

# Clinical application of the 2011 IFPCPC colposcope terminology in the era of HPV vaccines

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## Research article

**Keywords:** 2011 IFPCPC terminology, colposcopy, minor changes , major changes , Lugol's staining

**Posted Date:** December 22nd, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-131820/v1>

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## Abstract

**Background** Colposcopy is the conjunction with screening and diagnosis of cervical precancerous lesions. However the diagnostic accuracy of colposcopy is unsatisfied. This study was to evaluate colposcopic accuracy according to the 2011 International Federation of Cervical Pathology and Colposcopy (IFCPC) terminology.

**Methods** A retrospective cohort study was performed in 1,838 patients who underwent colposcopy in Shandong Qianfoshan Hospital, Cheeloo College of Medicine, Shandong University from October 2013 to April 2018. Using conization or cervical biopsy pathology as the gold standard, the agreement between colposcopic diagnosis and pathologic diagnosis was calculated, and correlations between variables were analyzed.

**Results** As an authoritative and widely used terminology for colposcopy diagnosis, the 2011 IFCPC terminology has certain clinical practicality and diagnostic accuracy. However, some signs such as mosaic, punctuation, sharp border, inner border sign and ridge sign had high specificity but unsatisfactory sensitivity, which limited the diagnostic value. Therefore, we discussed the Lugol's staining, a very common sign in colposcopy, and analyzed the diagnostic significance of bright yellow staining in low-grade squamous intraepithelial lesion (LSIL) and mustard yellow staining in high-grade squamous intraepithelial lesion (HSIL). The results showed that mustard yellow may be a valuable indicator in the diagnosis of HSIL.

**Conclusion** With the wide acceptance of human papilloma virus (HPV) vaccines and HPV-based screening, there will be new challenges to accurately identify the signs of non-HPV16 and non-HPV18 infections and of minor lesions using colposcopy. In this study, we provide some recommendations in dealing with these challenges. More clinical research will be needed to further refine colposcopy terminology, improve diagnostic accuracy, and ensure that the World Health Organization's goal of eliminating cervical cancer worldwide by 2030 is achieved.

## Background

Results released by the International Agency for Research on Cancer show that in 2018, there were an estimated 570,000 new cases of cervical cancer worldwide and 310,000 deaths from cervical cancer. Among them, nearly 110,000 new cases of cervical cancer and nearly 50,000 deaths occurred in China [1]. However, persistent infection with high-risk human papilloma virus (hrHPV) appears to be the major driver of cervical cancer development. It is a long process from precancerous lesions initiated by HPV infection to cervical cancer, so the diagnosis and treatment of precancerous lesions are particularly important. With the role of identifying the lesion, guiding biopsy and helping to plan treatment and follow-up, colposcopy, in conjunction with cervical screening has played an important role in reducing the incidence of cervical cancer. However, colposcopy is considered as subjective procedure which is highly dependent on the knowledge and skill of the observer [2-5]. Therefore, standardizing the colposcopy evaluation has always been the subject of concern and discussion. The Reid Colposcopic Index (RCI), the modified RCI, and the Swede score have all been used historically in colposcopic diagnosis. Although there are various colposcopy scoring systems, there is no consensus on the standardization [6-9]. The International Federation of Cervical Pathology and Colposcopy (IFCPC), which is the current authoritative international organization of cervical pathology and colposcopy, has presented four versions of colposcopic terminology: in 1975, 1990, 2002, and 2011 with the purpose of promoting uniform colposcopy terminology and practice. The American Society for Colposcopy and Cervical Pathology (ASCCP) proposed ASCCP Colposcopy Standards in 2017 based on colposcopy practice in the United States. On the one hand, all the colposcopy terminology changes reflect the continuous development of colposcopy technology in recent years and the improvement in our understanding of colposcopy; on the other hand, there are no accurate colposcopy standards that have been widely accepted and applied worldwide. Therefore, colposcopy standards will continue to evolve moving forward. In this study, we discuss the advantages and disadvantages of the 2011 IFCPC colposcopy terminology in clinical applications in the era of HPV vaccines.

## Methods

### Subjects and procedures

A retrospective study of 1,838 patients with abnormal cervical cytology, positive high-risk HPV testing, symptoms of contact bleeding, vaginal discharge, or suspicious-looking cervixes was carried out. All patients underwent colposcopy in Shangdong Qianfoshan Hospital, Cheeloo College of Medicine, Shandong University from October 2013 to April 2018. All selected cases had a pathological diagnosis based on a cervical biopsy or a cervical cone resection. Mean patient age was 41.73 years (41.73±10.63 years). Leisegang BG/LED Y/C optoelectronic integrated digital colposcope was used, and images were obtained using a Canon EOS600D camera. Patients received colposcopic diagnoses according to the 2011 IFPC colposcopic terminology by two colposcopists with 5–7 years working experience in colposcopy. Routine colposcopy was performed, which involved a general view of the cervix without reagent, a 3% acetic acid test, and a 5% Lugol's iodine staining test.

