Clinical Characteristics of High-grade Cervical Lesions and Diagnostic Value of Endocervical Curettage in Women Under 30 Years of Age: A Study [Postprint]

Authors: Jing Chen, Wang Chaoxing, Qian Ruiya, Yong Liu, Ruiya Qian, Yong Liu

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Abstract

Background Since the domestic approval and market launch of the human papillomavirus (HPV) vaccine in 2017, some young women have completed HPV vaccination. However, it remains unclear whether HPV vaccination affects the detection of cervical high-grade squamous intraepithelial lesion (HSIL) in young women and the diagnostic value of endocervical curettage (ECC) during colposcopy. Objective To investigate the clinical characteristics of cervical HSIL detection in women under 30 years of age and to evaluate the value of

Full Text

Clinical Characteristics of High-Grade Squamous Intraepithelial Lesion and Diagnostic Value of Endocervical Curettage in Women Aged Under 30

CHEN Jing[1], **WANG Chaoxing**[2], **QIAN Ruiya**[1*], **LIU Yong**[1*]

[1]Department of Gynecology, Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Beijing 100026, China
[2]Department of Gynecology, Xingyi People' s Hospital, Xingyi 562400, Guizhou Province, China

*Corresponding authors: QIAN Ruiya, Chief Physician; E-mail: qry126@ccmu.edu.cn; LIU Yong, Chief Physician; E-mail: youngleu@ccmu.edu.cn

Abstract

Background: Since the approval of human papillomavirus (HPV) vaccines in China in 2017, an increasing number of young women have completed HPV vaccination. However, whether HPV vaccination affects the detection of high-grade squamous intraepithelial lesion (HSIL) in young women, and the diagnostic value of endocervical curettage (ECC) under colposcopy, remain unclear.

Objective: To investigate the clinical characteristics of HSIL detection in women under 30 years of age and to explore the value of ECC under colposcopy in detecting HSIL.

Methods: A retrospective analysis was conducted on 427 patients under 30 years of age who underwent colposcopy-guided cervical biopsy and/or ECC at the Colposcopy Clinic of Beijing Obstetrics and Gynecology Hospital, Capital Medical University, between June 2021 and June 2022. All patients underwent cytology and high-risk HPV testing and were referred for colposcopy due to abnormal screening results. Using pathological results as the diagnostic gold standard, cervical intraepithelial lesions were diagnosed according to the WHO 2014 two-tier classification system for HSIL and low-grade squamous intraepithelial lesion (LSIL). The HSIL detection rate was defined as the number of cases with HSIL detected by cervical biopsy and/or ECC divided by the total number of cases. The biopsy detection rate was defined as the number of cases with HSIL detected by cervical biopsy divided by the total number of cases. The ECC detection rate was defined as the number of cases with HSIL detected by ECC divided by the total number of cases. The additional HSIL detection rate of ECC was defined as the number of cases where HSIL was detected by ECC but not found in cervical biopsy divided by the total number of cases, to evaluate the diagnostic value of ECC. Multivariate Logistic regression analysis was used to explore factors influencing HSIL detection in women under 30.

Results: Among the 427 patients, 155 (36.3%) underwent cervical multi-point biopsy only, detecting HSIL in 19 cases; 272 (63.7%) underwent both multi-point biopsy and ECC, detecting HSIL in 76 cases, of which 2 were additionally detected by ECC alone. The overall HSIL detection rate was 22.2% (95/427), the biopsy detection rate was 21.8% (93/427), the ECC detection rate was 1.6% (7/427), and the additional HSIL detection rate by ECC was 0.5% (2/427). Multivariate Logistic regression analysis showed that cytological HSIL (OR=7.274, 95%CI=1.901-27.828) and HPV 16/18 positivity (OR=10.833, 95%CI=1.317-89.135) were risk factors for HSIL detection ($P<0.05$).

Conclusion: In women under 30 years of age, cytological HSIL and HPV 16/18 infection are independent risk factors for HSIL detection. Younger age group (<25 years), colposcopic transformation zone type, and HPV vaccination are not relevant influencing factors. ECC has limited additional value for detecting HSIL in this age group. It is recommended that ECC may be omitted in women under 30 who do not have these two independent risk factors, regardless of transformation zone visibility and vaccination status.

