Value of high-risk human papillomavirus detection combined with colposcopy in the diagnosis of cervical cancer and precancerous lesions

PING WANG[1], DONGXIA GAO[2], XIAONI YU[2] and GAOXIANG ZHU[2]

[1]Jinan Licheng District Maternal and Child Health Care Family Planning Service Center, Jinan, Shandong 250100;
[2]Department of Obstetrics and Gynecology, Qingdao Geriatric Hospital
[The West District of Qingdao Municipal Hospital (Group)], Qingdao, Shandong 266002, P.R. China

Received January 11, 2023; Accepted August 21, 2023

DOI: 10.3892/ol.2024.14318

Abstract. In the present study, the diagnostic value of high risk-human papillomavirus (HR-HPV) combined with colposcopy for the detection of cervical cancer and precancerous lesions was evaluated. A total of 397 patients with confirmed cervical disease were enrolled between August 2020 and December 2021. According to the pathological diagnosis, the patients were divided into cervical intraepithelial neoplasia grade I (CIN I; n=153 cases), CIN II (n=101 cases), CIN III (n=86 cases) and cervical cancer (n=57 cases) groups. The HR-HPV-positive rate of the patients with different lesion types was compared, and the consistency of colposcopy and pathological examination results were assessed. For cervical cancer and precancerous lesions, the diagnostic value and efficacy of HR-HPV testing, colposcopy and combined HR-HPV testing and colposcopy examination were compared using pathological examination results as the gold standard. The results of the present study demonstrated that in patients with cervical cancer, the positive rate of HR-HPV (100.00%; n=57/57) was higher than that in patients with precancerous lesions, and the positive rate of HR-HPV in patients with CIN I type (36.60%, n=56/153) was lower than that in patients with CIN II (83.17%, n=84/101) and CIN III (82.56%, n=71/86) types (P<0.05). There was no significant difference in the HR-HPV-positive rate between patients with CIN II and CIN III (P>0.05). Cohen's κ coefficient for colposcopy examination and pathological examination of patients with cervical cancer and precancerous lesions was 0.622, the diagnostic accuracy was 90.43% (n=359/397), the positive predictive value was 65.57% (n=40/61), and the negative predictive value was 94.94% (n=319/336). Receiver operating characteristic curve analysis demonstrated that the area under the curve of the combined examination in the diagnosis of cervical cancer and precancerous lesions was 0.904, which was higher than that of colposcopy (0.820) or HR-HPV testing (0.802) alone (P<0.05). The results of the present study indicated that HR-HPV detection combined with colposcopy has diagnostic value for cervical cancer and precancerous lesions.

Correspondence to: Dr Gaoxiang Zhu, Department of Obstetrics and Gynecology, Qingdao Geriatric Hospital [The West District of Qingdao Municipal Hospital (Group)], 2 Chaocheng Road, Shinan, Qingdao, Shandong 266002, P.R. China
E-mail: zhushishunsui2022@163.com

Key words: high-risk human papillomavirus, colposcopy, cervical cancer, precancerous lesions, diagnostic value

Introduction

Cervical cancer is the fourth most common malignant tumor in the world and the most common malignant tumor of the female reproductive system (1). It is also the only malignant tumor with clear etiology that can be prevented early and for which intervention is possible through vaccination (2). In 2018, there were ~570,000 new cases of cervical cancer worldwide, accounting for 3.15% of all malignant tumors and ~310,000 deaths, accounting for 3.26% of all malignant tumor deaths (3). Clinically, cervical cancer has no obvious symptoms in the early stage, and the main symptoms in the middle and advanced stages include increased leucorrhea and vaginal contact bleeding (4). Early cervical precancerous lesions have no visible symptoms, such as watery vaginal secretions, postcoital bleeding and intermittent drip bleeding (5). The early symptoms of patients are often ignored due to the lack of specificity; therefore, early cervical cancer screening is of value for the prevention of cervical cancer (6). Persistent infection with HR-HPV has been reported to be the main cause of cervical cancer (7). HR-HPV is a small double-stranded DNA virus that can cause skin and mucous membrane lesions in humans. Based on its carcinogenic risk, HPV is divided into low- and high-risk HPV types (8,9). Persistent HR-HPV infection may progress to CIN and eventually to invasive cervical cancer (10). Clinical data have indicated that persistent infection with high-risk human papillomavirus (HR-HPV) is related to the incidence of cervical cancer (11). It has been reported that ≥70% of women will have ≥1 HPV infection in their lifetime, but such infections can be naturally cleared by the body's own immune system in most cases, and only

1-4% of persistent HPV infections will gradually develop into precancerous lesions or cervical cancer (12). Therefore, HPV infection can be regarded as being analogous to a 'common cold' of the cervix. Clinical data also show that high-grade cervical intraepithelial neoplasia (CIN) can potentially develop into invasive carcinoma (13,14).

CIN is an important stage in the prevention and treatment of cervical cancer. Early treatment of precancerous lesions and the blocking of their further development into cancer can effectively reduce the occurrence of cervical cancer (15). Colposcopy, an important method of examination for cervical cancer screening, supports the early detection and diagnosis of the disease. With digital colposcope amplification technology, changes in the surface of the cervix can be accurately and clearly observed, and the location of abnormal cells can be clearly identified through biopsy. However, false-negative phenomena may occur owing to the actions of the examiner themselves (16). Previous studies (12,17) have also reported that because of the confusion of normal and abnormal transformation areas, the difficulty in detecting endocervical lesions and the lack of specificity in images and other factors, colposcopy can lead to misdiagnosis. Therefore, it is necessary to explore a more accurate examination method to improve the rate of cervical cancer detected by early screening. In previous study (18), HR-HPV testing combined with colposcopy was used to diagnose cervical cancer. In the present study, the receiver operating characteristic (ROC) curve was used to analyze the diagnostic value of HR-HPV testing combined with colposcopy in differentiating cervical cancer from precancerous lesions, and to provide a reference for the clinical diagnosis and identification of this disease.