### 2011 IFPC colposcopic diagnosis

The 2011 IFPC terminology was applied to the colposcopy image description and diagnosis as follows: 1) General assessment: adequate or inadequate; squamocolumnar junction visibility: completely, partially, not visible; transformation zone types(TZ) 1, 2, 3; 2) Normal colposcopic findings: original squamous epithelium; columnar epithelium; ectopy; metaplastic squamous epithelium; nabothian cysts; crypt openings; 3) Abnormal colposcopic findings: general principles (location of the lesion, size of the lesion and size of the lesion as percentage of cervix); Grade 1 (minor): thin acetowhite epithelium, fine mosaic, fine punctation, irregular, geographic border; Grade 2 (major): dense acetowhite epithelium, coarse mosaic, coarse punctuation, sharp border, inner border sign, ridge sign, rapid appearance of acetowhitening, cuffed crypt openings; nonspecific: Leukoplakia, erosion, Lugol's staining; suspicious for invasion: atypical vessels, necrosis, ulceration, tumor or gross neoplasm; miscellaneous findings included: condyloma, polyp, inflammation, stenosis, endometriosis; 4) Colposcopic diagnoses were classified as normal or benign, low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL), or invasive carcinoma.

### Pathological diagnosis

Pathological diagnosis can be divided into: normal or benign, LSIL, HSIL, and carcinoma. Cervical biopsy diagnosis was used as the pathological diagnosis for those without conization, while the final histopathologic diagnosis was applied to patients who underwent conization or a hysterectomy.

### Statistical methods

Categorical variables were presented as frequencies (percentages). The estimated agreement between colposcopic and histological diagnoses was determined using weighted kappa statistics. The association between lesion size and pathological diagnosis was conducted using the Mantel–Haenszel  $\chi^2$  test. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), Youden's index(YI), and their 95% confidence intervals (CIs) were used to assess accuracy. The area under the curve (AUC) was used in logistics analysis to compare the diagnostic value of bright yellow for LSIL and mustard yellow for HSIL. Data analysis was performed using SAS 9.4, while the Delong test was used to compare receiver operating characteristic (ROC) curves using MedCalc statistical software. A two-sided  $P < 0.05$  was set as being statistically significant.

## Results

### Agreement between colposcopic and histological diagnoses

Table 1  
Agreement between colposcopic diagnosis and cervical histopathology.

Colposcopic diagnosis	Histopathological diagnosis				Total
	Normal or benign	LSIL	HSIL	Carcinoma	
Normal or benign	252	93	10	2	357
LSIL	307	482	116	2	907
HSIL	24	65	385	15	489
Carcinoma	0	0	8	77	85
Total	583	640	519	96	1838

**LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion;**

Because of several studies showed poor reliability of Lugol's staining, it was removed from the "minor grade" category to the "nonspecific" category [7, 10, 11]. In this study, Lugol's staining negativity had a high sensitivity and NPV while the specificity was low. The data are shown in the Table 6. But compared with rare sharp border, inner border sign, ridge sign and even mosaic, punctuation, Lugol's staining negativity was very common.

Table 2  
Accuracy of colposcopic diagnoses in distinguishing cervical histopathology at different cutoffs.

	Sensitivity (95%CI)	Specificity (95%CI)	Positive predictive value(95%CI)	Negative predictive value(95%CI)	Youden index
LSIL/HSIL/carcinoma vs. normal or benign	43.22% (39.26%~47.28%)	91.63% (89.97%~93.05%)	70.59% (65.66%~75.08%)	77.65% (75.46%~79.70%)	0.3485
HSIL/carcinoma vs. LSIL/normal or benign	92.72% (91.12%~94.05%)	78.86% (75.46%~81.91%)	89.72% (87.91%~91.28%)	84.49% (81.30%~87.23%)	0.7158
<b>LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion;</b>					

The sensitivity, specificity, PPV, NPV and YI of colposcopic diagnosis for normal cervix from any cervical lesion (LSIL, HSIL and carcinoma) and HSIL<sup>+</sup> (HSIL and carcinoma) form LSIL<sup>-</sup> (LSIL/normal or benign) were 43.22%, 91.63%, 70.59%, 77.65%, 0.34 and 92.72%, 78.86%, 89.72%, 84.49%, 0.7158 respectively. The accuracy of colposcopic diagnoses in distinguishing cervical histopathology at different cutoffs is shown in Table 2.