Keywords: High-grade squamous intraepithelial lesion; Colposcopy; Endocervical curettage; Human papillomavirus vaccines; Women under 30 years of age

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Current research has confirmed that persistent infection with high-risk human papillomavirus (HPV) can lead to cervical precancerous lesions and progression to cervical cancer [1-3]. Women under 30 years of age have frequent sexual activity and high HPV infection rates, yet cervical cancer incidence remains low in this demographic. Through years of exploration, combining domestic clinical experience [4-5] with screening guidelines from European and American countries [6-7], China currently recommends initiating cervical cancer screening at age 25, with high-risk HPV testing as the preferred primary screening method [8]. However, due to various factors, women under 25 are also actively seeking cervical cancer screening, leading to an increased number of screened women in this younger age group.

Furthermore, since the approval of HPV vaccines in China in 2017, some women under 30 have completed vaccination. Whether vaccination affects the detection of high-grade squamous intraepithelial lesion (HSIL) under colposcopy in this population, and the significance of endocervical curettage (ECC) for HSIL detection in this group, remain unclear. This study retrospectively analyzed the clinical and pathological data of women under 30 years of age, exploring the characteristics and influencing factors of HSIL detection in this age group, as well as the significance of ECC under colposcopy, to provide evidence for clinical practice.

1 Materials and Methods

1.1 Study Subjects

A retrospective review was conducted of 455 patients under 30 years of age who underwent colposcopy-guided cervical biopsy and/or ECC at the Colposcopy Clinic of the Gynecology Outpatient Department, Beijing Obstetrics and Gynecology Hospital, Capital Medical University, between June 2021 and June 2022. After excluding cases with incomplete clinical data, pregnancy, or lactation, 427 cases were included. Ages ranged from 20 to 29 years, with a mean age of (26.6$\pm$2.2) years. All cases underwent cytology and high-risk HPV testing. According to the *Guidelines for Comprehensive Prevention and Control of Cervical Cancer* (2nd edition) [9], patients with abnormal screening results indicating referral for colposcopy underwent colposcopic examination.

This study was approved by the Ethics Review Committee of Beijing Obstetrics and Gynecology Hospital, Capital Medical University (Approval No.: 2024-KY-080-01) and conducted in accordance with the principles of the Declaration of Helsinki. As this was a retrospective observational study using anonymized data, the requirement for written informed consent was waived.

1.2 Methods

1.2.1 Cytological Preparation and Diagnosis: Cervical cells were collected from the endocervix and ectocervix using a cervical brush, smeared onto glass slides and fixed, or prepared using liquid-based cytology techniques with appropriate instrumentation and standardized protocols. Microscopic examination was performed according to the 2014 Bethesda System [10], with cytology results classified into nine categories: negative for intraepithelial lesion and malignancy (NILM), atypical squamous cells of undetermined significance (ASC-US), low-grade squamous intraepithelial lesion (LSIL), atypical squamous cells cannot exclude high-grade lesion (ASC-H), high-grade squamous intraepithelial lesion (HSIL), squamous cell carcinoma (SCC), atypical glandular cells (AGC), adenocarcinoma in situ (AIS), and adenocarcinoma. For statistical analysis, NILM, ASC-US, and LSIL were grouped as low-grade abnormalities (LSIL), while ASC-H, HSIL, SCC, AGC, AIS, and adenocarcinoma were grouped as high-grade abnormalities (HSIL).

1.2.2 High-risk HPV Testing: PCR technology was used to detect 14 high-risk HPV genotypes, including 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68. HPV status was categorized as HPV 16/18 positive, non-16/18 high-risk HPV positive (HPV-HR), or HPV negative.

1.2.3 HPV Vaccination Status: Receipt of one or more doses of any HPV vaccine type was defined as vaccinated.

1.2.4 Colposcopic Examination: Indications for colposcopy included: normal cytology with HPV 16/18 positivity; persistent HPV-HR infection for more than one year without HPV 16/18; ASC-US cytology with positive HPV; or cytology showing LSIL or higher. All colposcopic examinations followed standard procedures, with assessment of transformation zone type and presence of suspicious lesions using 2011 International Federation of Cervical Pathology and Colposcopy (IFCPC) terminology [11]. Two to four biopsies were taken from abnormal areas, and ECC was performed when indicated (for women under 30 years, ECC was indicated when colposcopic findings were inconsistent with HSIL referral cytology, when the examination was unsatisfactory, or when cytology showed AGC or AIS). The curette was inserted into the cervical canal, gentle pressure applied, and the canal scraped circumferentially to obtain endocervical tissue. Care was taken to avoid extending sampling beyond the external os to minimize contamination with ectocervical tissue.