Materials and methods

Clinical data. A total of 397 patients with cervical cancer or precancerous lesions, aged 26-71 years (average, 38.60±6.15 years (mean ± SD), were diagnosed from August 2020 to December 2021 in Jinan Licheng District Maternal and Child Health Care Family Planning Service Center, China and were included in the present study. The patients have 0-6 previous pregnancies with a mean of (2.15±1.26) and the number of live births was 0-5 times with a mean of (1.31±1.17 times. There were 136 cases with smooth cervix, 118 grade I cervical erosion, 100 grade II cervical erosion, and 43 grade III cervical erosion (19). There were also 10 cases of menopause and 387 cases of non-menopausal. Pathological diagnosis was divided into CIN I (mild dysplasia; n=153 cases), CIN II (moderate dysplasia; n=101 cases), CIN III (severe dysplasia and carcinoma *in situ*; n=86 cases) and cervical cancer (n=57) (20). The present study was reviewed and approved by the ethics committee of Jinan Licheng District Maternal and Child Health Care Family Planning Service Center, Jinan, Shandong, China . Samples are collected and processed in February 2022.

Inclusion criteria. Patients who fulfilled the following criteria were included in the present study: i) HR-HPV DNA detection and colposcopy; ii) reported subjective symptoms, such as sexual intercourse bleeding or increased leucorrhea; iii) complete clinical and imaging data; iv) age ≥18 years and had sexual experience; and v) patient consented to participate in the present study.

Exclusion criteria. The following criteria were used to exclude patients from the present study: i) Treatment with radiotherapy and/or chemotherapy; ii) pregnancy or breastfeeding; iii) history of cervical surgery; iv) other gynecological tumors; v) infections with other viruses; vi) vaginal infectious lesions; vii) autoimmune diseases; viii) history of hysterectomy; ix) <24 h since last sexual intercourse; x) Within 48 h of vaginal medication; and xi) active menstruation.

HR-HPV detection. The cervix was fully exposed with a vaginal speculum, and a special HPV sampling brush rotated around the cervix counterclockwise 3-5 times for ~10 sec. The sampling brush was then removed and put in Digene sample storage solution .The upper part of the sampling brush was discarded, and the reagent bottle was covered with a cap. A total of 13 types of HR-HPV including types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 and 68 were assessed using the hybridization capture method using an HCII-HPV-DNA genetic hybridization detection system (hybrid capture II) (21,22) and an HCII reagent kit (Shanghai Yaoyun Biotechnology Co., Ltd.), which was performed according to manufacturer's protocols. All detection procedures and results were strictly determined in accordance with the kit instructions. The positive determination criteria were relative light unit (RLU)/cut off (CO) ≥1.0 of the specimen.

Colposcopy. The domestic VIZ-GD optical and electronic integrated colposcopy system (Beijing Siwei Saiyang Technology Co., Ltd.) was used to examine patients in the non-menstrual phase of the menstrual cycle who had not had cervical intercourse and neither drug administration, smear and irrigation, nor other gynecological examinations were performed within 24 h before the examination. Patients with acute inflammation were examined at a later time, after recovery. Patients were placed in lithotomy position, the bladder was drained and the cervix was exposed using a vaginal speculum. The cervical surface secretions were wiped with cotton balls for preliminary analysis, then 3% glacial acetic acid was applied to the cervix for 1 min. Compound iodine solution was applied to columnar and squamous epithelia, and their transformation areas. The suspicious parts or iodine-free areas were identified under colposcopy, and cervical canal scratching or biopsy was performed. Biopsies were collected at the 3, 6, 9 and 12 o'clock positions on the cervix (23).

A total of 12 sagittal sections were taken at 12 o'clock in the cervical cone section, which were quickly frozen and fixed with 10% formaldehyde. Then hematoxylin was nucleated for 3-5 min. After washing, 0.5% weak ammonia water returned to blue, eosin was re-stained to cytoplasm for 1 min. After washing, gradient ethanol was dehydrated, xylene transparent and neutral gum tablets were sealed, and the sections were observed under a light microscope. The pathological results were diagnosed by two senior pathologists, and the results of the colposcopy were described and diagnosed according to the new colposcopy terms of the 2011 International Federation for Cervical Pathology and Colposcopy (24). The pathological diagnostics were based on the International

Table I. Comparison of HR-HPV testing results in patients with cervical cancer, CIN I, CIN II and CIN III.

HR-HPV type	CIN I (n=153)	CIN II (n=101)	CIN III (n=86)	Cervical cancer (n=57)	χ^2	P-value
16, n	12	17	10	13		
18, n	3	3	5	2		
31, n	1	2	10	7		
33, n	3	7	5	8		
35, n	2	2	6	2		
39, n	0	2	3	1		
45, n	0	5	3	1		
51, n	0	6	2	0		
52, n	0	5	6	0		
56, n	1	2	2	4		
58, n	0	6	3	1		
59, n	1	2	2	0		
68, n	18	3	1	0		
Multiple HR-HPV	15	22	13	17		
Total, n (%)	56 (36.60)	84 (83.17)[a]	71 (82.56)[a,b]	56 (98.25)[a,b]	110.9	<0.001

[a]P<0.05 vs. CIN I; [b]P<0.05 vs. cervical cancer. CIN, cervical intraepithelial neoplasia; HR-HPV, high-risk human papillomavirus.

