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Diagnostic Accuracy of Colposcopy in Cervical Intraepithelial Neoplasia and Its Influencing Factors: A Retrospective Study

Yehong HUANG, Lujuan YUAN, Bili WU*

The Second Affiliated Hospital, School of Medicine, The Chinese University of Hong Kong, Shenzhen & Longgang District People's Hospital of Shenzhen, Guangdong, 518172, P.R. China.Corresponding Author

Abstract

Objective: To evaluate the diagnostic accuracy of colposcopy for cervical intraepithelial neoplasia (CIN) and identify influencing factors. **Methods**: A retrospective analysis of 493 cases where colposcopy and biopsy were performed, with pathological confirmation as the gold standard. Sensitivity, specificity, positive and negative predictive values of colposcopy were assessed, along with concordance between colposcopy and biopsy. Factors like HPV types, TCT results, transformation zone types, and lesion size were examined for their impact on accuracy. Logistic regression was used to identify key influencing factors. **Results**: Colposcopy showed a sensitivity of 78.11%, specificity of 81.06%, positive predictive value of 91.86%, and negative predictive value of 57.53%, with a Kappa value of 0.525 ($P < 0.001$). The agreement between colposcopy and biopsy was 70.79%. HPV subtype, transformation zone type, age, and lesion size influenced diagnostic accuracy. Logistic regression identified types II and III transformation zones as independent risk factors for diagnostic errors. **Conclusion**: Colposcopy has limitations in diagnosing CIN. Clinical judgment, supplemented by random biopsy, is crucial to avoid omissions, particularly in patients with unsatisfactory colposcopy results.

Keywords cervical intraepithelial neoplasia; colposcopy diagnosis; cervical cancer

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Cervical cancer is a common malignant tumor in women that poses a serious threat to women's health. Statistically, approximately 600,000 new cases of cervical cancer are diagnosed globally each year, representing 5% of all new cancer diagnoses[1]. In 2020, China recorded about 120,000 new cases, constituting one-fifth of the global total[2,3].

The clinical signs of precancerous cervical lesions and early-stage cervical cancer are subtle and typically detectable only through screening. Currently, HPV testing and/or cytology form the cornerstone of cervical cancer screening. Colposcopy is used to further diagnose and pinpoint lesions, with biopsy under colposcopic guidance providing a definitive diagnosis or exclusion of cervical cancer and precancerous conditions, thus guiding treatment and follow-up care.

Despite its significance in cervical cancer prevention and treatment, recent studies have highlighted colposcopy's suboptimal accuracy in identifying precancerous and early-stage cervical cancer. These studies note the risks of both missed and erroneous diagnoses[4-6]. This study assesses the diagnostic accuracy of colposcopy for cervical intraepithelial neoplasia (CIN) and explores factors associated with improving its clinical utility.

1 Materials and Methods

1.1 General Information

Colposcopic examinations were conducted in the colposcopy room of Longgang District People's Hospital, Shenzhen, from January 1, 2022, to December 31, 2022. The initial assessments were deemed "satisfactory." Biopsies were performed on lesions identified by colposcopy or through random biopsies after informed consent was obtained from patients with clinical indications but no colposcopic abnormalities.

1.1.1 Inclusion criteria

1. Women aged 25-65 years with a history of coitus.
2. Cytologic screening results and HPV-DNA test results available prior to colposcopy.
3. Pathological diagnosis results of cervical biopsy guided by colposcopy.

1.1.2 Exclusion criteria

1. Patients with a history of cervical surgery or hysterectomy.
2. Patients with a history of treatment for cervical precancerous lesions.
3. Non-cervical squamous epithelial lesions or cervical cancer cases.

1.2 Colposcopy and Biopsy

Colposcopies were conducted by a specialist and reviewed by two or more associate director physicians at our hospital using an electronic colposcope (Leisegang Feinemchanik-OP; Leisegang

3ML/F.F.P.). Observations focused on changes in the cervical epithelium and blood vessels at varying magnifications, particularly in the transformation area. If no suspicious lesions were observed under direct colposcopic view and clinical indications were present, biopsies were randomly taken from the transformation area at the 3, 6, 9, and 12 o'clock positions. If the transformation area was not fully exposed, or if lesions extended into the cervical canal, endocervical curettage (ECC) was performed. Colposcopy diagnoses were classified as: normal cervix, low-grade intraepithelial neoplasia, high-grade intraepithelial neoplasia, and suspicious carcinomatosis[7].