1.2.5 Diagnostic Criteria: All specimens were submitted separately. Cervical intraepithelial lesions were diagnosed according to the WHO 2014 two-tier classification system for HSIL and LSIL [12]. The HSIL detection rate was defined as cases detected by cervical biopsy and/or ECC. The biopsy detection rate was defined as cases detected by cervical biopsy. The ECC detection rate was defined as cases detected by ECC. The additional HSIL detection rate of ECC was defined as cases where HSIL was detected by ECC but not found in cervical biopsy.

1.3 Statistical Analysis

SPSS 27.0 software was used for statistical analysis. Categorical data were expressed as relative numbers (percentages), with intergroup comparisons using χ^2 tests. Multivariate Logistic regression analysis was used to explore influencing factors for HSIL detection. A significance level of $\alpha = 0.05$ was used.

2 Results

2.1 General Characteristics

This study included 427 patients, of whom 68 (15.9%) were under 25 years and 359 (84.1%) were 25-29 years; 11 (2.6%) had cytological HSIL and 416 (97.4%) had LSIL; 220 (51.5%) were HPV 16/18 positive, 186 (43.6%) were HPV-HR positive, and 21 (4.9%) were HPV negative; 148 (34.7%) had received at least one dose of HPV vaccine and 279 (65.3%) were unvaccinated; 223 (52.2%) had visible transformation zones (Type 1) and 204 (47.8%) had Type 2/3 transformation zones; 155 (36.3%) underwent cervical multi-point biopsy only, detecting HSIL in 19 cases; 272 (63.7%) underwent both multi-point biopsy and ECC, detecting HSIL in 76 cases (including 2 additional cases detected by ECC only), and detecting LSIL or lower in 196 cases. The overall HSIL detection rate was 22.2% (95/427), the biopsy detection rate was 21.8% (93/427), the ECC detection rate was 1.6% (7/427), and the additional ECC detection rate was 0.5% (2/427).

2.2 Univariate Analysis of HSIL Detection in Women Under 30

No significant differences were found in HSIL detection rates among different age groups, colposcopic transformation zones, or vaccination status ($P > 0.05$). Significant differences were found in HSIL detection rates among different cytological results and HPV status groups ($P < 0.05$), as shown in Table 1 .

2.3 Multivariate Logistic Regression Analysis of HSIL Detection in Women Under 30

Using histopathological results as the dependent variable (LSIL=0, HSIL=1) and cytological results (LSIL=0, HSIL=1) and HPV status (HPV negative=0, HPV-HR=1, HPV 16/18 positive=2) as independent variables, multivariate Logistic regression analysis showed that cytological HSIL and HPV 16/18 positivity were risk factors for HSIL detection ($P < 0.05$), as shown in Table 2 .

2.4 Detection of HSIL by ECC Under Colposcopy

This study included 272 cases undergoing cervical multi-point biopsy plus ECC. HSIL was detected in the cervical canal in 7 cases (2.6%), with 2 cases (0.7%) additionally diagnosed by ECC alone, as shown in Table 3 .

Discussion

There has been ongoing controversy regarding the optimal starting age for cervical cancer screening. Different countries have variations in HPV vaccination coverage, peak age of cervical cancer incidence, screening methods and capacity, and government funding for prevention programs, leading to recommended screening initiation ages ranging from 20-30 years globally [13-14]. This study comprehensively examined screening age, cytology, HPV screening results, HPV vaccination status, and colposcopic findings to investigate the diagnostic significance of colposcopy-guided multi-point biopsy and ECC for HSIL in women under 30, as well as the clinical characteristics associated with HSIL diagnosis in this age group.