Cooperation on Cancer Reporting (25); pathological diagnosis is the gold standard for diagnosis of cervical cancer. Under colposcopy, white acetic acid epithelium, with the severity of the lesion positively associated with the whiteness of the epithelium, white glands and rings, heterogenous vessels and punctured vessels were observed. The Reid colposcopy index (RCI) score was proposed by Reid in 1984; it can reduce the subjectivity of colposcopy diagnosis and is currently the most widely accepted colposcopy scoring system (26). Previous studies (27,28) reported that colposcopy diagnosis using RCI has a good consistency with histopathological diagnosis. RCI was adopted for diagnosis and scored as follows: 1-2 points was regarded as CIN I; 3-4 points was regarded as CIN II; and 5-6 points was regarded as CIN III.

Data comparison. Observation indicators were as follows: i) HR-HPV-positive rate was compared among patients with different lesion types, and the consistency of colposcopy and pathological examination results was analyzed; ii) the diagnostic value and efficacy of HR-HPV testing, colposcopy and combined examination for cervical cancer and precancerous lesions were compared using pathological examination results as the gold standard; and iii) the detection rates were compared among patients with different types of cervical lesions by colposcopy, and the association between HR-HPV-positive rate and the severity of cervical lesions was analyzed.

Statistical analysis. Data were processed using SPSS (version 22.0; IBM Corp.). The positive rate of HR-HPV and sensitivity, specificity were expressed as percentage, and the difference between groups was compared using the χ^2 test. The measurement data were expressed as mean ± SD after Kolmogorov-Smirov normality testing. The diagnostic value of HR-HPV testing, colposcopy and combined examination for cervical cancer and precancerous lesions was analyzed using the receiver operating characteristic (ROC) curve, sensitivity and specificity were calculated according to the Jorden index (29). MedCalc (version 19.4; Beijing Huanzhong Ruichi Technology Co., Ltd.) software was used to analyze z-score, and the diagnostic efficiency of combined diagnosis and individual diagnosis of each index was compared. Cohen's κ coefficient test was used to analyze the consistency between the results of colposcopy and pathological examination. P<0.05 was considered to indicate a statistically significant difference.

Table II. Consistency comparison between vaginal examination results and pathological examination results in patients with cervical cancer and precancerous lesions.

Examination method	Pathological result		Total, n
	Positive	Negative	
Colposcopy			
Positive	40	21	61
Negative	17	319	336
Total, n	57	340	397

Results

HR-HPV testing results in patients with cervical cancer and precancerous lesions. The positive rate of HR-HPV in patients with cervical cancer was significantly higher than that in patients with precancerous lesions, and the positive rate of HR-HPV in patients with CIN I was significantly lower than that in patients with CIN II and CIN III (both P<0.05; Table I). There was no significant difference in the HR-HPV-positive rates between patients with CIN II and CIN III (P>0.05).

Table III. Differential value analysis of colposcopy combined with HR-HPV testing for cervical cancer and precancerous lesions.

Examination method	Area under the curve	SEM	95% CI	Sensitivity, %	Specificity, %
HR-HPV	0.681[a]	0.031	0.620-0.742	98.25	37.94
Colposcopy	0.820[a]	0.037	0.747-0.893	93.82	70.18
Combination	0.868	0.027	0.816-0.920	70.18	93.82

[a]P<0.05 vs. combination. HR-HPV, high risk human papillomavirus.

Table IV. Comparison of detection rates of different types of cervical precancerous lesions by colposcopy.

Group	Patients, n	Detection rate, % (n)
CIN I	153	92.16 (141)[a]
CIN II	101	95.05 (96)[a]
CIN III	86	95.35 (82)[a]
Cervical cancer	57	70.18 (40)

[a]P<0.05 vs. cervical cancer. CIN, cervical intraepithelial neoplasia.

These findings indicated that the detection rate of HR-HPV in patients with cervical cancer increased with increasing degree of lesion.

Consistency of vaginal and pathological examination results in patients with cervical cancer and precancerous lesions. Cohen's κ coefficient of vaginal examination results and pathological examination results in patients with cervical cancer and precancerous lesions was 0.622, the diagnostic accuracy was 90.43% (n=359/397), the positive predictive value was 65.57% (n=40/61) and the negative predictive value was 94.94% (n=319/336) (Table II). These findings indicated that colposcopy had high consistency with pathological examination of cervical cancer and precancerous lesions.

Differential value analysis of colposcopy combined with HR-HPV testing for cervical cancer and precancerous lesions. The area under the curve (AUC) of combined colposcopy and HR-HPV testing for the identification of cervical cancer and precancerous lesions was greater than that of colposcopy or HR-HPV testing alone (Table III; Fig. 1). This result indicated that combined examination was better than either HR-HPV testing and colposcopy alone in differentiating between cervical cancer and precancerous lesions. Combined diagnosis is superior to HR-HPV diagnosis alone (z=8.749, P<0.0001); Combined diagnosis is better than colposcopic diagnosis alone (z=3.620; P=0.0003).

Comparison of the detection rate of different types of precancerous cervical lesions by colposcopy. The detection rate of cervical cancer by colposcopy was lower than the detection rates for CIN I, CIN II and CIN III (P<0.05; Table IV; Fig. 2-6). This result indicated that the rate of precancerous lesions detected by colposcopy was higher than that of cervical cancer.

