Necessity of Colposcopy and Biopsy prior to Large Loop Excision of the Transformation Zone (LLETZ)

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Abstract. Background: The clinical value of colposcopy and biopsy prior to large loop excision of the cervical transformation zone (LLETZ) with respect to negative histology and positive specimen margin rates, was evaluated. Patients and Methods: A total of 2,050 consecutive patients who had undergone LLETZ from 1997 to 2005, were included. As diagnostic work-up prior to LLETZ, 290 patients underwent repeat PAP test only and 1,760 patients had undergone colposcopy/biopsy. Results: The diagnostic approach using colposcopy/biopsy reduced the rates of negative histology and positive margins from 6.0% to 1.9% (p<0.001) and from 28.2% to 21.7% (p=0.002), respectively. The rates of invasive carcinomas were not different between the groups (6.6% vs. 6.5%; p=0.9). Conclusion: Performing colposcopy and biopsy prior to LLETZ reduces unnecessary surgical procedures and decreases positive margin rates.

The optimal cervical cancer screening strategy and the subsequent management of abnormal PAP tests would eliminate cervical cancer with the least necessary surgical interventions (1). While a number of clinical guidelines have been published regarding cervical dysplasia, adherence to these guidelines has been reported to be low (2).

Colposcopy and colposcopically directed cervical punch biopsy are regarded as the cornerstones of the management of abnormal PAP tests (3). However, this approach has been challenged citing overtreatment, unnecessary morbidity, increased health care costs, and a low sensitivity of colposcopy and/or biopsy in detecting high grade dysplasia (4, 5). It has been suggested that abnormal PAP tests, that is any PAP test indicative of a high grade squamous intraepithelial lesion (HSIL) or recurrent PAP tests indicative of low grade squamous intraepithelial lesion (LSIL), are sufficiently indicative for large loop excision of the transformation zone (LLETZ) (6).

Although LLETZ is widely regarded as minor surgery and can be performed on an outpatient basis, this intervention carries a significant morbidity including a number of short- and long-term complications, such as cervical stenosis, bleeding, premature rupture of the membranes, preterm delivery, low birthweight, and an increased risk of caesarean section (7, 8). Furthermore, a LLETZ specimen with positive margins causes patient anxiety and a number of subsequent medical interventions. Therefore, diagnostic work-up strategies prior to LLETZ have been developed and tested in order to minimize the number of LLETZ specimens with negative histology and positive resection margins. Whether or not routine colposcopy and biopsy is associated with a significant reduction of the number of LLETZ specimens with negative histology and with positive resection margins, however, is unknown.

In the present study, the effect of colposcopy and biopsy prior to LLETZ on negative histology and positive margin rates was evaluated in a series of 2,050 consecutive patients.

Patients and Methods

Clinical data were collected retrospectively from files at the Medical University of Vienna, Department of Obstetrics and Gynecology. A total of 2,050 consecutive patients undergoing LLETZ for cervical dysplasia from January 1997 to December 2005, were included.

The patients had been referred to the outpatient clinic of our Department of Obstetrics and Gynecology by their treating physicians for the treatment of abnormal PAP tests. No strict policy was implemented on the required examinations prior to LLETZ was implemented and the senior physician in charge of the outpatient clinic on the respective day decided on the scheduled examinations on any particular day. Some of the
patients underwent repeat PAP test only (group A, n=290) while the others underwent repeat PAP test and colposcopy with (n=1,287) or without (n=473) colposcopically directed cervical punch biopsy (group B). Biopsies were not performed in patients with no visible cervical lesion on colposcopy, with anticoagulation therapy, and in patients not consenting to a cervical biopsy.

In group B after examination of the vulva, a speculum was inserted into the vagina and the cervix was visualized. The examination was started at a low magnification after cleaning the cervix and removing any excess cervical mucus. The repeat PAP test was then taken. In cases of a non-visible transformation zone, a separate endocervical PAP test was taken. For the patients in group B, a 3% acetic acid solution was next applied to the cervix and a complete colposcopic examination was performed including observation of the original squamous epithelium, the entire transformation zone, the squamocolumnar junction and as much of the columnar epithelium of the cervix as possible. Only if the squamocolumnar junction was completely visible, that is if the internal – endocervical – limit of the normal or atypical squamous epithelium was entirely apparent, was the colposcopy regarded as satisfactory. For the patients who underwent cervical punch biopsy at least one biopsy was taken under colposcopic guidance, if an acetic-white and/or iodine-negative lesion was present. After completion of the colposcopic examination, all observations were entered in a structured colposcopy chart.

