Significance of diagnostic of hpv testing and cytoscopic studies in the aspect of gynecological screening detecting cervical pathology in women

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Abstract. The purpose of this article was to identify the diagnostic significance of HPV testing and cytoscopic examination in terms of cervical pathology. In the course of this study during 2020-2021. 10,716 women aged 25-65 years were examined, who did not present complaints, indicating gynecological pathology and did not have a history of erosive lesions of the cervix. In the course of the study, the sensitivity, specificity and diagnostic significance of the HPV PCR test and cytoscopic examination were calculated in terms of detecting cervical pathology in women during the screening examination. A colposcopic examination was considered a method of verifying the diagnosis. HPV by PCR in the cervical mucosa during the screening process is detected in 23.77% of women. The frequency of infection decreases with increasing age of the subjects. The combination of positive HPV and cytology as a risk marker does not increase the diagnostic value of primary screening based on the use of methods in isolation.

1 Introduction

There is a clear increase in the incidence in young women under 40 years of age. In Uzbekistan, cervical cancer is the second most common cancer among women of all ages and the second most common cause of death among women of childbearing age after breast cancer. Most of these deaths are due to late diagnosis. In this regard, the most pressing issues are to improve the detection, diagnosis and prevention of precancerous and cancerous diseases of the cervix.

Human papillomavirus (HPV) is a DNA-containing virus that infects epithelial cells. There are more than 200 types of HPV, which clinical manifestations of infection vary from asymptomatic, the development of simple papillomas and genital warts to squamous and invasive carcinomas of the mucous membranes.

A likely mechanism linking HPV infection and the development of CC is the ability of the virus to epigenetically inhibit the tumor suppressor gene [1, 2] and disrupt the regulation of cell mitotic activity, affecting the G1 phase of the cell cycle [3] by methylating cell DNA [4, 5]. Also, HPV, like other viruses, penetrating into the cells of the

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immune system, triggers the methylation of signaling proteins, changing their informative function and disrupting the complex cascade of interactions of specific immunity effectors [6, 7].

The prevalence of HPV is up to 40% in the general population, peaks between the ages of 14 and 30, when transient HPV infection predominates, and declines with age. Among patients with cervical cancer, the incidence of HPV is 99.7% [8].

Today, in many countries, primary screening programs have been reorganized in favor of high-risk HPV (rHPV) testing, especially in women over 30 years of age.

The use of rHPV tests as primary screening for cervical cancer has several advantages.Randomized controlled trials and meta-analyses of randomized data demonstrate level A evidence that the HPV test has higher sensitivity and negative predictive value in detecting advanced stages of the disease compared to cytology. Screening based on HPV is 60-70% more informative in terms of detecting invasive cervical cancer in women older than 30 years compared to cytology [9-15]. This advantage is especially pronounced in relation to glandular lesions. Higher sensitivity allows for a longer screening interval: typically 5 years for a negative result, compared to 3-5 years and even more often for cytological screening. rHPV is an objective test with high inter and intra variability. The test can be carried out in centralized laboratories to ensure quality control. Also, the test practically does not require special technical skills to evaluate the result. This reduces the requirements for staff, in particular the presence of a cytopathologist with specific skills that require periodic retraining and recertification. hrHPV test allows to reduce the number of unsatisfactory screening results, self-collection of material with a sensitivity comparable to a medical procedure, with somewhat less specificity, is possible. Self-collection of material is a good alternative for countries with a low level of healthcare organization, as well as for women living in remote and hard-to-reach regions.

2 Materials and methods

In the course of this study during 2020-2021. 10,716 women aged 25-65 years (mean age - 43.28±3.82 years) were examined, who did not present complaints, indicating gynecological pathology and did not have a history of erosive lesions of the cervix. All examined women underwent a PCR test to detect HPV DTCs in the cells of the cervical mucosa. Cells were obtained by taking with a special brush. As a result, groups of HPV-positive (HPV+) and HPV-negative (HPV-) women were identified. Also, all the subjects underwent an examination of the cervix in gynecological mirrors to visually determine the state of the mucosal epithelium and cytological examination by the Papanicolaou method. During the examination, all examined women were divided into a group with unchanged cervical mucosa (PAP-) and a group with erosive changes in the cervical mucosa.

All women included in the HPV+ and PAP+ groups underwent colposcopy and biopsy of the cervical mucosa. In case of detection of LSIL, electrocoagulation of the affected area of the cervix mucosa was performed, HSIL - electroconization, carcinomas - hysterectomy.