### Significance of the individual colposcopic findings in the IFCCP nomenclature

Table 3  
Correlation of colposcopic findings in the 2011 IFCCPC nomenclature with histological diagnoses(%)

Colposcopic finding	Histopathological diagnosis			
	Normal or benign (N = 583)	LSIL(N = 640)	HSIL(N = 519)	Carcinoma(N = 96)
<b>Adequate or inadequate of cervix</b>				
adequate	541 (31.99)	600 (35.48)	476 (28.15)	74 (4.38)
inadequate	42 (28.57)	40 (27.21)	43 (29.25)	22 (14.97)
<b>Transformation zone type</b>				
1	99 (32.04)	138 (44.66)	72 (23.3)	0 (0)
2	9 (36)	9 (36)	7 (28)	0 (0)
3	475 (31.58)	493 (32.78)	440 (29.26)	96 (6.38)
<b>Squamocolumnar junction visibility</b>				
completely visible	108 (32.34)	147 (44.01)	79 (23.65)	0 (0)
partially visible	195 (26.17)	279 (37.45)	261 (35.03)	10 (1.34)
not visible	280 (36.89)	214 (28.19)	179 (23.58)	86 (11.33)
<b>Size of the lesion as percentage of cervix</b>				
< 30%	572 (34.15)	621 (37.07)	443 (26.45)	39 (2.33)
30%~67%	10 (8.26)	17 (14.05)	71 (58.68)	23 (19.01)
> 67%	1 (2.38)	2 (4.76)	5 (11.9)	34 (80.95)
<b>Aceto-white epithelium</b>				
Thin aceto-white epithelium	362 (34.54)	557 (53.15)	127 (12.12)	2 (0.19)
Dense aceto-white epithelium	21 (3.89)	64 (11.85)	380 (70.37)	75 (13.89)
<b>Punctation</b>				
Fine punctation	38 (17.19)	93 (42.08)	89 (40.27)	1 (0.45)
Coarse punctation	6 (2.79)	29 (13.49)	148 (68.84)	32 (14.88)
<b>Mosaic</b>				
Fine mosaic	1 (9.09)	4 (36.36)	6 (54.55)	0 (0)
Coarse mosaic	3 (2.5)	9 (7.5)	88 (73.33)	20 (16.67)
Inner border sign	0 (0)	2 (15.38)	11 (84.62)	0 (0)

LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion;

	Histopathological diagnosis			
Ridge sign	1 (6.67)	1 (6.67)	12 (80)	1 (6.67)
Sharp border	0 (0)	4 (10.81)	25 (67.57)	8 (21.62)
Cuffed crypt (gland) openings	26 (8.64)	77 (25.58)	184 (61.13)	14 (4.65)
Iodine negativity	474 (27.72)	627 (36.67)	514 (30.06)	95 (5.56)
Leukoplakia	0 (0)	2 (25)	4 (50)	2 (25)
Atypical vessel	0 (0)	2 (2.6)	22 (28.57)	53 (68.83)
Erosion	1 (6.25)	0 (0)	2 (12.5)	13 (81.25)
Necrosis	0 (0)	0 (0)	1 (3.45)	28 (96.55)
Tumor or gross neoplasm	1 (1.79)	0 (0)	1 (1.79)	54 (96.43)
Condyloma	1 (4)	17 (68)	7 (28)	0 (0)
Polyp	52 (55.32)	26 (27.66)	15 (15.96)	1 (1.06)
Contact bleeding	26 (15.95)	30 (18.4)	54 (33.13)	53 (32.52)
Endometriosis	8 (72.73)	1 (9.09)	2 (18.18)	0 (0)
LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion;				

The correlation of colposcopic findings in the 2011 IFCPC nomenclature with histological diagnoses is shown in Table 3.

## General assessment of colposcopic findings

Of the 1,838 patients, 1,691 (1691/1838, 92.00%) had adequate cervical screening and 147 (147/1838, 8.00%) had inadequate cervical screening. The squamocolumnar junction was completely, partially and not visible in 334 (334/1838, 18.17%), 745 (745/1838, 40.53%) and 759 (759/1838, 41.29%) cases respectively.

Transformation zone types 1, 2, 3 account for 16.81% (309/1838, 16.81%), 1.36% (25/1838, 1.36%) and 81.83% (1504/1838, 81.83%).

## Abnormal colposcopic findings

Of the 1,838 patients, 1,675 had abnormal colposcopic findings on < 30% of the visible cervix (91.13%, 1675/1838), 121 had abnormal findings on 30–67% of the visible cervix (6.58%, 121/1838), and 42 on > 67% of the visible cervix (2.29%, 42/1838). The linear trend test of lesion size and pathological diagnosis showed the larger the size of the lesion, the more serious the disease ( $\chi^2 = 261.869$ ,  $P < 0.001$ ).