The PAP tests were scored using the Bethesda classification. The histology was reported as negative, mild (cervical intrapithelial neoplasia, CIN I), moderate (CIN II) or severe (CIN III) cervical dysplasia, condylomata acuminata or invasive cervical cancer.

On the basis of the test results, patients were scheduled for LLETZ or were managed conservatively. The LLETZ procedures were conducted as inpatient surgery under general anesthesia. The size and shape of the cone was designed according to the colposcopic findings.

The evaluated outcome parameters were the rate of negative histology and the rate of positive margins of the LLETZ specimens. Patients’ age, training status of surgeon, and colposcopy result as independent parameters. P-values of <0.05 were considered statistically significant. The statistical software SPSS 11.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

Results

The mean age of the patients was 35.9 (SD 10.2) years.

The LLETZ histologies in group A were: complete negative histology, n=19 (6.5%); condylomata acuminata, n=2 (0.7%); CIN I, n=49 (16.9%); CIN II, n=63 (21.7%); CIN III, 138 (47.6%) and invasive cervical cancer, n=19 (6.6%). LLETZ histologies in group B were: complete negative histology: n=33 (1.9%), condylomata acuminate: n=5 (0.3%), CIN I: n=176 (10.0%), CIN II: n=400 (22.7%), CIN III: 1031 (58.6%), invasive cervical cancer: n=115 (6.5%). The patients in group A and B had complete negative histology rates of 6.5% and 1.9%, respectively (p<0.001). Within group B, an unsatisfactory colposcopy was associated with a significantly higher negative histology rate (5.9%) compared with a satisfactory colposcopy (1.2%, p<0.001). The rates of invasive carcinomas were not different between the groups (6.6% vs. 6.5%; p=0.9).

Positive LLETZ specimen margins were noted in 28.2% and 21.7% of patients in group A and B, respectively (p=0.002). Within the group undergoing colposcopy, the patients with an unsatisfactory colposcopy had a significantly (p<0.001) higher positive LLETZ specimen margin rate (25.2%) than those with a satisfactory colposcopy (18.2%). The influence of the following parameters on positive LLETZ specimen margin rate was evaluated in a multivariate Cox regression model: patients’ age < vs. ≥30 years, training of surgeon (resident vs. attending physician) and diagnostic work-up prior to LLETZ (Table I). The patients’ age and the diagnostic work-up prior to LLETZ independently influenced positive LLETZ specimen margin rate.

Table I. Predictors of positive margins of LLETZ specimen.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Positive LLETZ margin rate (%)</th>
<th>Univariate p</th>
<th>Multivariate p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>22.6%</td>
<td>0.002</td>
<td>0.02</td>
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<tr>
<td>Diagnostic work-up prior to LLETZ</td>
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<td></td>
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<tr>
<td>Repeat PAP smear only</td>
<td>28.2%</td>
<td></td>
<td></td>
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<tr>
<td>Repeat PAP, colposcopy, biopsy</td>
<td>21.7%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age ≥30 yrs</td>
<td>25.4%</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age &lt;30 yrs</td>
<td>16.0%</td>
<td></td>
<td></td>
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<tr>
<td>Training status of surgeon</td>
<td></td>
<td>0.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Resident</td>
<td>22.9%</td>
<td></td>
<td></td>
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<tr>
<td>Attending physician</td>
<td>22.4%</td>
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Discussion

Benefit of the colposcopy/biopsy strategy was clearly shown compared to PAP test alone regarding negative histology and positive LLETZ specimen margins, in the present study. This effect was retained in all the subgroup analyses and in the multivariate Cox regression analysis. The data in the colposcopy/biopsy group with respect to negative histology were excellent and better than those previously published. On average fifteen colposcopies would be performed to prevent one unnecessary LLETZ procedure. The relatively high positive margin rate was similar to previously published series. It should be noted that our data cannot be compared with those of "see and treat" approaches using PAP tests and colposcopy to decide on excisional procedures.

The strength of our study was the large number of LLETZ procedures evaluated and the clearly defined outcome parameters while the major shortcoming of our data is the retrospective and non-randomized study design. However, as no strict policy regarding pre-LLETZ diagnostic procedures was implemented in our Department the data should not have been unduly influenced by selection bias. The fact that patient’s characteristics were equally balanced between the groups (group A vs. B) supports the validity of our findings.

Acknowledgements

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References