1.3 Pathological Examination

All cervical tissue specimens underwent pathological examination by our hospital's qualified pathologists. Diagnoses were reviewed and finalized by two senior pathologists. Following the WHO 2014 classification of female reproductive tumors, a secondary classification system was recommended, distinguishing between LSIL and HSIL. LSIL corresponds to CIN1, while HSIL typically includes most cases of CIN2 and CIN3. CIN2 was triaged using immunohistochemical P16 staining; negative results were treated as LSIL, and positive results were managed as HSIL.

1.4 Statistical Approach

SPSS 22.0 software was utilized for data coding and statistical analysis. A Chi-square test was used to analyze the data, and multivariate logistic regression was employed to identify statistically significant influencing factors, isolating independent risk factors that impacted the accuracy of colposcopy diagnoses. The threshold for statistical significance was set at $\alpha = 0.05$, with $P < 0.05$ deemed significant.

2 Results

2.1 Accuracy of Colposcopy in Diagnosing CIN

This study included 493 patients with a median age of 37 years (range: 25-65 years). Of these, 426 patients (86.41%) were under 50 years old, and 67 patients (13.59%) were over 50. There were 63 cases (12.78%) of high-grade cervical lesions and 430 cases (87.22%) of non-high-grade lesions. HPV16/18 was positive in 241 cases (48.88%), and non-HPV16/18 was positive in 252 cases (51.12%).

Regarding the transformation zone type, there were 325 cases (65.93%) of type I, 117 cases (23.73%) of type II, and 51 cases (10.34%) of type III. Cervical lesion area was less than 1/2 in 225 cases (45.64%) and greater than or equal to 1/2 in 268 cases (54.36%).

Diagnostically, 186 cases (37.73%) had a normal cervix (including inflammation), 242 cases (49.09%) had low-grade lesions, and 65 cases (13.18%) had high-grade lesions. The pathological diagnoses were as follows: normal cervix (including inflammation) in 132 cases (26.67%), CIN1 in 269 cases (54.56%), and CIN2 in 92 cases (18.66%).

Table 1 Basic characteristics of the research objects

variate	Number of patients n (%)
Total number of patients	**N=493**
age	
＜50，n（%）	426（86.41）
≥50，n（%）	67（13.59）
TCT results	
High grade lesion，n（%）	63(12.78)
Non-high grade lesions，n（%）	430(87.22)
HPV-DNA results	
HPV16/18，n（%）	241（48.88）
Non-HPV16/18，n（%）	252（51.12）
Transformation zone type	
Type 1 transformation zone，n（%）	325（65.92）
Type 2 transformation zone，n（%）	117（23.73）
Type 3 transformation zone，n（%）	51（10.34）
Cervical lesion area	
＜1/2	225（45.64）
≥1/2	268（54.36）
Diagnostic results of colposcopy	
Normal cervix， n（%）	186（37.73）
Low grade lesion，n（%）	242（49.09）
High grade lesion，n（%）	65（13.18）
Pathological diagnosis results	
Normal cervix， n（%）	132 （26.77）
Low grade lesion， n（%）	269（54.56）
High grade lesion， n（%）	92（18.66）

2.1.1 Sensitivity and Specificity of Colposcopy Using the pathological diagnosis as the gold standard, colposcopy achieved a sensitivity of 78.11%, specificity of 81.06%, positive predictive value of 91.86%, and negative predictive value of 57.53% (Kappa value 0.525, P < 0.001). (Table 2).