Table 4  
Accuracy of colposcopic minor changes in predicting low-grade lesion

	<b>Sensitivity (95% CI)</b>	<b>Specificity (95% CI)</b>	<b>Positive predictive value (95% CI)</b>	<b>Negative predictive value (95% CI)</b>	<b>Youden index</b>
<b>Thin aceto- white epithelium</b>	87.03% (84.20%~89.42%)	59.02% (56.21%~61.77%)	53.15% (50.12%~56.15%)	89.49 (87.15%~91.45%)	0.4605
<b>Fine mosaic</b>	0.625% (0.18%~1.66%)	99.42% (98.77%~99.74%)	36.36% (14.98%~64.81%)	65.19% (62.97%~67.34%)	0.045
<b>Fine punctuation</b>	14.53% (12.00%~17.48%)	89.32% (87.43%~90.95%)	42.08% (35.76%~48.67%)	66.17% (63.83%~68.44%)	0.035

Table 5  
Accuracy of colposcopic major changes in predicting high-grade lesion

	<b>Sensitivity (95% CI)</b>	<b>Specificity (95% CI)</b>	<b>Positive predictive value (95% CI)</b>	<b>Negative predictive value (95% CI)</b>	<b>Youden index</b>
<b>Dense aceto-white epithelium</b>	73.22% (69.24%~76.85%)	87.87% (85.99%~89.53%)	70.37% (66.38%~74.07%)	89.29% (87.49%~90.86%)	0.6109
<b>Coarse mosaic</b>	16.96% (13.96%~20.43%)	97.57% (96.58%~98.29%)	73.33% (64.76%~80.46%)	74.91% (72.81%~76.91%)	0.1453
<b>Coarse punctuation</b>	28.52% (24.80%~32.55%)	94.92% (93.59%~95.99%)	68.84% (62.35%~74.66%)	77.14% (75.03%~79.12%)	0.2344
<b>Sharp border</b>	4.82% (3.25%~7.04%)	99.09% (98.04%~99.50%)	67.57% (51.38%~80.45%)	72.57% (70.46%~74.58%)	0.039
<b>Inner border sign</b>	2.12% (1.14%~3.80%)	99.85% (99.41%~99.99%)	84.62% (56.54%~96.90%)	72.16% (70.06%~74.17%)	0.0197
<b>Ridge sign</b>	2.31% (1.28%~4.04%)	99.77% (99.30%~99.96%)	80% (54.05%~93.72%)	72.19% (70.09%~74.20%)	0.0208
<b>Cuffed crypt openings</b>	35.45% (31.46%~39.66%)	91.13% (89.47%~92.55%)	61.13% (55.51%~66.46%)	78.20% (76.07%~80.20%)	0.2658

The thin acetowhite epithelium, fine punctuation and fine mosaic were regarded as minor changes for LSIL. In grade 1, the sensitivity, specificity, PPV, NPV and YI of detecting LSIL were 87.03%, 59.02%, 53.15%, 89.49% and 0.4605. Those of the fine mosaic and fine punctuation are shown in Table 4. In grade 2, the sensitivity, specificity, PPV, NPV and YI of thick white

acetate epithelium in the diagnosis of HSIL were 73.22%, 87.87%, 70.37%, 89.29% and 0.6109. Other data are shown in the Table 5. As it is generally believed that thick white acetate epithelium had high diagnostic value. The sensitivity of coarse mosaic, coarse punctuation, cuffed crypt openings, sharp border, inner border sign and ridge sign were all higher than 90%. Although rare, inner border sign and ridge sign—two new colposcopic criteria had high PPV of 84.62% and 80% respectively, prior to the other criteria including thick white acetate epithelium.

Table 6

Accuracy of colposcopic Lugol's staining negativity in predicting normal or benign, low-grade lesion, high-grade lesion and carcinoma

	<b>Sensitivity (95% CI)</b>	<b>Specificity (95% CI)</b>	<b>Positive predictive value (95% CI)</b>	<b>Negative predictive value (95% CI)</b>	<b>Youden index</b>
<b>Normal or benign</b>	81.30% (77.93%~84.27%)	1.51% (0.96%~2.37%)	27.72% (25.65%~29.89%)	14.84% (9.63%~22.10%)	-0.1719
<b>LSIL</b>	97.97% (96.52%~98.84%)	9.60% (8.05%~11.41%)	36.67% (34.41%~38.98%)	89.84% (83.28%~94.09%)	0.0757
<b>HSIL</b>	99.04% (97.70%~99.56%)	9.33% (7.87%~11.02%)	30.06% (27.93%~32.27%)	96.09% (90.94%~98.56%)	0.0837
<b>Carcinoma</b>	98.96% (93.77%~99.99%)	7.29% (6.16%~8.61%)	5.56% (4.56%~6.75%)	99.22% (95.27%~99.99%)	0.0622
<b>LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion;</b>					

Because of several studies showed poor reliability of Lugol's staining, it was removed from the "minor grade" category to the "nonspecific" category [7, 10, 11]. In this study, Lugol's staining negativity had a high sensitivity and NPV while the specificity was low. The data are shown in the Table 6. But compared with rare sharp border, inner border sign, ridge sign and even mosaic, punctuation, Lugol's staining negativity was very common.

