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Comparison of the Grade of CIN in Colposcopically Directed Biopsies with that in Outpatient Loop Electrosurgical Excision Procedure (LEEP) Specimens – A Retrospective Review

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ABSTRACT

Background: It has been suggested that LEEP should be the standard for the diagnosis of cervical dysplasia, rather than colposcopically directed biopsy as traditionally so, since it is both diagnostic and therapeutic.

Patients: Seventy-eight patients who underwent LEEP at the Gynaecological Cancer Centre, KK Hospital from 1 January 1995 to 31 December 1997 for cervical dysplasia diagnosed by colposcopically directed biopsy were retrospectively reviewed. The mean age of the patients was 40.3 years (SD 8.4), with 78.2% of them with CIN I or CIN II. The mean operating time was 11.8 minutes (SD 4.9) and 53.8% (42/78) were given prophylactic antibiotics, with the only complication being moderate postoperative haemorrhage in 3.8% (3/78). The mean follow-up period was 19.1 months (SD 9.3) with the cure rate being 97.4% (76/78).

Results: Only half of the patients had corresponding histologies on biopsy and LEEP, with 28.2% (22/78) undergraded and 21.8% (17/78) overgraded.

Conclusion: Significant discrepancies may be found between the results of colposcopically directed biopsy and loop excision, and LEEP, which is safe and effective may be the choice procedure for the diagnosis of cervical dysplasia.

Keywords: LEEP, colposcopically directed biopsy, CIN, significant discrepancies

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INTRODUCTION

The incidence of cervical cancer can be reduced with screening by cervical Papanicoloau smears applied in an organised fashion, together with treatment of pre-cancerous dysplasias[1]. Colposcopically directed biopsy of the cervix has been the standard for the diagnosis of cervical intraepithelial neoplasia (CIN) for years and treatment is often based on histopathological reports of such specimens. The introduction and development of loop electrosurgical excision procedure (LEEP) has brought about a plethora of studies disputing the accuracy and reliability of diagnosing CIN with colposcopically directed biopsy. Reports have demonstrated significant discrepancies between histology from colposcopically directed biopsy and from LEEP specimens[2-4], suggesting that reliance on colposcopically directed biopsy alone for the diagnosis of CIN may be potentially damaging as women with more advanced cervical dysplasia subsequently found in LEEP specimens will initially have been treated inadequately. The aim of our study was to review our cases to ascertain if, indeed, there is significant discrepancy between the histology of colposcopically directed biopsy and LEEP.

METHOD

This is a retrospective analysis of women who underwent LEEP at the Gynaecological Cancer Centre, KK Hospital, for cervical dysplasia, from 1 January 1995 to 31 December 1997. All the patients were diagnosed by colposcopically directed biopsies.

LEEP was performed with the LEEP System 6000 machine, with power setting between 25 and 50 watts. Loop size ranged from 1.0 cm x 1.0 cm to 2.0 cm x 1.0 cm and current was blended to cut and coagulate. Haemostasis was attained with either ferric subsulphate (Monsell) or roller ball coagulation.

Records of all cases were traced and reviewed for patient characteristics, operating time, the use of prophylactic antibiotics, complications, follow-up period, outcome and the histopathology of colposcopically direct biopsy specimens and the corresponding LEEP specimens. Data collected was dependant on the adequacy of documentation in the records, bearing in mind that this is a retrospective study. All continuous data were expressed as mean.

Cohen's K was used for the measurement of agreement between the grade of dysplasia diagnosed or colposcopically directed biopsy and that obtained from the LEEP specimen.

RESULTS

There were 78 patients who underwent LEEP in the 3 years of our study, all of whom had their diagnosis confirmed by colposcopically directed biopsies at the site most suspicious of dysplasia or the most dysplastic area. The ages ranged from 23 years to 67 years of age (mean 40.3, SD 8.40). 89.7% (70/78) were Chinese, 2.6% (2/78) were Malays, 1.3% (1/78) were Indians and 6.4% (5/78) were of other races. The operating times ranged from 5 minutes to 30 minutes (mean 11.8, SD 4.9).

Prophylactic antibiotics were not administered to all patients. The antibiotics of choice were either Doxycycline 100 mg bd and Metronidazole 200 mg tds, or Amoxycillin 250mg tds in combination with Metronidazole. The antibiotics were prescribed for a period of 1 week postoperatively. 53.8% (42/78) were prescribed either of the combinations of antibiotics. The only complication recorded in our study was postoperative haemorrhage. Haemorrhage was classified as mild when bleeding was slight, moderate when admission was necessary for haemostasis (either by vaginal packing, with Monsell solution application, or by diathermy), and severe when transfusion was necessary. 3.8% (3/78) reported to have had this complication, all of whom were in the moderate bleeding group.

One of the patients had been prescribed prophylactic Doxycycline and Metronidazole, whilst the others had not been given any prophylaxis. All 3 were admitted for only 24 hours with a vaginal pack, and were discharged well.

Table I illustrates the histopathological distribution of the cases by colposcopically directed biopsy. 78.2% (61/78) were CIN I or CIN II. There were 6 cases of CIN III. Of these, 4 were confirmed to have CIN III with clear margins on LEEP histology. However, 2 were diagnosed with invasive cancer. The first was diagnosed with invasive, well differentiated adenocarcinoma on LEEP biopsy. An extended hysterectomy was scheduled for Stage 1A1 cervical adenocarcinoma, but at laparotomy, the left obturator and para-aortic lymph nodes were found to be enlarged. The operation was abandoned, and the patient underwent a course of radiotherapy. The second patient had microinvasive squamous cell carcinoma for which a vaginal hysterectomy was performed. Histology of the specimen confirmed microinvasion with clear margins. Both patients are presently well, with no recurrence.