Table 2 The specificity and sensitivity of colposcopy images in the diagnosis of CIN n (%)

Diagnosis by colposcopy	Pathological diagnosis (standard)		total	
	positive	negative		
positive	282	25	307	positive prediction rate 91.86%
negative	79	107	186	negative prediction rate 57.53%
total	361	132	493	
	sensitivity 78.11%	specificity 81.06%		

*Kappa value 0.525，$P<0.001$

2.1.1 Concordance Between Colposcopy and Pathological Diagnosis

The overall concordance rate between colposcopy and pathological biopsy diagnosis was 70.79% (349/493; see Table 3).

Table 3 Comparison of colposcopy diagnosis and pathological diagnosis (n)

Diagnosis by colposcopy	pathological diagnosis			total
	Normal cervix	Low grade lesion	High grade lesion	
Normal cervix	107	65	14	186
Low grade lesion	16	195	31	242
High grade lesion	9	9	47	65
total	132	269	92	493

2.2 Univariate Analysis Affecting Diagnostic Accuracy of Colposcopy Factors such as age, HPV16/18 status, type of cervical transformation zone, and cervical lesion area were identified as influencing the diagnostic accuracy of colposcopy (Table 4).

2.2 Multivariate Logistic Regression Analysis on Diagnostic Concordance of Colposcopy

A multivariate logistic regression analysis (full model) was conducted with the dependent variable (0 = concordance, 1 = no concordance), using significant variables ($P < 0.05$) from the univariate analysis as independent variables. The analysis identified type II (OR = 6.906) and type III (OR = 16.653) transformation zones as independent risk factors affecting the accuracy of colposcopic diagnosis of cervical epithelial neoplasia (see Table 5).

3 Discussion

Cervical cancer is a common gynecological malignancy with a well-understood etiology and progression, making prevention feasible. Effective screening for detecting precancerous lesions and ensuring timely interventions is essential for preventing cervical cancer[8]. Currently, cervical cytology (TCT) and HPV testing are the primary screening methods[9-11]. Positive screening results necessitate colposcopy and colposcopically guided cervical biopsies to confirm diagnoses, guide treatment, and manage cases, which are crucial for preventing and treating cervical cancer[12]. Thus, improving the accuracy of colposcopy and biopsy remains a key focus of ongoing research and development.

3.1 Role of Colposcopy in Diagnosing CIN

Colposcopy is a crucial intermediary between screening and diagnosis in cervical cancer management. Key metrics such as specificity, sensitivity, positive predictive value, negative predictive

Table 4 Univariate analysis affecting diagnostic accuracy of colposcopy

risk factor	number of cases(n)	Consistency(n)	inconformity(n)	χ^2value	*P* value
age					
≥50	67	37	30	9.087	0.003
＜50	426	312	114		
HPV16/18					
yes	241	185	56	8.133	0.004
no	252	164	88		
Cytological test					
High grade lesion	63	43	20	0.225	0.635
Non-highgrade lesion	430	306	124		
Transformation zone type					
Type 1	325	280	45	115.430	＜0.001
Type 2	117	55	62		
Type 3	51	14	37		
Cervical lesion area					
＜1/2	225	171	54	5.431	0.020
≥1/2	268	178	90		

value, and the concordance rate between colposcopic and biopsy diagnoses, as well as the risks of over-diagnosis and under-diagnosis, are central concerns in colposcopy practice.

In this study, the diagnostic concordance rate of colposcopy was 70.79%, significantly higher than the approximately 50% accuracy rate reported for direct visual biopsy in the literature[13]. For instance, in a study by Hopman et al., 23 experienced colposcopists provided presumptive diagnoses based on colposcopic images and biopsy site selection, achieving a concordance rate of 66.7% between colposcopy and pathology diagnoses[14]. Similarly, Benedet et al. reported a 50% concordance rate in a multi-center study involving 84,244 patients across 24 colposcopy centers[15].