Table 7

Accuracy of colposcopic Lugol's staining bright yellow in predicting normal or benign, low-grade lesion, high-grade lesion and carcinoma

	<b>Sensitivity (95%CI)</b>	<b>Specificity (95%CI)</b>	<b>Positive predictive value(95%CI)</b>	<b>Negative predictive value(95%CI)</b>	<b>Youden index</b>
<b>Normal or benign</b>	70.33% (66.49%~73.89%)	35.78% (33.17%~38.47%)	33.72% (31.11%~36.42%)	72.19% (68.53%~75.57%)	0.0611
<b>LSIL</b>	75.63% (72.15%~78.80%)	38.90% (36.18%~41.69%)	39.80% (37.09%~42.58%)	74.92% (71.36%~78.17%)	0.1453
<b>HSIL</b>	49.90% (45.62%~54.19%)	27.45% (25.10%~29.92%)	21.30% (19.09%~23.69%)	58.20% (54.28%~62.01%)	-0.2265
<b>Carcinoma</b>	65.63% (55.67%~74.38%)	33.81% (31.63%~36.07%)	5.18% (4.06%~6.58%)	94.69% (92.62%~96.22%)	0.0622
<b>LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion;</b>					

Table 8

Accuracy of colposcopic Lugol's staining mustard yellow in predicting normal or benign, low-grade lesion, high-grade lesion and carcinoma

	<b>Sensitivity (95%CI)</b>	<b>Specificity (95%CI)</b>	<b>Positive predictive value(95%CI)</b>	<b>Negative predictive value(95%CI)</b>	<b>Youden index</b>
<b>Normal or benign</b>	10.98% (8.68%~13.79%)	65.74% (63.07%~68.31%)	12.96% (10.26%~16.22%)	61.38% (58.75%~63.95%)	0.0611
<b>LSIL</b>	22.34% (19.28%~25.73%)	70.70% (68.06%~73.21%)	28.95% (25.12%~33.10%)	63.02% (60.41%~65.56%)	-0.0699
<b>HSIL</b>	49.13% (44.85%~53.42%)	81.88% (79.71%~83.87%)	51.62% (47.22%~56.00%)	80.36% (78.15%~82.40%)	0.3101
<b>Carcinoma</b>	33.33% (24.68%~43.26%)	73.48% (71.36%~75.50%)	6.48% (4.60%~9.03%)	95.24% (93.49%~96.54%)	0.0681
<b>LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion;</b>					

Table 9

Accuracy of colposcopic Lugol's staining bright yellow in predicting LSIL<sup>-</sup> (LSIL and normal or benign) and Lugol's staining mustard yellow in predicting HSIL<sup>+</sup> (HSIL and carcinoma)

	<b>Sensitivity (95%CI)</b>	<b>Specificity (95%CI)</b>	<b>Positive predictive value(95%CI)</b>	<b>Negative predictive value(95%CI)</b>	<b>Youden index</b>
<b>Lugol's staining bright yellow/LSIL<sup>-</sup></b>	73.10% (70.54%~75.51%)	47.64% (43.72%~51.59%)	73.52% (70.97%~75.92%)	47.11% (43.21%~51.03%)	0.2074
<b>Lugol's staining mustard/HSIL<sup>+</sup></b>	46.67% (42.76%~50.62%)	83.07% (80.87%~85.07%)	58.10% (53.70%~62.37%)	75.60% (73.23%~77.82%)	0.2974
<b>LSIL, low-grade squamous intraepithelial lesion; HSIL, high-grade squamous intraepithelial lesion;</b>					