During the study, the number of women with indications for various treatment options for cervical pathology was recorded, depending on the algorithm of diagnostic tactics.

3 Results and discussions

In the course of the study, the sensitivity, specificity and diagnostic significance of the HPV PCR test and cytoscopic examination were calculated in terms of detecting cervical pathology in women during the screening examination. A colposcopic examination was

considered a method of verifying the diagnosis. The general methodology and calculation results for various pathologies of the cervical epithelium are presented in Table 1.

As can be seen from the presented data, in terms of detecting the pathology of the cervical epithelium, both in general and in individual variants, the HPV test had a higher sensitivity (above 94%) compared to the cytological study, which showed high sensitivity only for detecting ACSUS. (91.07%) and low sensitivity in terms of identifying other pathology variants (28.57%-57.23%).

Table 1. Specificity, sensitivity and diagnostic significance of the HPV test and cytological examination in terms of detecting the pathology of the cervical epithelium.

Detectable pathology	critical+	critical-	Sensitivity	Specificity	Diagnostic significance
Method of calculation					
Pathology+	a	c	a/(a+c)	d/(b+d)	(a+d)/ (a+b+c+d)
Pathology-	b	d			
Epithelial pathology (cervical cancer)					
PCR	1322	63	95.45	86.87	87.98
	1225	8106			
Cytology	940	445	67.87	98.32	94.38
	157	9174			
acsus					
PCR	644.00	39.00	94.29	81.03	81.88
	1903.00	8130.00			
Cytology	622.00	61.00	91.07	99.07	98.56
	93.00	9940.00			
LSIL					
PCR	477	21	95.78	79.74	80.49
	2070	8148			
Cytology	285	213	57.23	99.94	97.96
	6	10212			
hsil					
PCR	194	3	98.48	77.63	78.01
	2353	8166			
Cytology	86	111	43.65	99.97	98.94
	3	10516			
Carcinoma					
PCR	7	0	100.00	76.28	76.30
	2540	8169			
Cytology	2	5	28.57	100.00	99.95
	0	10709			

The specificity of the PCR test (76.3%-21.03%, in general - 86.87%), on the contrary, turned out to be significantly lower than that of the cytological study (99.07-100%, in general - 98.32%). The diagnostic significance also turned out to be higher in the cytological study compared to the HPV test.

The indicators of sensitivity, specificity and diagnostic significance of the combination of positive results of the HPV test and cytological examination were also calculated. The combination of a positive HPV test and a cytological study occurred in 536 women. Of these, 532 colposcopically revealed pathology of the epithelium of the cervix.

Thus, the sensitivity of this combination in terms of detecting pathology was 38.41%, specificity - 99.96%, diagnostic significance - 92.00%. The highest sensitivity was noted in the aspect of diagnosing ASCUS (47.02%), specificity - cervical cancer (one hundred%). The diagnostic significance was comparable for all variants of epithelial pathology and exceeded 94% (Table 2).

Table 2. Specificity, sensitivity and diagnostic significance of a combination of a positive HPV test and a cytological examination in terms of identifying various pathologies of the cervical epithelium.

Detectable pathology	critical+	critical-	Sensitivity	Specificity	Diagnostic significance
ascus	300 / 81	338 / 9997	47.02	99.20	96.09
lsil	105 / 4	393 / 10074	21.08	99.96	94.99
hsil	43 / 1	154 / 10077	21.83	99.99	94.44
c-r	2 / 0	5 / 10078	28.57	100.00	94.06

Note: (the calculation method is given in Table 2, in the numerator - pathology +, in the denominator - pathology -)

Thus, the study showed that in terms of detecting the pathology of the cervical epithelium, a positive HPV test has high sensitivity, but low specificity, and a positive result of a cytological study has high specificity, but low sensitivity. The informativeness of the combination of positive results of HPV and cytological tests does not have an advantage with a cytological examination.

4 Conclusion

HPV by PCR in the cervical mucosa during the screening process is detected in 23.77% of women. The frequency of infection decreases with increasing age of the subjects. The sensitivity of HPV as a screening for HSIL is 98.48%, CC is 100%, specificity is 77.63% and 76.28%, diagnostic significance is 78.01% and 76.30%, respectively. The combination of positive HPV and cytological examination as a risk marker does not increase the diagnostic value of primary screening based on the use of methods in isolation (sensitivity as a screening for HSIL 21.83%, cervical cancer - 28.57%, specificity - 99.99% and 100%, diagnostic significance - 94.44% and 94.06%, respectively).

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