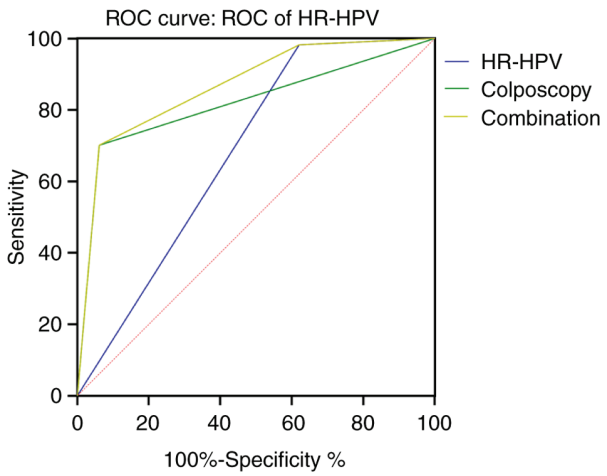

Figure 1. Receiver operating characteristic curve analysis of colposcopy combined with HR-HPV testing for the differentiation of cervical cancer and precancerous lesions. HR-HPV, high-risk human papillomavirus.

Discussion

Previous studies have reported that HR-HPV infection was closely associated with cervical cancer and precancerous lesions, and that HR-HPV could be found in almost all samples from patients with cervical cancer (27,30). Therefore, the HR-HPV-positive rates in patients with different cervical lesions were analyzed in the present study. The results demonstrated that the HR-HPV-positive rate in patients with cervical cancer was significantly higher than that in patients with precancerous lesions, and HR-HPV-positive rate in patients with CIN I was significantly lower than that in patients with CIN II and CIN III, which suggested that the HR-HPV-positive rate of patients may be related to the degree of the cervical lesion.

Further analysis in the present study demonstrated that the HR-HPV-positive rate was associated with the severity of cervical precancerous lesions, which indicated that the more severe the cervical lesions were, the higher the HR-HPV-positive rate might be, which may be related to the fact that persistent HR-HPV infection is a major risk factor for cervical cancer. However, previous studies have reported that HR-HPV quantification is not related to the severity of cervical lesions, and HR-HPV infection was not exactly related to the degree of cervical lesions (31,32). The degree of cervical lesions increased, the differentiation and maturity of abnormal squamous cells decreased, and the tumor cells appeared apoptotic and necrotic, followed by HPV loss. However, the host DNA-integrated virus in cervical cancer cells increased,

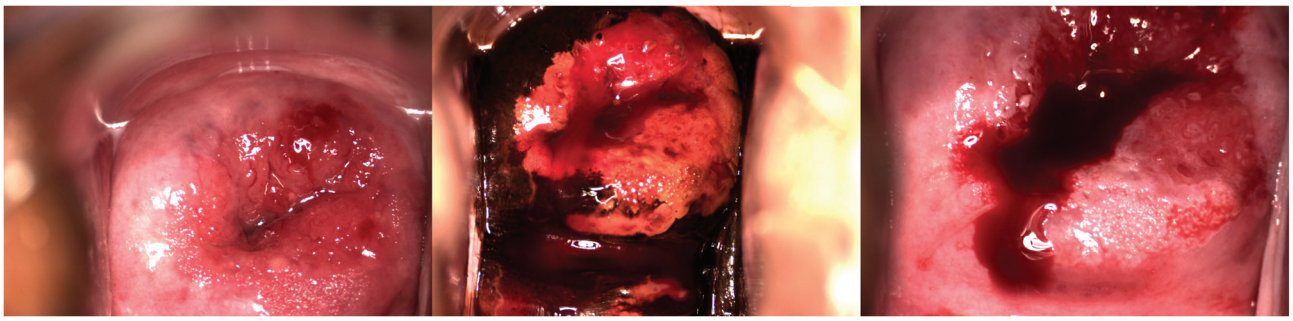

Figure 2. Cervical intraepithelial neoplasia I precancerous lesion of cervical cancer.

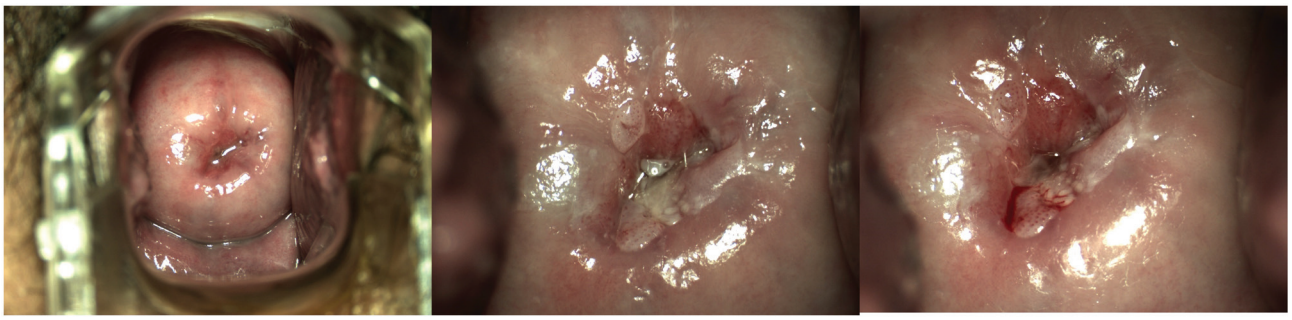

Figure 3. Cervical intraepithelial neoplasia II precancerous lesion of cervical cancer.