## LSIL<sup>-</sup> (LSIL and normal or benign); HSIL<sup>+</sup> (HSIL and carcinoma)

According to the degree of yellow, the Lugol's staining negativity was divided into bright and mustard yellow. The sensitivity and NPV of bright yellow to LSIL diagnosis were higher than fine mosaic and fine punctation, only lower than thin acetowhite epithelium which is shown in Table 7. Mustard yellow had high specificity and NPV of HSIL diagnosis. The YI was lower than dense aceto-white epithelium but higher than coarse mosaic, coarse punctuation, cuffed crypt openings, sharp border, inner border sign and ridge sign. The data is shown in Table 8. The accuracy of colposcopic Lugol's staining bright yellow in predicting LSIL<sup>-</sup> (LSIL and normal or benign) and Lugol's staining mustard yellow in predicting HSIL<sup>+</sup> (HSIL and carcinoma) is shown in Table 9. The values of bright yellow and mustard yellow in diagnosing LSIL and HSIL were compared according to the logistics regression model. The results showed an odds ratio (OR) of mustard yellow for HSIL was 1.43, (1.06–1.94, P = 0.019). As a result, mustard yellow may be a valuable indicator for the diagnosis of HSIL. Invasive carcinoma was rare. Atypical vessels was classified as suspicious for invasion and it had certain diagnostic value for microinvasive carcinoma.

Miscellaneous findings included condyloma, polyp, inflammation, stenosis and endometriosis. Among 25 patients with condyloma, normal or benign was found in only 1 patients, LSIL in 17 and HSIL in 7 patients. Among 94 patients with polyp, normal or benign was found in 52 patients, LSIL in 26, HSIL in 15 and carcinoman in 1 patients. In those with endometriosis, most (8/11) were diagnosed with inflammation.

## Discussion

Hans Hinselmann invented colposcopy in 1925. It is a realtime visualization of the cervix, with magnification and illumination, especially the transformation zone for the detection of cervical intraepithelial neoplasia (CIN) and invasive cancer. It is also used for vaginal or vulvar evaluation. The basis for colposcopy is to find suspicious lesions and biopsy through 3–5% acetic acid and Lugol iodine solution. The acetowhite epithelium, lesion borders and size, vascular patterns, crypt openings and ect are visualized [6, 8, 12, 13]. Before colposcopy was widely used, many women with serious cytological abnormalities underwent conization or hysterectomy as both diagnosis and therapy. The application of colposcopy with targeted biopsies provided accurate assessment and unnecessary excision was avoided [14, 15].

With the purpose of unifying the nomenclature of colposcopy for comparative studies and improving the accuracy of diagnosis, IFCCP presented its first International Colposcopic Classification in 1975, its second nomenclature in 1990 and third in 2002. In 2011, the IFCCP committee examined the past IFCCP terminologies and proposed an evidence-based terminology by reviewing publications. It was recommended that the 2011 terminology should replace all other terminologies and be implemented immediately for diagnosis, treatment and research [12]. So far, the 2011 IFCCP terminology has been proposed for several years. It has certain clinical practicability. Several studies demonstrated it can improve the colposcopic accuracy. However, the reproducibility of transformation zone and the predictive value of a few signs remained to be questioned. Meanwhile, with the popularized of HPV vaccine and changes in cervical cancer screening strategies, colposcopy presents new challenges. First, long-term effects of HPV vaccination has led to decreased the incidence of high grade CIN in Australia, America and Europe. It will be the trend in developing country, such as in china. In addition, the update of the guidelines tends to reduce the screening of low-risk women with longer intervals [16–19]. The impact of vaccination and referral patterns may lead to a trend of colposcopy volume reduction. This was confirmed in a study in the United States, which showed that the average monthly visits (75.3) dropped to nearly one-third of the 218 visits per month in July 2010. [20]. Secondly, cytology-based screening is being replaced by HPV-based screening. In HPV-screening with higher sensitivity than cytology, the number with minor abnormalities at colposcopy is likely to increase. Otherwise, colposcopic signs of HPV-16 infection are more typical than other types of HPV infection [16]. This was confirmed in other studies [21, 22]. In the vaccinated and HPV-based screening population, colposcopy may become increasingly difficult [23]. Recognizing the limitations of the terminology, in 2017 ASCCP presented recommendations for colposcopy practice and procedures and the quality assurance measures in America [24, 25]. ASCCP claimed 2017 ASCCP terminology was compatible with the IFCCP terminology and was an adapted and simplified version. Although some changes were obvious, such as removal of the classification of cervical transformation zone and emphasis of risk-based colposcopy practise. Of course, ASCCP also expressed their expectation to continue constructive dialogue with IFCCP [26]. We would like to see such kind of academic controversy because it leads to thinking and problem solving. The world health organization has set a goal of eliminating cervical cancer worldwide by 2030. This year, the 17th World Congress for Cervical Pathology and Colposcopy will be held in India. The theme is “Eliminating Cervical Cancer all for Action”. A new edition of IFCCP colposcopy terminology will be released. Of the moment, we conclude, look ahead, explore the likely changes of colposcopy practice in this era because no matter which screening program is selected, colposcopy will still be the tool for diagnosing precancerous lesions after the screening is positive [23]. Therefore, colposcopic skills and basic training are still very important [27].

