

# Risk of Occult Invasive Cervical Cancer According to Preoperative CIN Grade

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## Summary

Cervical intraepithelial neoplasia grade 2 (CIN2) and grade 3 (CIN3) are both categorized as high-grade squamous intraepithelial lesions (HSIL) in current classification systems. However, the biological behavior and the likelihood of harboring occult invasive cervical cancer may differ substantially between these two entities. Clarifying this difference is clinically important for optimizing treatment strategies and avoiding overtreatment. In this retrospective study, we evaluated patients who underwent cervical conization after biopsy-proven CIN between 2015 and 2025. Cases diagnosed as adenocarcinoma in situ (AIS) were excluded. The study cohort consisted of 35 patients with preoperative CIN1, 95 patients with CIN2, and 564 patients with CIN3. To strengthen the CIN2 cohort, an additional independent dataset of 44 patients diagnosed with CIN2 over a separate 5-year period was incorporated, resulting in a total of 139 CIN2 cases. The primary endpoint was the presence of invasive cervical cancer in the final pathological diagnosis after excisional treatment. The analysis revealed marked differences in occult invasive cancer rates according to preoperative CIN grade. Invasive cancer was identified in 1 of 35 CIN1 cases (2.9%), 0 of 139 CIN2 cases (0%), and 61 of 564 CIN3 cases (10.8%). These findings indicate that the risk of occult invasion in CIN2 is extremely low, whereas CIN3 carries a clinically significant risk of underlying invasive disease. These findings suggest that, despite being grouped under the same HSIL category, CIN2 and CIN3 have substantially different invasive potential. This distinction may have important implications for risk-adapted clinical management and treatment decision-making in cervical precancerous lesions.

## Result

738 patients who underwent cervical conization at our institution

colposcopy-directed biopsy	no	CIN1	CIN2	CIN3 severe	CIN3 CIS	1a1	1a2	1b1 or higher	total
CIN1	0	17	10	4	3	1	0	0	35
CIN2	5	13	61	48	12	0	0	0	139
CIN3 SD	4	15	35	170	81	13	0	1	319
CIN3 CIS	0	2	9	48	139	40	1	6	213
total	9	47	115	270	235	54	1	7	738

- ▶ The concordance rate between the preoperative biopsy diagnosis and the final pathological diagnosis after cervical conization was 69.9% (516/738).
- ▶ The rate of occult invasive cancer detected after cervical conization was 1/35 (2.9%) in patients with a preoperative diagnosis of CIN1, 0/139 (0%) in those with CIN2, and 61/532 (11.5%) in those with CIN3.
- ▶ The rate of pathological upstaging after cervical conization was 18/35 (51.4%) in patients with a preoperative diagnosis of CIN1, 60/139 (43.2%) in those with CIN2, and 61/532 (11.5%) in those with CIN3.

Analysis of Cases Preoperatively Diagnosed with CIN2 Over the Most Recent Five Years (2020–2025)

age	smear	biopsy	Conization	HPV	cut end	recurrence
29	HSIL	CIN2	CIN3	+	-	+
31	ASC-US	CIN2	CIN2	+	+	+
59	HSIL	CIN2	CIN3	+	+	+
53	ASC-H	CIN2	CIN1	-	-	-
35	LSIL	CIN2	CIN1	-	-	-
38	HSIL	CIN2	CIN2	+	-	-
38	HSIL	CIN2	CIN1	-	-	-
45	ASC-H	CIN2	CIN2	+	+	-
40	LSIL	CIN2	CIN2	+	-	-
47	LSIL	CIN2	no SIL	-	-	-
41	ASC-H	CIN2	CIN3	-	-	-
54	HSIL	CIN2	CIN3	+	-	-
23	ASC-H	CIN2	CIN1	+	-	-
41	HSIL	CIN2	CIN3	+	+	-
49	ASC-H	CIN2	CIN3	+	-	-
44	LSIL	CIN2	CIN3	+	-	-
44	ASC-H	CIN2	CIN2	-	-	-
46	HSIL	CIN2	CIN2	-	-	-
50	LSIL	CIN2	no SIL	-	-	-
51	ASC-H	CIN2	CIN3	+	-	-
44	ASC-H	CIN2	CIN3	+	-	-
39	ASC-H	CIN2	CIN3	+	-	-
45	HSIL	CIN2	CIN3	-	-	-
40	HSIL	CIN2	CIN3	+	-	-
49	HSIL	CIN2	no SIL	-	-	-
48	ASC-US	CIN2	CIN3	-	-	-

- ▶ Among preoperative CIN2 cases, the diagnostic concordance with post-conization pathology was low (23.1%), while 46.2% were upgraded to CIN3, indicating the heterogeneous nature of CIN2 and the potential underestimation by biopsy.
- ▶ HPV positivity was more frequent in the CIN3-upgraded group than in the non-CIN3 group (83.3% vs. 35.7%), suggesting that HPV positivity may be a predictive factor for higher-grade lesions.
- ▶ All recurrent cases were HPV-positive, and most showed positive margins or CIN3 pathology, suggesting that these factors may be associated with recurrence risk.

CIN2 lesions showed marked pathological heterogeneity, with a low concordance rate between biopsy and post-conization pathology. Nearly half of the cases were upgraded to CIN3 after conization, suggesting the potential underestimation of lesion severity by biopsy alone. In particular, HPV-positive cases and those with high-grade cytology (HSIL/ASC-H) were more likely to harbor higher-grade lesions, indicating their potential value for risk stratification.

## Review of the Literature

- ▶ Previous studies reported concordance rates between punch biopsy and conization pathology of approximately 50–70%. Our concordance rate of 69.9% was consistent with these findings.
- ▶ Several reports have suggested substantial heterogeneity of CIN2 lesions, with frequent upgrading after excision. In our cohort, 43.2% of CIN2 cases were upgraded to CIN3 or higher.
- ▶ Few studies have directly compared occult invasive cancer risk across CIN grades. Our findings demonstrated no invasive cancer in CIN2, whereas CIN3 showed a clinically significant risk.
- ▶ The association between CIN2 cases and HPV was 94.1% in the CIN3 group and 75% in the non-CIN3 group, indicating a tendency for a higher rate of CIN3 in HPV-positive cases.
- ▶ CIN2 lesions exhibit high heterogeneity, suggesting that a certain number of cases are underestimated by biopsy.

## Conclusion

Although classified as the same HSIL category, CIN2 showed no occult invasive cancer but frequent upgrade to CIN3 after conization, indicating marked biological heterogeneity. Risk-adapted management may help avoid overtreatment while identifying higher-risk CIN2 lesions.

COI Disclosure Information  
**Lead Presenter** : Haruka Wada  
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