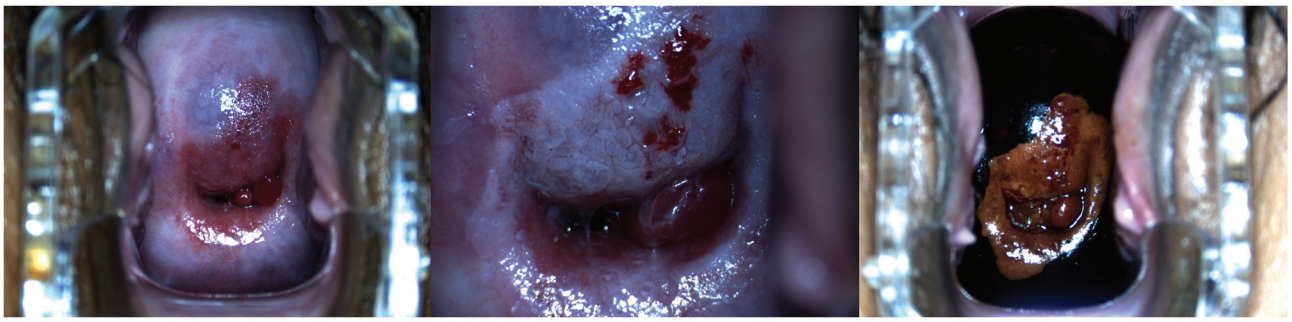

Figure 4. Cervical intraepithelial neoplasia III precancerous lesion of cervical cancer.

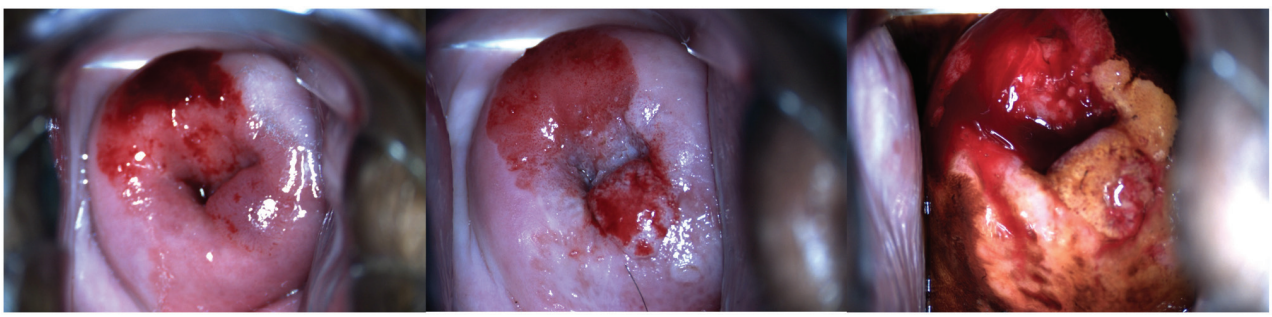

Figure 5. Cervical cancer.

and the detection value decreased (33,34). The results of the present study demonstrated that there was no significant difference in the HR-HPV-positive rates of patients with CIN II and CIN III, which indicated that CIN II and CIN III could not be differentiated by detection of the HR-HPV-positive rate. This may be because there are other factors, in addition to HPV infection, that affect the progression of cervical lesions, such as age at first sexual intercourse, number of sexual partners, multiparity, oral contraceptives, smoking, obesity, nutrition and exercise (35).

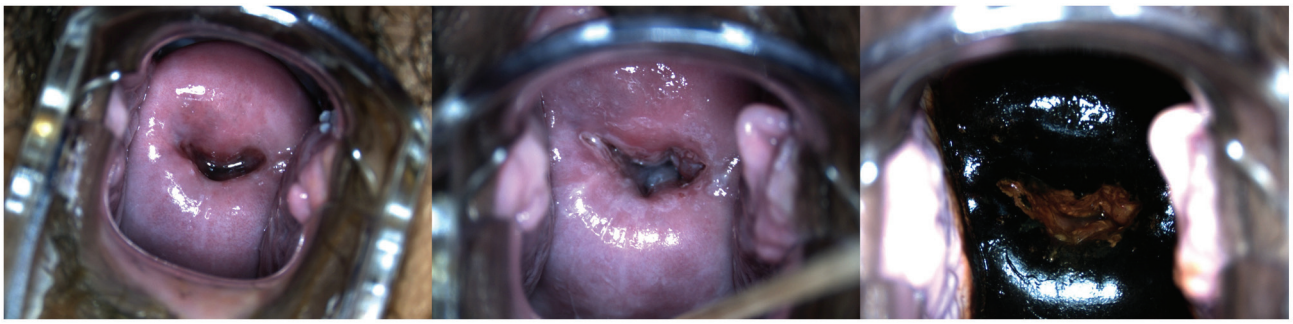

Figure 6. Cervical inflammation.

Patients with cervical precancerous lesions often have no visible symptoms and lack of characteristic cervical morphological changes, which make it difficult to diagnose early. Colposcopy is a non-invasive examination instrument that can replace biopsy examination, improve the accuracy of biopsy and reduce the misdiagnosis rate (36). Colposcopy technology uses strong light to penetrate several layers of epithelial cells into the stroma, which is then reflected to form an image. By observing the color, configuration, blood vessels and iodine staining of the image, the location and severity of cervical lesions can be determined. For smooth uterus or mild erosion of the cervix, colposcopy can also be used to find early underlying issues in a timely manner, and localization and biopsy can be performed under a microscope (37,38). Previous study (39) have pointed out that colposcopy also leads to missed diagnosis of cervical lesions. Under colposcopy, the mucosa of the cervix and vagina is magnified 10-40 times, allowing physicians to directly observe the morphology and structure of cervical blood vessels and surface epithelium, and to identify suspicious lesion areas that are difficult to be confirmed with the naked eye. However, colposcopy has certain limitations. For example, physicians observe the changes of the cervical epithelium under the action of acetic acid in just a few minutes during a patient's examination, which is subjective, and changes in the cervical epithelium may also be affected by factors such as solution application method, volatilization degree and action time, which may lead to misdiagnosis and missed diagnosis (40,41). The present study demonstrated that the accuracy and positive predictive value of colposcopy in the diagnosis of cervical cancer and precancerous lesions were both high, but the negative predictive value of colposcopy was low, which suggested that false negative phenomenon could be expected to occur in the diagnosis of cervical cancer. This is possibly related to its dependence on the subjectivity of the physician at the time of diagnosis, therefore, patients need colposcopy and HPV joint diagnosis. Furthermore, the present study demonstrated that the detection rate of cervical cancer using colposcopy was lower than that for CIN I, CIN II and CIN III, which indicated that the diagnostic accuracy of cervical cancer by colposcopy was lower than that of precancerous lesions.

