

Inner Border—A Specific and Significant Colposcopic Sign for Moderate or Severe Dysplasia (Cervical Intraepithelial Neoplasia 2 or 3)

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■ Abstract

Objective. Investigation of the correlation between the colposcopic sign inner border and cervical intraepithelial neoplasia (CIN) 2 or 3 and its association with specific human papillomavirus (HPV) types and the age of the patient.

Study Design. Colpophotographs or cervicograms were taken from 947 women referred due to an abnormal cervical finding. Occurrence of the colposcopic sign inner border was evaluated retrospectively by 2 independent colposcopists. Histologic evaluation was based on punch or cone biopsies. Human papillomavirus testing was done using Hybrid Capture I or a polymerase chain reaction–based HPV test.

Results. The prevalence of the colposcopic phenomenon inner border in women with an atypical transformation zone was 7.6% (53/695). In 70% of women with inner border, CIN 2 or 3 was confirmed histologically. The sensitivity of the colposcopic sign inner border for detection of CIN 2 or 3 was 20%, and the specificity was 97%. In patients with inner border, the odds ratio for CIN 2 or 3 was 7.7 (95% CI = 4.2–14.3). There was no significant association between inner border and any high-risk HPV

type. Cervical intraepithelial neoplasia 2 or 3 associated with inner border was significantly more frequent in patients younger than 35 years.

Conclusion. Inner border is a rare colposcopic phenomenon but highly specific for CIN 2 or 3 in young women. ■

Key Words: colposcopy, grading, CIN, human papillomavirus

Colposcopy is used to grade ectocervical disease [1] and to delineate the extent of the lesion [2]. Assessment of cervical disease is completed by colposcopic guided biopsies [3] using 5% acetic acid and Lugol uptake (Schiller test). The application of grading criteria such as color, surface pattern, iodine uptake, presence or absence of abnormal vessels, and demarcation [4] on an atypical transformation zone remains challenging because only 20% of these atypical transformation zones contain cervical intraepithelial neoplasia (CIN) [5]. Thus, colposcopic signs that are highly correlated with CIN can be useful in clinical practice especially for trainees in colposcopy.

The colposcopic phenomenon of inner border has been described as an “internal demarcation” or an “internal border” by several colposcopists [6, 7] and is defined as a sharp acetowhite demarcation within a less opaque acetowhite area.

Because the association of the colposcopic sign inner border with moderate/severe cervical intraepithelial

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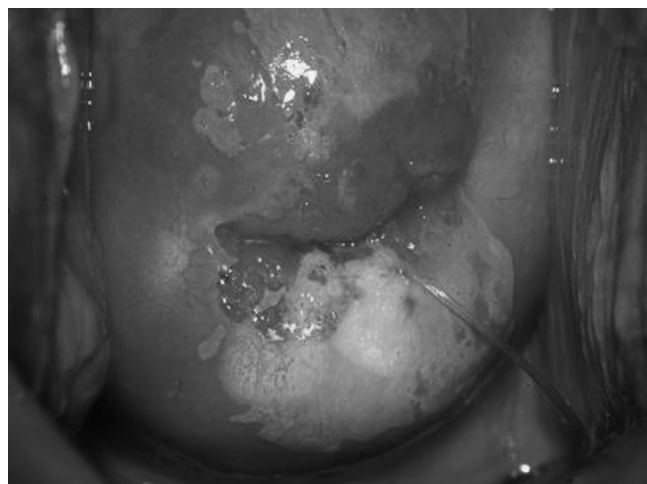


Figure 1. Colpophotograph of a 31-year-old woman with an intrauterine device. The sign of inner border can be seen between 5 and 6 o'clock. Cytology was normal, HPV testing was positive for HPV 16, and histology confirmed CIN 3.