In this study, we analyzed the clinical applicability of the 2011 IFCCP nomenclature in predicting cervical disease. The results showed the agreement between histopathology and colposcopy was 65.07% with weighted kappa = 0.5966. It was

equal to Li *et al*'s of 64.95% with consistency of kappa = 0.436, Fan *et al*'s of 65.5% with weighted kappa strength 0.494 and Prabhakaran's of 65.7% [28–30]. Although IFCPC nomenclature was only moderate, it was better than Swede Score, RCI, modified RCI and 2002 IFCPC nomenclature [7, 8, 31–35]. In our study, we found that the 2011 IFCPC colposcopic terminology had a high sensitivity (92.72%) in differentiating HSIL<sup>+</sup> from LSIL<sup>-</sup>, a little higher than that reported in previous studies (30–91.3%) [36]. The specificity for detecting HSIL<sup>+</sup> was 78.86%, a little lower than previously reported (79–96.5%) [34, 37, 38]. The PPV and NPV of colposcopy to diagnose HSIL<sup>+</sup> were 89.72% and 84.49%, both comparable to the previous findings [34, 36–38]. The term of cervical colposcopy in 2011 begins with “general assessment” with the purpose of emphasizing the level of reliability of this colposcopic examination [12]. In our study, 1.25% (147/1838) of all patients had inadequate colposcopic examination. The main reason was bleeding, others included scarring of lacerations, vaginal wall relaxation, changes in cervical position (hysteromyoma compression, adhesion), inflammation and neoplasm. This reminds us colposcopic operation should be gentle, so as not to artificially caused contact bleeding, especially near the endocervical canal. For changes in cervical position, we can use tools such as cervical clamp when necessary to help fully exposing the cervical transformation zone. If there is cervical neoplasm, it should be pushed in different directions in order to see the transformation zone at 360°. The squamocolumnar junction was completely visible in 334 (334/1838, 18.17%). “Partially visible” and “not visible” are respectively defined as mostly visible and most or all invisible of the squamocolumnar junction because it is in the endocervical canal. We think the definitions of “partially visible” and “not visible” are ambiguous. The degree of “most of the squamocolumnar junction visible and not visible” is difficult to grasp. We suggest the visibility of squamocolumnar junction in the range of 0°–360° is defined as “partially visible” with visible rang indicated as necessary. For example, the squamocolumnar junction is partially visible from 90° to 180°. It is also suggested “not visible” means the squamocolumnar junction can not be seen at all.

Once the highlight but now the controversy of 2011 IFCPC nomenclature is cervical TZ. The authors' supposition of TZ is that it advances a closer relationship to therapeutic strategies and leads to individualized treatment [39]. Type1, 2, 3 excisions with removal of different rang of ectocervical and endocervical tissue resect type 1, 2, 3 TZ. However, in clinical practice of several years, the reproducibility of TZ in different examiners has been questioned. In this study, transformation zone types 1, 2, 3 accounted for 16.81% (309/1838, 16.81%), 1.36% (25/1838, 1.36%) and 81.83% (1504/1838, 81.83%). Li *et al*'s study of 525 cases indicated types 1, 2, and 3 of TZs accounted for 22.29%, 7.24%, and 70.48% [28]. Fan *et al*'s research showed 1005 cases (44.4%, 1005/2262) were classified as type 2 TZ, 887 (39.2%, 887/2262) as type 1 and 370 (16.4%, 370/2262) as type 3 TZ [29]. It was significantly different between the distributions of the three types TZ in our and Fan *et al*'s studies, especially of type 2 TZ. In the Germany analysis of 3761, 2153 cases (57%) were classified as type 2 TZ, 906 cases (24%) were type 1 TZ, 702 cases (19%) were type 3 TZ, and significant heterogeneity of TZs in different clinics was showed [40]. In 2017, ASCCP claimed that literature suggested the use of TZ type unrepeatable, especially for type 2 TZ, and there was no evidence showed TZ type can improve the prediction or management of cervical disease [35, 40]. Therefore, TZ types were not incorporated in the 2017 ASCCP terminology. We suggest on one hand, more studies should focus on the precise extent especially the “length” of excision for different TZ types, the necessity of existence of type 2 TZ and more precise anatomic distinction between types 1 and 2 TZ. On the other hand, if evidence-based research suggests that the TZ has clinical significance, further effort to reduce heterogeneity in the classification of TZ types between individual examiners is of importance. The squamocolumnar junction is the inner margin of cervical TZ. Correctly identifying the mature columnar epithelium and then confirming the squamocolumnar junction is the key to correctly identifying the TZ.