Colposcopy provides a basis for the final diagnosis of cervical lesions by locating suspicious lesions and obtaining biopsy tissues (42). Previous reports indicate that colposcopy may lead to misdiagnosis of cervical precancerous lesions (43,44). Colposcopy magnifies the cervical lesion site aiding the evaluation of the surface blood vessels and epithelial morphology, which enables preliminary judgment on the lesion nature and supports diagnosis through biopsy sampling. However, the accuracy of the examination results of this method is affected by the subjective experience of physicians, which may lead to misdiagnosis (45-47). HR-HPV testing has become an important screening method for cervical cancer; it not only improves the sensitivity of cytological screening, but also predicts the development of disease in patients with normal cytology or atypical squamous cell lesions, reduces the number of tests in HPV-negative women with abnormal cytology and reduces medical waste (48-50). In the present study, the two examination methods were applied in the clinical diagnosis of cervical cancer and precancerous lesions. AUC of combined examination in the identification of cervical cancer and precancerous lesions was significantly greater than that of colposcopy or HR-HPV testing alone. The AUC value of the combined examinations was ≥0.9. which suggested that the combined examination had a high diagnostic value for cervical cancer and precancerous lesions and may be used in the differential diagnosis of cervical cancer and precancerous lesions.

In conclusion, HR-HPV testing combined with colposcopy has diagnostic value for cervical cancer and precancerous lesions, and the HR-HPV-positive rate was associated with the severity of cervical lesions. The limitations of the present study include: i) A total of 13 types of HR-HPV were detected in the present study, and it is suggested that future prospective studies should detect more types of HR-HPV, which will provide reference for clinical diagnosis of cervical cancer and precancerous lesions caused by HR-HPV; and ii) colposcopy is affected by the subjective experience of physicians, which is prone to false negative results. It is suggested that the final results should be decided after discussions with the physicians, rather than drawing arbitrary conclusions.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