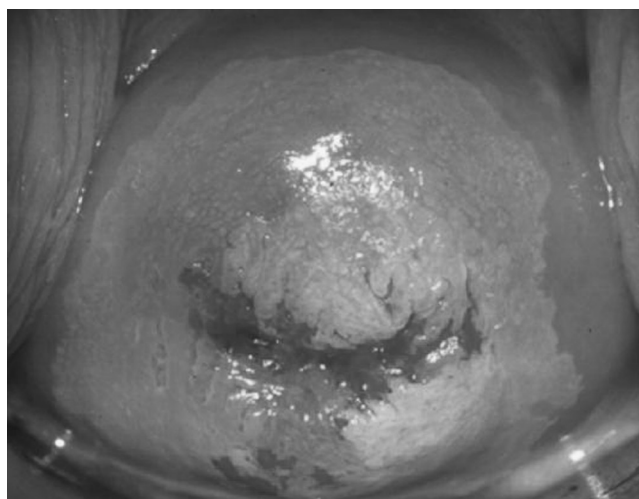


Figure 3. Colpophotograph of a 23-year-old patient. Inner border can be seen between 10 and 6 o'clock. Human papillomavirus 16 was detected in the cervical smear, and biopsy was diagnosed as CIN 3 by histology.

lesions has not been investigated systematically, it is our objective to evaluate specificity and sensitivity of this phenomenon. In addition, human papillomavirus (HPV) type and age of the patient were correlated with the presence or absence of inner border.

PROCEDURE

Two independent colposcopists reviewed the colposcopic photographs and cervicograms of 947 women (mean age, 32 years; range 15–79 years) referred to the col-

poscopy clinic of the Friedrich-Schiller-University in Jena, Germany. Patients were referred due to an abnormal cervical finding based on an atypical or abnormal cytology result and/or abnormal colposcopic finding and/or cervical smear positive for high-risk HPV. Both colposcopists evaluated retrospectively the occurrence of the colposcopic sign inner border (Figures 1–3). When inner border was diagnosed by one colposcopist only, the colposcopic photograph was reviewed by both colposcopists, and agreement was reached. Histologic evaluation was based on colposcopy-directed punch or cone biopsies, and examination was performed by a certified pathologist using CIN classification, whereas neither colposcopists nor pathologist had any information about clinical data or cytologic results of the patient.

Before biopsy, a cervical smear was taken for HPV DNA detection. Human papillomavirus detection and typing were performed using Hybrid capture I (Digene,

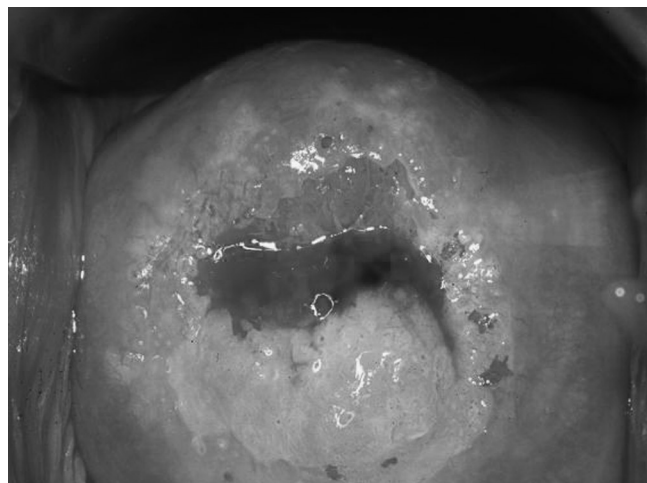


Figure 2. Colpophotograph of a 27-year-old patient. Inner border can be seen between 3 and 9 o'clock. Human papillomavirus 16 was detected in the cervical smear, and punch biopsy was diagnosed as CIN 3 by histology.

Table 1. Histologic Findings Associated With Inner Border

Colposcopy	Histology		Total
	CIN 2 or 3	CIN 1 or Less	
"inner border"	37	16	53
No "inner border"	148	494	642
	185	510	695

Association of inner border with CIN 2 or 3: $p < .001$.
CIN, cervical intraepithelial neoplasia.

Gaithersburg, MD) or GP5+/bioGP6 + polymerase chain reaction–enzyme immunoassay [8]. The statistical analysis was done by calculation of odds ratio with 95% CI and χ^2 test.

RESULTS

An atypical transformation zone was found in 73% (695/947) of all patients referred to the colposcopy clinic. The prevalence of the colposcopic sign inner border in these women was 7.6% (53/695). In women with inner border, the histologic diagnosis was CIN 1 in 10 women; in 6 women, metaplasia or inflammatory changes were diagnosed; and in 37 women with inner border, CIN 2 or 3 was proven histologically (Table 1). Thus, in 20% (37/185) of all CIN 2 or 3, inner border was seen.