Acetowhite epithelium is a core finding in colposcopy. Dense aceto-white epithelium had good specificity, PPV and NPV for HSIL. Major changes such as coarse mosaic, coarse punctuation, cuffed crypt openings and sharp border all had high specificity for HSIL. Two new signs, inner border sign and ridge sign also showed good diagnostic value. Compared with the major changes, the diagnostic value of minor changes signs was not satisfactory. The specificity of thin aceto-white epithelium was 59.02% and PPV 53.15%. The sensitivity of fine punctuation and fine mosaic were quite low. It should be pointed out that the definition of the dense or thin aceto-white is subjective and relative, which should be combined with

the type of HPV infection, the patient's age and so on. Massad et al. suggested all acetowhite lesions should be biopsied to improve sensitivity [32]. ASCCP recommended that for high-risk screening results, the biopsy of mild or translucent acetowhite changes was also necessary [25]. Actually, several signs such as punctation, mosaic, sharp border and even the new signs of both major and minor changes were highly specific and less sensitive because they occurred less frequently in cases. This makes them less diagnostic in daily clinical practice. Therefore, we attempted to find a sign with high frequency as acetowhite changes. As we all know, the significance of Lugol's staining was diminishing, from major changes section, minor changes section to the "nonspecific" category of the "abnormal colposcopic findings" section in 2011 Colposcopic Terminology. Our study confirmed Lugol's staining negativity had a high sensitivity and NPV while the specificity was low. Although we suggested Lugol's staining was useful in delineating the boundaries of normal and abnormal tissue, identifying vaginal lesions and lesions of no obvious acetowhite changes after menopause. Lugol's staining had high NPV. Lugol's staining negativity was divided into bright and mustard yellow. We investigated the diagnostic value of bright yellow for LSIL and mustard yellow for HSIL. As a result, mustard yellow may be a valuable indicator for the diagnosis of HSIL. We believe Lugol's staining still has certain diagnostic value of colposcopy and is the necessary procedure in colposcopic performance.

## Conclusion

Going forward, we provide some recommendations to improve colposcopic diagnostic accuracy in an environment of HPV vaccination and HPV-based screening. Firstly, colposcopic terminology needs to be further refined. Signs of non-HPV 16 infection and new valuable signs need to be found. Further research is needed to confirm the existence of TZ. Secondly, colposcopy referrals should be further clarified to avoid excessive examination and insufficient examination in HPV-based screening. Thirdly, with the proper help of some biomarkers such as p16, improve the quality control of cytology, HPV detection and histopathology, so as to provide more accurate and objective clinical data for colposcopists. Fourthly, colposcopy technique is always an evolutionary process. Novel colposcopy techniques such as optical spectroscopy, computer-assisted colposcopy, electrical impedance spectroscopy, dynamic spectral imaging, confocal endomicroscopy and optical coherence tomography will need to improve and develop [41]. Last but not least, ensure the quality control of colposcopy, improve the diagnosis level of colposcopists. Adequate high-quality training and certification process for colposcopists need to be implemented. Practice makes perfect. Colposcopists should have adequate expertise and support to fulfill their role. For example, if sufficient studies confirm that the TZ is guiding for the extent of cervical conization, then we should improve the ability to accurately identify the TZ rather than denying its existence due to poor repeatability. There is no better choice than colposcopy, but there is no better choice for colposcopy than more standardized quality assurance. In this way, the benefits of changes in screening strategies can truly translate into the reduction in the incidence and mortality of cervical cancer [23].

## Abbreviations

IFCPC, International Federation of Cervical Pathology and Colposcopy; HPV, human papilloma virus; HSIL, high-grade squamous intraepithelial lesion; LSIL, low-grade squamous intraepithelial lesion; RCI, Reid Colposcopic Index; ASCCP, American Society for Colposcopy and Cervical Pathology; TZ, transformation zone types

## Declarations

### Ethics approval and consent to participate

All patients signed an Informed Consent Form after being informed about the project, understanding the terms, and clarifying possible questions about the research. The study received ethical approval from the Medical Ethics Committee of Shandong Provincial Qianfoshan Hospital, Shandong University(2020S554).

## Consent for publication

All authors have given consent to publish.

## Availability of data and materials

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

## Competing interests

All authors have declared no competing interests.

## Funding

This study was supported by Shandong Medical and Health Science and Technology Development Project (No.2017WSB04051) mainly on the data collection , manuscript writing and editing.

## Authors' contributions

BZ and FNR were responsible for the conception and design of the study. BZ, GHZ, SHH collected the data. BZ, SHH analyzed the data. BZ interpreted the data. BZ wrote the manuscript. All authors have read and approved the manuscript.

## Acknowledgements

The authors would like to thank Dr Fang Tang and Yafei Liu for their help in data analysis. The authors also acknowledge the assistance of Mark Abramovitz, PhD for editing the English text of a draft of this manuscript.

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