PW performed the investigation and data curation and drafted the original manuscript. DG developed the methodology used and drafted the original manuscript. XY designed the research, wrote, reviewed and edited the final manuscript. GZ conceived the study, and reviewed and edited the original manuscript. PW and GZ confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was reviewed and approved by the hospital ethics committee of Jinan Licheng District Maternal and Child Health Care Family Planning Service Center, Jinan, Shandong, and was conducted in accordance to the tenets of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Singh D, Vignat J, Lorenzoni V, Eslahi M, Ginsburg O, Lauby-Secretan B, Arbyn M, Basu P, Bray F and Vaccarella S: Global estimates of incidence and mortality of cervical cancer in 2020: A baseline analysis of the WHO global cervical cancer elimination initiative. Lancet Glob Health 11: e197-e206, 2023.
2. Li M, Du X, Lu M, Zhang W, Sun Z, Li L, Ye M, Fan W, Jiang S, Liu A, *et al*: Prevalence characteristics of single and multiple HPV infections in women with cervical cancer and precancerous lesions in Beijing, China. J Med Virol 91: 473-481, 2019.
3. Lin S, Gao K, Gu S, You L, Qian S, Tang M, Wang J, Chen K and Jin M: Worldwide trends in cervical cancer incidence and mortality, with predictions for the next 15 years. Cancer 127: 4030-4039, 2021.
4. Shami S and Coombs J: Cervical cancer screening guidelines: An update. JAAPA 34: 21-24, 2021.
5. Awolude OA, Oyerinde SO, Ayeni AO and Adewole IF: Human papillomavirus-based cervical precancer screening with visual inspection with acetic acid triage to achieve same-day treatments among women living with human immunodeficiency virus infection: test-of-concept study in Ibadan, Nigeria. Pan Afr Med J 40: 48, 2021.
6. Zhao H, He Y, Fan B, Wang Y and Wu YM: Human papillomavirus E6E7 mRNA and TERC lncRNA in situ detection in cervical scraped cells and cervical disease progression assessment. Virol J 19: 18, 2022.
7. Dong A, Xu B, Wang Z and Miao X: Survival-related DLEU1 is associated with HPV infection status and serves as a biomarker in HPV-infected cervical cancer. Mol Med Rep 25: 77, 2022.
8. Lyu Y, Ding L, Gao T, Li Y, Li L, Wang M, Han Y and Wang J: Influencing factors of high-risk human papillomavirus infection and DNA load according to the severity of cervical lesions in female coal mine workers of China. J Cancer 10: 5764-5769, 2019.
9. Horn J, Denecke A, Luyten A, Rothe B, Reinecke-Lüthge A, Mikolajczyk R and Petry KU: Reduction of cervical cancer incidence within a primary HPV screening pilot project (WOLPHSCREEN) in Wolfsburg, Germany. Br J Cancer 120: 1015-1022, 2019.
10. Jary A, Teguete I, Sidibé Y, Kodio A, Dolo O, Burrel S, Boutolleau D, Beauvais-Remigereau L, Sayon S, Kampo M, *et al*: Prevalence of cervical HPV infection, sexually transmitted infections and associated antimicrobial resistance in women attending cervical cancer screening in Mali. Int J Infect Dis 108: 610-616, 2021.
11. Hu H, Zhao J, Yu W, Zhao J, Wang Z, Jin L, Yu Y, Han L, Wang L, Zhu H and Li F: Human papillomavirus DNA, HPV L1 capsid protein and p16(INK4a) protein as markers to predict cervical lesion progression. Arch Gynecol Obstet 299: 141-149, 2019.
12. Bedell SL, Goldstein LS, Goldstein AR and Goldstein AT: Cervical cancer screening: past, present, and future. Sex Med Rev 8: 28-37, 2020.
13. Chen L, Dong B, Zhang Q, Mao X, Lin W, Ruan G, Kang Y and Sun P: HR-HPV viral load quality detection provide more accurate prediction for residual lesions after treatment: A prospective cohort study in patients with high-grade squamous lesions or worse. Med Oncol 37: 37, 2020.
14. Sargent A, Fletcher S, Bray K, Kitchener HC and Crosbie EJ: Cross-sectional study of HPV testing in self-sampled urine and comparison with matched vaginal and cervical samples in women attending colposcopy for the management of abnormal cervical screening. BMJ Open 9: e025388, 2019.
15. Okunade KS: Human papillomavirus and cervical cancer. J Obstet Gynaecol 40: 602-608, 2020.
16. Hernández-López R, Lorincz AT, Torres-Ibarra L, Reuter C, Scibior-Bentkowska D, Warman R, Nedjai B, Mendiola-Pastrana I, León-Maldonado L, Rivera-Paredez B, *et al*: Methylation estimates the risk of precancer in HPV-infected women with discrepant results between cytology and HPV16/18 genotyping. Clin Epigenetics 11: 140, 2019.
17. Santesso N, Mustafa RA, Schünemann HJ, Arbyn M, Blumenthal PD, Cain J, Chirenje M, Denny L, De Vuyst H, Eckert LO, *et al*: World health organization guidelines for treatment of cervical intraepithelial neoplasia 2-3 and screen-and-treat strategies to prevent cervical cancer. Int J Gynaecol Obstet 132: 252-258, 2016.
18. Zehua W: Obstetrics and gynecology (5th edition). Obstetrics Gynecol (5th Edition) 2004.
19. Perkins RB, Guido RS, Castle PE, Chelmow D, Einstein MH, Garcia F, Huh WK, Kim JJ, Moscicki AB, Nayar R, *et al*: 2019 ASCCP risk-based management consensus guidelines for abnormal cervical cancer screening tests and cancer precursors. J Low Genit Tract Dis 24: 102-131, 2020.
20. Zhou Y: Investigation of the clinical application value of HR-HPV DNA combined with liquid based cytology in colposcopy of cervical cancer. Contrast Media Mol Imaging 2022: 5054507, 2022.
21. Abdel Aziz MT, Abdel Aziz MZ, Atta HM, Shaker OG, Abdel Fattah MM, Mohsen GA, Ahmed HH and El Derwi DA: Screening for human papillomavirus (HPV) in Egyptian women by the second-generation hybrid capture (HC II) test. Med Sci Monit 12: MT43-MT49, 2006.
22. Poljak M, Marin IJ, Seme K, Brinovec V, Maticic M, Meglic-Volkar J, Lesnicar G and Vince A: Second-generation Hybrid capture test and Amplicor monitor test generate highly correlated hepatitis B virus DNA levels. J Virol Methods 97: 165-169, 2001.
23. Knoepp SM, Kuebler DL and Wilbur DC: Resolution of equivocal results with the Hybrid Capture II high-risk HPV DNA test: A cytologic/histologic review of 191 cases. Diagn Mol Pathol 16: 125-129, 2007.
24. Burness JV, Schroeder JM and Warren JB: Cervical colposcopy: Indications and risk assessment. Am Fam Physician 102: 39-48, 2020.
25. Zhou Q, Zhang F, Sui L, Zhang H, Lin L and Li Y: Application of 2011 international federation for cervical pathology and colposcopy terminology on the detection of vaginal intraepithelial neoplasia. Cancer Manag Res 12: 5987-5995, 2020.
26. Kudela E, Laucekova Z, Nachajova M, Visnovsky J, Bielik T, Krivus S, Biringer K, Balharek T and Zubor P: Colposcopic scoring indexes in the evaluation of cervical lesions with the cytological result of atypical squamous cells, cannot exclude high-grade lesion. J Obstet Gynaecol Res 46: 314-319, 2020.
27. McCluggage WG, Judge MJ, Alvarado-Cabrero I, Duggan MA, Horn LC, Hui P, Ordi J, Otis CN, Park KJ, Plante M, *et al*: Data set for the reporting of carcinomas of the cervix: Recommendations from the international collaboration on cancer reporting (ICCR). Int J Gynecol Pathol 37: 205-228, 2018.
28. Zhao X, Song S, Wang Y, Mu X and Zhang L: Effects of photodynamic therapy in the treatment of high-grade vaginal intraepithelial lesions following hysterectomy and HPV infection. Photodiagnosis Photodyn Ther 42: 103336, 2023.
29. Li Y, Lu F and Yin Y: Applying logistic LASSO regression for the diagnosis of atypical Crohn's disease. Sci Rep 12: 11340, 2022.