Colposcopy improves diagnostic accuracy by detecting small lesions that are invisible to the naked eye. The magnified view and enhanced visualization of the cervical squamo-columnar junction, transformation zone, and iodine-stained morphological changes contribute to this improvement. In this study, colposcopy demonstrated a sensitivity of 78.11%, specificity of 81.06%, positive predictive value of 91.86%, and negative predictive value of 57.53%. These results suggest that colposcopy is highly specific and provides a strong positive predictive value, allowing

Table 5 Multivariate logistic regression analysis of factors affecting the diagnostic accuracy of colposcopy

influence factor		*β*	S.E	Wald	*P* value	*OR* value	*OR*（95%*CI*）	
HPV16/18	yes	Reference				1.000		
	no	-0.187	0.232	0.652	0.420	0.829	0.526	1.307
Zone of transformation	type I	Reference				1.000		
	type II	1.932	0.253	58.235	＜0.001	6.906	4.204	11.344
	type III	2.813	0.381	54.472	＜0.001	16.653	7.891	35.145
age	＜50	Reference				1.000		
	≥50	-0.245	0.332	0.544	0.461	0.783	0.408	1.501
Cervical lesion area	＜1/2	Reference				1.000		
	≥1/2	0.289	0.234	1.526	0.217	1.335	0.844	2.110
constant term		-1.907	0.511	13.921	＜0.001	0.148		

effective triage of patients and facilitating early interventions for those diagnosed with cervical intraepithelial neoplasia (CIN).

However, the low negative predictive value of 57.53% highlights a risk of missed or underdiagnosed cases, particularly for low-grade cervical squamous intraepithelial neoplasia. Such lesions often present with subtle or indistinct features, making them difficult to detect and prone to misdiagnosis.

Clinicians must meticulously observe colposcopic images, especially for patients with negative TCT and HPV results or those who lack typical colposcopic features. By combining a thorough analysis of images with patient history and current health status, clinicians can improve diagnostic accuracy and continue to build their diagnostic experience.

3.2 Factors Influencing the Diagnostic Accuracy of Colposcopy

This study analyzed several factors that may influence colposcopy outcomes, including HPV detection, cytology, transformation zone type, patient age, and cervical lesion area. The findings showed that the detection of specific HPV subtypes (HPV16/18 positive and non-HPV16/18 positive), transformation zone type, patient age, and cervical lesion area significantly affected the accuracy of colposcopy. However, thin-layer liquid-based cytology results did not significantly impact colposcopy's accuracy in diagnosing CIN.

3.2.1 Effect of HPV Subtypes on Colposcopy Accuracy

In this study, 241 cases (48.88%) were in the high-risk HPV16/18 positive group, while 252 cases were in the non-HPV16/18 high-risk group. The diagnostic coincidence rates were 76.76% (185/241) for the HPV16/18 positive group and 65.08% (164/252) for the non-HPV16/18 group.

A significant difference was observed between the two groups ($\chi^2 = 8.113$, $P = 0.004$), confirming that the diagnostic accuracy was significantly higher in the HPV16/18 positive group.

Research by Nam et al.[16] suggests that colposcopic lesion size varies with different HPV types, with HPV16 being associated with larger lesions, making them easier to detect. Similarly, Stoler et al.[17] found that HPV16/18 infection enhances colposcopy accuracy, likely due to the cytopathic effects of E6 and E7 proteins produced by HPV16/18. These proteins degrade P53 and Rb, leading to chromosome mutations, uncontrolled cell proliferation, and cancer. The cytopathic effects are more easily identifiable during colposcopy, improving diagnostic accuracy.

Additionally, clinicians may subconsciously focus more on HPV16/18 positive cases, further increasing detection rates in this group. Therefore, it is essential to remain vigilant for missed or underdiagnosed cases in patients with non-HPV16/18 positive results.

3.2.2 Effect of Transformation Zone on Diagnostic Accuracy of Colposcopy

Cervical precancerous lesions and cervical cancer commonly occur in the cervical transformation zone. Lesions in type I transformation zones are fully exposed, while those in type II zones can be exposed with instrumental assistance. In contrast, lesions in type III zones may extend into the cervical canal, with some or all of the lesions not clearly visualized. The visibility of lesions directly impacts the examination's accuracy—less exposed lesions are more likely to be missed by colposcopy.