There was a 58-year-old woman whose colposcopically directed punch biopsy showed a squamous lesion for which invasion could not be excluded. LEEP biopsy confirmed a moderately differentiated squamous cell carcinoma.

A Wertheim's operation was performed for Stage 1B cervical cancer. The patient is presently well with no recurrence one and half years later.

Table II illustrates the comparison of colposcopically directed biopsy histology with LEEP histology.

Fifty percent (39/78) of cases had histologies which corresponded whilst 28.2% (22/78) and 21.8% (17/78) were undergraded and overgraded respectively by colposcopically directed biopsy. The Cohen's K statistical analysis for the agreement between colposcopically directed biopsy and LEEP biopsy histology was 0.36 ($p < 0.001$) indicating a moderate correlation. Of the 17 overgraded, 8 were CIN I and 9, CIN II, accounting for 25.8% (8/31) of CIN I and 30% (9/30) of CIN II. None of the cases with CIN III on colposcopically directed biopsy was overgraded.

Amongst the 22 who had LEEP histologies more severe than suggested by colposcopically directed biopsy, there was no significant difference in the frequency of undergrading noted amongst the different histologies ($p < 0.05$). Table III summarises the frequency of discrepancy between colposcopically directed biopsy and LEEP histologies.

The follow-up period ranged from 3 months to 35 months (mean 19.1, SD 9.3). 97.4% (76/78) remained free of disease at the time of the study. Of the 2 patients with disease, one was discovered to have CIN III on colposcopy 18 months post-LEEP, after regular follow-up was negative. Cone biopsy confirmed CIN III with clear margins. The second case was one of persistent CIN II for 6 months post-LEEP. Again, cone biopsy confirmed CIN II. Both patients are well.

Table I – Histopathological distribution by colposcopically directed biopsy (n = 78)

Histology	Frequency
HPV	9 (11.5%)
CIN I	31 (39.7%)
CIN II	30 (38.5%)
CIN III	6 (7.7%)
Cervicitis	1 (1.3%)
Suspicious of invasion	1 (1.3%)
Total	78 (100%)

HPV = Human Papilloma Virus

CIN = Cervical Intraepithelial Neoplasia

DISCUSSION

It is acknowledged widely that most cervical cancers develop from cervical dysplasias, the higher the grade of dysplasia, the higher the malignant potential[5]. Given the clear malignant potential of untreated high grade dysplasias, and the difficulty in identifying accurately CIN I on cervical punch biopsy[6], it seems to be prudent to treat all women with CIN I regardless of the grade of dysplasia.

Many reports have illustrated significant discrepancy between colposcopically directed biopsy and LEEP histology[7,8]. Loop excision has been shown to result in the diagnosis of microinvasion not identified by colposcopic biopsy[2]. Our study concurs with the observations.

Only 50% of our patients had similar histologies on colposcopic biopsy and LEEP. 28.2% were undergraded, a significant percentage which is disturbing as these patients might not have been given

Table II – Comparison of colposcopically directed biopsy histology with LEEP histology

Colposcopically directed biopsy	LEEP HPV	CIN I	CIN II	CIN III	Cervicitis	Cancer	Total
HPV	7	0	1	1	0	0	9
CIN I	2	12	7	4	6	0	31
CIN II	2	4	14	7	3	0	30
CIN III	0	0	0	4	0	2	6
Cervicitis	0	0	0	0	1	0	1
Suspicious of invasion	0	0	0	0	0	1	1
Total	11	16	22	16	10	3	78

Table III – Frequency of discrepancy between colposcopically directed and LEEP histology

Colposcopically directed biopsy histology	Undergraded (n = 22)	Overgraded (n = 17)
HPV	2	0
CIN I	11	8
CIN II	7	9
CIN III	2	0
Cervicitis	0	0
Invasive cancer	0	0

the appropriate treatment. This is potentially catastrophic since it has been reported that the occurrence of progression of CIN lesions to either a more severe form, or invasive cancer ranges from 1.4% to 60%[8]. Of the 17 cases which were overgraded, 8 were CIN I, that is, 25.8% (8/31) of all the CIN I on colposcopic biopsy had no residual disease on LEEP.

This is consistent with studies which show that perhaps up to 80% of low grade dysplasias will either regress or remain the same[9]. Furthermore, the biopsy itself may actually alter the growth behaviour of the dysplastic cells, particularly in very localised lesions. The moderate degree of correlation (k = 0.36) between colposcopic biopsy and LEEP is consistent with other studies[10] and lends support to the suggestion that LEEP may be the method of choice for the diagnosis of cervical dysplasia[11]. The low complication rate (3.8%), high cure rates (97.4%) and relatively short operating time (mean 11.8 minutes) have been favourable factors in further establishing LEEP as an attractive alternative to colposcopically directed biopsy.

However, several factors precludes generalising the results observed. Firstly, our study was a fairly small one, and was a retrospective study, entailing the review of patients' records which often are not well documented. The site of biopsy and the number of biopsy specimens taken were not documented. Obviously a more experienced colposcopist would have been more likely to biopsy the correct site. Furthermore, the more the number of biopsies taken, the less the likelihood of missing the diagnosis, a factor which might have altered the rate of underdiagnosis.

Secondly, the operators' experiences ranged widely from registrars to senior consultants, a fact which could possibly explain the high degree of discrepancies in the histologies.

In conclusion, our study has shown that there is significant discrepancy in the histology of colposcopically directed biopsy and LEEP. All women with apparent low grade dysplasia or colposcopic biopsy should be treated and LEEP may be the method of choice since it is both diagnostic and therapeutic, and it is a safe and efficient procedure that can be done in the outpatient setting[12].

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