30. Rajaram S and Gupta B: Screening for cervical cancer: Choices & dilemmas. Indian J Med Res 154: 210-220, 2021.
31. Ping W: Application value of HPV test in cervical cancer screening of rural women. J Community Med 14: 2, 2016.
32. Rohner E, Edelman C, Sanusi B, Schmitt JW, Baker A, Chesko K, Faherty B, Gregory SM, Romocki LS, Sivaraman V, *et al*: Extended HPV genotyping to compare HPV type distribution in self- and provider-collected samples for cervical cancer screening. Cancer Epidemiol Biomarkers Prev 29: 2651-2661, 2020.
33. Jespersen MM, Booth BB and Petersen LK: Can biopsies be omitted after normal colposcopy in women referred with low-grade cervical cytology? A prospective cohort study. BMC Womens Health 21: 394, 2021.
34. Wang J, Du Y, Dong J, Zhou Y, Wang P, Zhang X, Chen Y and He P: Clinical significance of genotyping for human papillomavirus (HPV) 16 18/45 combined with cytology in cervical exfoliated cells in HPV oncogenic mRNA-positive women. Gynecol Oncol 153: 34-40, 2019.
35. Zhu XH, Li XM, Zhang WL, Liao MM, Li Y, Wang FF, Shang B, Peng LG, Su YJ, You ZJ, *et al*: Application of artificial intelligence-assisted diagnosis for cervical liquid-based thin-layer cytology. Zhonghua Bing Li Xue Za Zhi 50: 333-338, 2021 (In Chinese).
36. Wittenborn J, Weikert L, Hangarter B, Stickeler E and Maurer J: The use of micro RNA in the early detection of cervical intraepithelial neoplasia. Carcinogenesis 41: 1781-1789, 2020.
37. Zhang SK, Luo XP, Li ZF, Su Z, Xia JC, Hu GY, Zhu YJ, Xie LX, Feng XX, Sun XB, *et al*: Performance of human papillomavirus typing test in cervical precancer lesions and cervical cancer screening. Zhonghua Zhong Liu Za Zhi 42: 252-256, 2020 (In Chinese).
38. Newman H, Hu J, Li X, He J, Bradford L, Shan S, Wu X, Zhu B, Yang W, Fu B, *et al*: Evaluation of portable colposcopy and human papillomavirus testing for screening of cervical cancer in rural China. Int J Gynecol Cancer 29: 23-27, 2019.
39. Cong Q, Song Y, Wang Q, Zhang H, Gao S and Sui L: A retrospective study of cytology, high-risk HPV, and colposcopy results of vaginal intraepithelial neoplasia patients. Biomed Res Int 2018: 5894801, 2018.
40. Luo GP, Zeng X, Cao HY, Tang D and Xi MR: The clinical significance of HPV L1/PD-L1 tests combined with colposcopy for cervical precancerous lesions and cervical cancer. Sichuan Da Xue Xue Bao Yi Xue Ban 52: 516-522, 2021 (In Chinese).
41. Liu Y, Liao J, Yi X, Pan Z, Pan J, Sun C, Zhou H and Meng Y: Diagnostic value of colposcopy in patients with cytology-negative and HR-HPV-positive cervical lesions. Arch Gynecol Obstet 306: 1161-1169, 2022.
42. Luo Q, Lang L, Han N, Liang L, Shen L and Zhang H: Prevalence and genotype distribution of high-risk human papillomavirus infection among women with cervical cytological abnormalities in Chongqing, China, 2014-2020. Diagn Cytopathol 49: 1237-1243, 2021.
43. Painter H, Erlinger A, Simon B, Morroni C, Ramogola-Masire D and Luckett R: Impact of cervicitis on performance of cervical cancer screening using HRHPV testing and visual evaluation in women living with HIV in Botswana. Int J Gynaecol Obstet 151: 144-146, 2020.
44. Liu G, Sharma M, Tan N and Barnabas RV: HIV-positive women have higher risk of human papilloma virus infection, precancerous lesions, and cervical cancer. Aids 32: 795-808, 2018.
45. Vodicka EL, Chung MH, Zimmermann MR, Kosgei RJ, Lee F, Mugo NR, Okech TC, Sakr SR, Stergachis A, Garrison LP Jr and Babigumira JB: Estimating the costs of HIV clinic integrated versus non-integrated treatment of pre-cancerous cervical lesions and costs of cervical cancer treatment in Kenya. PLoS One 14: e0217331, 2019.
46. Husaiyin S, Han L, Wang L, Ma C, Ainiwaer Z, Rouzi N, Akemujiang M, Simayil H, Aniwa Z, Nurimanguli R and Niyazi M: Factors associated with high-risk HPV infection and cervical cancer screening methods among rural Uyghur women aged >30 years in Xinjiang. BMC Cancer 18: 1162, 2018.
47. Garza-Rodríguez ML, Oyervides-Muñoz MA, Pérez-Maya AA, Sánchez-Domínguez CN, Berlanga-Garza A, Antonio-Macedo M, Valdés-Chapa LD, Vidal-Torres D, Vidal-Gutiérrez O, Pérez-Ibave DC and Treviño V: Analysis of HPV integrations in mexican pre-tumoral cervical lesions reveal centromere-enriched breakpoints and abundant unspecific HPV regions. Int J Mol Sci 22: 3242, 2021.
48. Dong B, Chen L, Lin W, Su Y, Mao X, Pan D, Ruan G, Xue H, Kang Y and Sun P: Cost-effectiveness and accuracy of cervical cancer screening with a high-risk HPV genotyping assay vs. a nongenotyping assay in China: An observational cohort study. Cancer Cell Int 20: 421, 2020.
49. Ferrera A, Valladares W, Cabrera Y, de la Luz Hernandez M, Darragh T, Baena A, Almonte M and Herrero R: Performance of an HPV 16/18 E6 oncoprotein test for detection of cervical precancer and cancer. Int J Cancer 145: 2042-2050, 2019.
50. Suwanthananon C and Inthasorn P: A comparison of the associations of reid colposcopic index and swede score with cervical histology. J Obstet Gynaecol Res 46: 618-624, 2020.