In this study, the coincidence rates of colposcopy with cervical biopsy pathology in type I, II, and III transformation zones were 86.15%, 47.01%, and 27.45%, respectively. The highest rate was observed in type I transformation zones at 86.15%, while the rates for types II and III were below 50% (47.01% and 27.45%). Significant differences in diagnostic accuracy were observed across the various transformation zone types, and these differences were statistically significant ($P < 0.001$).

Research by Guo Shuang[18] indicated concordance rates of 78.73%, 71.52%, and 57.27% for types I, II, and III transformation zones, respectively, with type III showing the lowest accuracy. Similarly, He Yu[19] reported concordance rates of 72.46%, 71.3%, and 43.5% for types I, II, and III, highlighting that colposcopy accuracy decreases as the visibility of the transformation zone diminishes.

The lower diagnostic accuracy in type III zones aligns with the findings of Guo Shuang and He Yu, suggesting that reduced visibility in the transformation zone increases the difficulty of performing accurate colposcopy and cervical biopsy, potentially leading to missed diagnoses. Consequently, endocervical curettage (ECC) is essential as an adjunctive diagnostic tool for patients with type II and III transformation zones, where lesions may extend into or be situated entirely within the cervical canal.

3.2.3 Effect of Age on Diagnostic Accuracy of Colposcopy

The average age of menopause is around 50 years. In this study, patients were divided into two groups: those under 50 years and those 50 years or older. The diagnostic concordance rates

of colposcopy were 73.24% and 55.22%, respectively, with a statistically significant difference ($P = 0.003$). This finding is consistent with other research, such as Costa et al.[20], which suggests that the rate of missed diagnoses in colposcopy is positively correlated with age, particularly in patients over 50, due to reduced visibility of the squamo-columnar junction.

Post-menopause, the cervix tends to shrink and shorten, causing the epithelium at the squamo-columnar junction to recede into the cervical canal, leading to partial or complete obscuration of the transformation zone. Additionally, as age increases, ovarian function declines, estrogen levels decrease, and vaginal tissues atrophy. These changes make unexposed areas harder to visualize, complicating colposcopy and reducing diagnostic accuracy.

3.2.4 Effect of Cervical Lesion Area on Diagnostic Accuracy of Colposcopy

This study analyzed the impact of cervical lesion size on colposcopy accuracy. Statistical analysis comparing lesions with an area $\geq$1/2 of the cervix to those $<$1/2 revealed a statistically significant difference in diagnostic accuracy ($P = 0.020$). Previous studies, such as Pretorius et al.[21], have similarly indicated that colposcopy accuracy correlates with the size of the lesion.

Smaller lesions often present fewer distinctive features under colposcopy, making it challenging to accurately biopsy the affected tissue and increasing the likelihood of a missed diagnosis. This underscores the importance of thorough imaging reviews in clinical practice, even when lesions are small or undetected. Incorporating TCT and HPV testing, along with multi-point random biopsies, may improve the accuracy of pathological diagnoses.

4 Limitations

Most prior studies assessing the accuracy of colposcopy have used pathological outcomes from cervical conization specimens as the benchmark for evaluating colposcopy-directed cervical biopsy in diagnosing precancerous lesions. In many studies, the interval between colposcopy-guided biopsy and cervical conization is not well-documented, potentially introducing verification bias. While this study successfully addresses this issue, the literature on this topic remains limited. Although the research perspective is innovative, the methodology may still introduce some bias in the findings.

5 Conclusion

In conclusion, colposcopy plays a crucial role in preventing and treating cervical cancer, but it has limitations. To minimize missed diagnoses, it is essential to mitigate inadequate diagnostic assessments and perform random biopsies when necessary. Effective colposcopy examinations should consider factors such as HPV subtypes, transformation zone types, patient age, and other clinical conditions to improve diagnostic accuracy.

6 Ethics Statement

This study was approved by the Institutional Ethics Committee of Longgang District People's Hospital of Shenzhen (Ethics Approval Number: 2022093). The data were derived from previous clinical diagnoses and treatments as part of retrospective studies. Medical records and specimens explicitly refused by patients were excluded, and patients were not required to provide written informed consent for data release.

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