the first indication of cervical neoplasia and we have previously shown (20) that up to one-third of patients with doubtful smears may harbour significant cervical neoplasia; in the present study 95.8% had CIN, with three quarters being severe dysplasia/carcinoma-in-situ. Cervical neoplasia ranging from severe dysplasia to invasive cancer occured at a rate of 88.7% and 94.4% in those with suspicious and positive smears respectively; in a local study by Ong and Zarina (21) similar disease occured in only 30% and 70-80% of those with suspicious and positive smears respectively who had conization without prior colposcopy. The higher rates of neoplasia in our study are due to the use of colposcopy and selective cone biopsy. Our rates of cervical neoplasia in cone biopsies approach those of Bjerre et al (18) who studied large numbers of patients and reported rates of similar disease in 74.2% of those with suspicious smears and 85.1% of those with positive smears.

There was a 2% rate of false-positive cytology in our study whereas there was none in the study by Ahlgren et al (22) who also performed colposcopy prior to conization. Without colposcopy, a high rate of false-positive cytology has been reported when all patients with abnormal smears were subjected directly to diagnostic conization (18,23). Colposcopy is therefore very useful when patients with abnormal smears are managed so that conization is avoided in those with false-positive cytology; colposcopy furthermore assures that in a very high proportion of cone specimens cervical neoplasia will be confirmed. In this study cervical neoplasia was found in 94.4%, in close agreement with the figures of 100% in Ahlgren's et al (22) study, who also utilized selective conization; it occurred in only 85.7% in Bjerre's et al (18) study who performed non-selective cone biopsy.

Conization as therapy for CIN necessitates determining whether excision is complete and this requires a careful and thorough histologic examination of resection margins; when cone biopsy margins are free of disease we share the opinion of Coppleson (24) that it is good evidence that conization is safe and adequate treatment. Complete excision of CIN was achieved in 94% of patients in this study. Schulman and Cavanaugh (25) consider disease-free margins alone to be unreliable without detailed examination of the cone specimen by serial step sections. The rate of CIN persistence is however very low even in those with involved margins; the studies of Kolstad and Klem (19) and Devereaux (26) report rates of only 16% and 12% respectively. In the present study, the numbers with involved margins were very small. Of 3 patients with involved margins who received no further treatment only one has persistent disease but more definitive in this respect is the recent study of Ahlgren et al (22) when disease persistence occurred in 42 such cases. Patients with cone biopsy margins involved by CIN who receive no further treatment however must be closely followed with regular smears and preferably also with colposcopy.

Complications of haemorrhage following conization requiring intervention may reach 25% (27) but are generally in the range of 3 to 11% (24). We had a rate of 2.8% whereas Ong and Zarina (21) reported a much higher rate of 8.5% closer to the 9.2% of Davis et al (28). Cervical stenosis occurred in 1% of our patients and is much lower than the rate of 7% reported by Hester (29). In none was there significant dysmenorrhoea following conization. Some studies (30, 31, 32) report significant adverse effects on fertility and subsequent pregnancies following cone biopsy. Cervical

incompetence and increased rate of premature delivery and cervical dystocia have been described. The reports of McCann et al (33) and Lee (34) describe few adverse effects whereas that of Larsson et al (31) describes a high rate of premature delivery in young women only, being 4.4% before and 30.6% after conization. The case control study of Jones et al (42) reported a 17% rate of preterm labour following cone biopsy compared to 3% in controls. However, our own experience in this study of the effect of conization is small because only 3 patients became pregnant, all of whom however suffered no complications. No definitive conclusions can be drawn from so few cases. Recent studies (33,34) however, suggest that the purported adverse effects of conization on subsequent pregnancy outcome may not be as great as might be anticipated but it is difficult to compare the various studies in the literature because some utilize selective conization following colposcopy which allows a reduction in the size and depth of the cone biopsy, reducing morbidity of the procedure. We feel that the issue is as yet unresolved and the morbidity of selective conization on subsequent reproductive function needs further study.

With the low complication rate of cone biopsy in our study we feel that the procedure is not associated with excessive morbidity and is acceptable when used selectively after colposcopy. Since there is an insufficient period of follow-up in the current analysis no valid conclusions on the long-term efficacy of cone biopsy as therapy for CIN can be made from the present study but the long-term studies reported by Bjerrre et al (18), Ahlgren et al (22), Andersch and Moinian (23) and Kolstad and Klem (19) are reassuring in this respect. We conclude that with the incorporation of colposcopy, the number of diagnostic cone biopsies has decreased, nearly all that are done will contain cervical neoplasia and the procedure following colposcopy is associated with little morbidity. Selective cone biopsy then becomes an essential and acceptable diagnostic and therapeutic procedure for those with cervical intraepithelial neoplasia.

ACKNOWLEDGEMENT

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