Among the 427 women undergoing colposcopy in this study, 95 were ultimately diagnosed with HSIL by histology, accounting for approximately 22.2%, slightly higher than the 17.75% HSIL detection rate reported in previous studies for women under 30 referred for colposcopy [15]. Of these, 88 cases (92.6%) were detected by cervical multi-point biopsy, 5 cases (5.3%) by both cervical biopsy and ECC, and only 2 cases (2.1%) by ECC alone. The incidence of endocervical lesions in women under 30 was only 1.6% (7/427), while the additional HSIL detection rate by ECC was merely 0.5% (2/427). Therefore, this study suggests that ECC has limited additional value for detecting HSIL in women under 30. MI Lan et al. [16] found no HSIL detected by ECC in women under 30, concluding that ECC has limited significance for this age group, which is consistent with our findings. LIU et al. [17] reported detecting HSIL in 10 of 99 women aged 21-29 who underwent ECC. PRETORIUS et al. [18] suggested that ECC should be performed in women 25 years and older with any abnormal cytology and/or HPV-HR positivity. Currently, as HPV vaccination reduces high-risk HPV infection rates in women under 30, the HSIL detection rate by ECC may further decrease in the future for patients under 30 with low-grade cytological abnormalities.

Cytological results have predictive value for HSIL detection. This study indicated that when cytology showed HSIL, 63.6% of patients had histologically detectable HSIL, whereas when cytology showed LSIL, the HSIL detection rate was only 21.2%. Cytological screening demonstrates high specificity but low sensitivity; in this study, only 7.4% (7/95) of women with HSIL had cytological HSIL results, consistent with current literature [15]. Multivariate Logistic regression analysis showed that when cytology indicated HSIL, the risk of detecting HSIL was 7.27 times higher than when cytology indicated LSIL, suggesting that cytological HSIL is an independent predictor of HSIL detection in women under 30.

HPV testing has high sensitivity but low specificity for diagnosing cervical HSIL. This study showed that among HSIL-detected cases, the HPV positivity rate reached 99.0%, with HPV 16/18 positivity at 67.4% and HPV-HR positivity at 31.6%, suggesting that HPV 16/18 positivity has higher predictive value for

HSIL, consistent with current literature [15]. Multivariate Logistic regression analysis showed that HPV 16/18 positivity carried a 10.833-fold increased risk of HSIL compared to HPV negativity, indicating that HPV positivity is an independent predictor of HSIL, and immediate referral for colposcopy is warranted when HPV 16/18 is positive.

Transformation zone type did not significantly affect HSIL detection. In this study of 427 cases, the HSIL detection rates for Type 1 and Type 2/3 transformation zones were 24.2% and 20.1%, respectively, with no statistically significant difference ($P = 0.307$), consistent with current literature [19]. This suggests that in young women, whether the transformation zone is visible is not a relevant factor affecting HSIL detection.

Numerous studies have demonstrated that HPV vaccination reduces HPV 16/18 infection rates and the incidence of histological cervical HSIL and above [20-21], leading some countries to reassess cervical cancer screening guidelines incorporating vaccination status. In 2020, the Polish Society of Colposcopy and Cervical Pathophysiology recommended including pre-colposcopy assessment, testing techniques, and HPV vaccination status to optimize colposcopy practice and achieve individualized management [22]. Since HPV vaccine approval in China in 2017, the cumulative estimated vaccination rate among eligible women aged 9-45 has been reported at only 2.24% [23]. In this study, the vaccination rate among women under 30 referred for colposcopy was only 34.7%, indicating a need for strengthened education regarding HPV vaccination among age-appropriate women. However, this study found no statistically significant difference in HSIL detection rates between vaccinated and unvaccinated groups ($P = 0.821$), consistent with the findings of GUO Jing et al. [24]. This suggests that current practice in China does not yet require modification of existing management protocols based on HPV vaccination status.

In conclusion, in women under 30 years of age, cytological HSIL and HPV 16/18 infection are independent risk factors affecting HSIL detection, while younger age group (<25 years), transformation zone visibility, and HPV vaccination are not relevant influencing factors. ECC has limited additional value for detecting HSIL in this population. It is recommended that ECC may be omitted in women under 30 who do not have these two independent risk factors, regardless of transformation zone visibility and vaccination status. This conclusion aligns with the 2023 ASCCP guidelines regarding indications for ECC in women under 30 [25].

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Note: Figure translations are in progress. See original paper for figures.