

# Outcomes of carbon dioxide laser conization for the treatment of cervical intraepithelial neoplasia grade III

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## Summary

**Purpose:** The aim of this study was to determine the rates of incomplete excision of cervical intraepithelial neoplasia (CIN) III after carbon dioxide laser conization, and the risk of reappearance of CIN depending on the excision margins.

**Methods:** A total of 153 women who underwent carbon dioxide laser conization for CIN III between 1988 and 1998 at our hospitals were eligible for inclusion in the study and their notes were retrospectively studied.

**Results:** Histological examination of the excision margins revealed complete excision in 134 (87.6%), uncertain margins in one, and extension of CIN to the margins in 18 (11.8%) cases. The treatment failure rate in the cases with clear margins was 2.2% (3 of 134), and in the cases with involved margins 44.4% (8 of 18) ( $p < .001$ ).

**Conclusion:** Carbon dioxide laser conization despite the worldwide use of LLETZ still has a place in the treatment of CIN. Very high rates of complete excision were achieved. As incomplete excision does not always result in treatment failure, neither do clear margins always indicate eradication of the disease.

**Key words:** Laser; CIN; Uterine cervix; Treatment failure.

## Introduction

Conservative treatment, either ablative or excisional, has become the treatment of choice for cervical intraepithelial neoplasia (CIN), and in combination with the introduction of cervical screening has resulted in a marked decrease in the incidence of cervical cancer [1]. Especially carbon dioxide laser conization has been used with success for over 20 years [2]. However women who have been treated for CIN, whatever the method of treatment, are still more likely than the general population to develop invasive cancer [3], and follow-up is necessary. It has been shown that the extension of the CIN to the excision margins is a major risk factor for treatment failure [4].

The aim of this retrospective study was to determine the rates of incomplete excision of CIN III after carbon dioxide laser conization, and the risk of reappearance of CIN depending on the excision margins.

## Materials and Methods

Women who underwent carbon dioxide laser conization for CIN III between 1988 and 1998 at our hospitals were eligible for inclusion in the study and their notes were retrospectively studied. The women had been referred for colposcopy because of one abnormal cervical smear suggestive of squamous intraepithelial lesion (SIL) or because of a repeated smear revealing atypical squamous cells of undetermined significance (ASCUS). In case of abnormal colposcopic findings a punch

biopsy under colposcopic guidance followed. The women in whom pathology would reveal CIN II-III underwent carbon dioxide laser conization. The equipment used was a product of ESC Sharplan, Israel. At the end of the procedure the crater edges were ablated to a depth of 1 mm for haemostasis and destruction of possible residual nests of dysplastic epithelium. A total of 153 women with CIN III were treated. These women were followed-up every six months with a Pap test and colposcopy for the first two postoperative years and annually thereafter. In cases with incomplete excision follow-up was every three months during the first two postoperative years. If, irrespectively of the marginal status, there were cytological and/or colposcopic indications of CIN (any grade) during the follow-up period the patient would undergo a biopsy. If it showed CIN the case was considered as treatment failure and a second procedure would be performed.

The excised cervical specimen was sent for pathological examination with attention to the excision margins. From each cervical specimen 12-16 paraffin blocks were created, and 4-5 sections were made and examined from each block.

The main outcome measures were the excision margin status, and the appearance of subsequent CIN during the follow-up period, and the grade of the residual lesion. Statistical analysis was done with the  $X^2$  test.

## Results

The mean age of the women was 33.7 years (standard deviation: 7.2, range: 27-48). Histological examination of the excision margins in the 153 women revealed complete excision of CIN III in 134 (87.6%) and extension of CIN to the margins in 18 (11.8%) cases. In one case the margins could not be evaluated because of thermal artifact.

Of the 134 women with clear margins 114 (85.1%) completed two years of follow-up, and 129 (96.3%) had at least one year. The appearance of subsequent CIN during the follow-up period was histologically confirmed in three of the 134 cases (2.2%). Of the 18 women with involved margins 14 (77.7%) completed two years of follow-up and 16 (88.8%) had at least one year. Subsequent CIN was diagnosed in 8 of 18 (44.4%). Recurrence rates between women with clear margins and women with involved margins differed significantly ( $p < .001$ ). The only patient with uncertain margins completed two years of follow-up and no further lesion was detected. The grade of the residual lesions is shown in Table 1.

Although 14 women became pregnant during the follow-up period, data on fertility and pregnancy outcome (spontaneous abortions, preterm labor, etc.) were limited.

Table 1. — *Follow-up cytology and colposcopy and grade of residual lesions.*

Follow-up	Clear margins n=134			Involved margins n=18		
	CIN I	CIN II	CIN III	CIN I	CIN II	CIN III
Cytology:+	1	2	0	1	1	3
Colposcopy:+						
Cytology:+	0	0	0	0	1*	0
Colposcopy:-						
Cytology:-	0	0	0	0	1	1
Colposcopy:+						
Total	1	2	0	1	3	4

+: abnormal test result; -: normal test result; \*A diagnostic second loop was performed due to cytology suggesting high grade SIL, while colposcopy was unsatisfactory.

## Discussion

The main advantage of excisional methods such as carbon dioxide laser conization, large loop excision of the transformation zone (LLETZ) and cold knife conization over ablative ones (laser ablation, electrocoagulation diathermy, cold coagulation and cryotherapy) is the pathological assessment of excision margins. It has been established and confirmed by our study that extension of CIN to the margins of excision is a major risk factor [4]. Therefore the women at increased risk for treatment failure can be identified and followed-up more intensively. In this study the rate of incomplete excision of CIN III after carbon dioxide laser conization was very low (11.8%) compared to reported rates after LLETZ [5]. This can be attributed to the accuracy with which the laser beam can be directed, so that the whole affected area can be included in the excision.

Incomplete excision does not always result in treatment failure. In only 44.4% of the women with involved margins was there evidence of residual CIN. This is in agreement with a study of 721 women who underwent LLETZ, where despite a just 56% rate of complete excision, the treatment success rate in the first three months was 95% [5]. A possible explanation or this could be the thermal destruction of the dysplastic epithelium at the

cervical crater edges by the laser beam or the diathermy loop either during the excision or during the haemostasis process [6]. Therefore in these women close follow-up is required in order to detect those who will have residual disease, but also to avoid unnecessary second excisions.

However, even clear margins do not always indicate eradication of the disease. In fact the risk of treatment failure in such cases ranges from 1.9 to 6% independent of the excisional method used [7-10]. In this study there was a 2.2% risk of treatment failure after complete excision which is within the above range.

Detailed data on the fertility and the pregnancy outcome of the women in this study are not presented. A case-control study would be required to evaluate the effects of laser conization on fertility and pregnancy. Although the amount of cervical tissue excised in laser conization is probably less than in cold knife conization, in one study it was shown that cones deeper than 10 mm are associated with adverse pregnancy outcome [11]. On the contrary studies on LLETZ have not shown any effects of LLETZ on fertility and pregnancy [12].

It seems that carbon dioxide laser conization despite the worldwide use of LLETZ still has a place in the treatment of CIN. The equipment may cost more and the procedure may last longer than LLETZ [13], but in the hands of an experienced gynecologist, it presents excellent results. Apart from extensive high grade lesions which should be preferably excised in one specimen, laser should also be considered as the treatment of choice in young women with glandular lesions where cold knife conization could result in excessive removal of healthy cervical tissue, and LLETZ might not reach the appropriate depth of excision.

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