The sensitivity of the colposcopic sign inner border for detection of CIN 2 or 3 was 20%, and the specificity was 97%. The positive predictive value was 70%, and the negative predictive value was 77%. In patients with inner border, the odds ratio for CIN 2 or 3 was 7.7 (95% CI = 4.2–14.3).

Of all the 185 women with CIN 2 or 3, 155 (83.2%) were positive for high-risk HPV, approximately half of them (92/155) were positive for HPV type 16 (HPV 16). There was no significant association between inner border and any high-risk HPV type (Table 2).

A significant age difference was found between women with CIN 2 or 3 and inner border compared with women with CIN 2 or 3 and without inner border (Table 3). Of women with CIN 2 or 3 and inner border, 78.4% were younger than 35 years compared with 59.5% with CIN 2 or 3 without inner border ($p < .05$).

DISCUSSION

The colposcopic phenomenon of inner border was associated with high-grade cervical lesions by several colposcopists and is integrated in various scoring systems [5, 6].

Table 2. Correlation of Inner Border With HPV

Colposcopy + Histology	HPV status		
	HPV 16 (+)	HPV 16 (-)/ HR-HPV (+)	HR-HPV (-)
Inner border + CIN 2 or 3	59.5%	27.0%	13.5%
No inner border + CIN 2 or 3	47.3%	35.1%	17.6%

HPV, human papillomavirus; CIN, cervical intraepithelial neoplasia.

Table 3. Age in Patients With CIN 2 or 3 in the Presence or Absence of Inner Border

Age in years	CIN 2 or 3 correlated with inner border	
	CIN 2 or 3 with inner border	CIN 2 or 3 without inner border
<35	29	88
>35	8	60

The use of scoring systems may improve the quality of colposcopy, but in daily practice, there is a need for practical selection criteria, which allow to find the most severe area for colposcopy-directed biopsies in a safe and quick way.

In our series, prevalence of inner border was low. This sign was found in 7.6% of all women with an atypical transformation zone referred to our colposcopy clinic due to abnormal cytology and/or suspicious colposcopic findings. Thus, inner border seems to be a rare phenomenon that resulted in a low sensitivity of 20% for detection of CIN 2 or 3. However, the positive predictive value to detect moderate and high-grade epithelial lesions was high, with a 7 out of 10 chances. Inner border is a valuable marker for high-grade CIN. On the other hand, there was no CIN 2 or 3 in 16 of 53 women with inner border, the majority (62.5%) being diagnosed with CIN 1. Further investigation is necessary to evaluate whether CIN 1 combined with inner border has a higher potential for progression.

Inner border was found most frequently in women younger than 35 years. This result is in accordance with findings of a previous study of age dependency of colposcopic signs: In women older than 34 years, CIN is colposcopically less conspicuous than in younger women. Thus, grading criteria are less pronounced and are more difficult to identify in women older than 34 years [9]. Because inner border is mostly caused by increased cellularity of CIN which leads to high opacity, this sign is less frequent in older patients. In addition, by definition, inner border appears within the transformation zone, which is especially in young women located at the ectocervix [10]. We were unable to analyze the histomorphologic basis for the colposcopic phenomenon of inner border because in most patients, punch and not cone biopsies were taken. Fields of various degrees of CIN “bordering” each other seem the most likely histopathologic explanation for the phenomenon [11]. The field with the highest opacity and highest histologic grade lies always more central toward the cervical canal.

In previous studies, it has been shown that there is no colposcopic sign specific for certain HPV types [2]. We also found in our series no significant association between HPV 16 and inner border combined with or without CIN 2 or 3, or any other high-risk HPV types and inner border combined with or without CIN 2 or 3.

Thus, we conclude that inner border is a rare but significant and highly specific marker for CIN 2 or 3 in young women.

Whenever inner border is seen, the colposcopist should direct the biopsy forceps to the most central lesion outlined by an inner border, and CIN 2 or 3 will be diagnosed in 7 of 10 patients by histology.

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