Preplanned Studies

Multiple Center Research on Relationship Between Screening Quality and Detection of Cervical Cancer — Six Provinces, China, June–December 2021

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Summary

What is already known about this topic?

The effective implementation of cervical cancer examination programs requires improved cervical cancer screening coverage and quality.

What is added by this report?

The detection rate of ≥ high-grade squamous intraepithelial lesion (HSIL) in 6 hospitals was 19.6%. Not having underwent screening in the last 5 years and abnormal screening results had a negative association with detection of ≥HSIL, and abnormal screening results would increase the risk of detection by 75% compared with normal screening results. Additionally, low grade, high grade, and cancer of colposcopic impression were associated with a higher risk for detecting ≥HSIL.

What are the implications for public health practice?

It is essential to disseminate health knowledge about cervical cancer control to women in order to increase their awareness and screening rates. Additionally, it is necessary to further strengthen the training of professional staff to improve the quality of cervical cancer prevention, including screening, colposcopic examination, and follow-up for target female populations.

The coverage and quality of screening are essential for reducing the incidence of cervical precancers and cervical cancer. This multicenter study aimed to investigate the relationship between screening quality and the detection of cervical precancers and cervical cancer. The study was conducted from June to December 2021 in six hospitals across six provinces. The 2,945 participants were non-pregnant women who underwent colposcopy examinations. The average age of participants was 40.9±11.5 years old. Only 6.9% of participants had received human papillomavirus (HPV) vaccination. A total of 92.6% of participants had abnormal cervical screening results. Of the participants, 577 had high-grade squamous intraepithelial lesion (HSIL) or worse (≥HSIL), with a detection rate of 19.6%. Univariate analysis indicated that a lack of cervical cancer screening history in the past five years, as well as positive cervical screening and abnormal colposcopic impression, were independent associated factors of the ≥HSIL detection rate. A multivariable logistic regression showed that positive cervical screening [odds ratio (*OR*) = 1.75, 95% confidence interval (*CI*): 1.07–2.86] was a risk factor for detecting ≥HSIL. Low-grade, high-grade, and cancer of colposcopic impression were associated with a higher risk for detecting ≥HSIL (*OR*=2.94, 95% *CI*: 2.13–4.08; *OR*=36.64, 95% *CI*: 26.07–51.48). It is important to disseminate health knowledge to improve public awareness of cervical cancer prevention and to enhance capacity building of professional staff to improve the quality of cervical cancer screening.

Cervical cancer was the second most common cancer and the second leading cause of cancer-related death among women of reproductive age worldwide in 2020, with 604,127 new cases and 341,831deaths (*1*). Of these, 88.1% of the new cases and 91.4% of the deaths occurred in low- and middle-income countries. In 2016, China reported 98,900 new cases and 30,500 deaths due to cervical cancer (*2*). Cervical cancer can be prevented through vaccination and screening with appropriate follow-up and treatment (*3*). Early detection and treatment of cervical precancers are also key to successful prevention. Cervical precancers include HSIL and adenocarcinoma in situ (AIS). Cervical cancer screening, colposcopy, and pathology are three steps for diagnosing cervical precancers. Therefore, the coverage and quality of screening are essential to reduce the incidence of cervical precancers. The objective of this multicenter study was to investigate the relationship between screening quality

and the detection of cervical precancers and cervical cancer in hospitals, providing evidence to improve cervical control for the target population in health facilities.

The study sites were six hospitals in six provinces: Peking University First Hospital, Sichuan Provincial Maternity and Child Health Care Hospital, Women's Hospital Zhengjiang University School of Medicine, Yanbian Maternal and Child Health-Care Hospital, Changzhou Maternal and Child Health Care Hospital, and The Maternal and Child Health Hospital of Guangxi Zhuang Autonomous. The participants were all non-pregnant women who underwent colposcopy examination in the study hospitals from June to December 2021. Biopsy was performed after colposcopy examination, followed by biopsy specimens for pathological diagnosis. The collected data included age, cervical cancer screening history, HPV vaccination, cervical cancer screening, colposcopy examination, and pathology results. All the colposcopy doctors in the six hospitals had received training in colposcopy operation. The study was approved by the Biomedical Research Ethics Committee of Peking University First Hospital, with the ethic code 2020[321]. Finally, among 3,637 women, 2,945 participants were analyzed. The exclusion criteria included incomplete data collection. The outcome of this study was the detection of cervical precancers and cervical cancer (≥HSIL). SPSS 26.0 software (IBM, Armonk, NY, USA) was used for statistical analyses, and $P<0.05$ was considered a statistically significant difference. Continuous variables were expressed as mean±standard deviation (SD); categorical variables were expressed as numbers and percentages; comparisons among groups were performed by Chi-square tests or Fisher exact tests as appropriate. Multivariable logistic regression models were used to evaluate the association between risk factors and detection of ≥HSIL.

The average age of participants was 40.9±11.5, ranged from 19 to 80 years old; 17.4% (511/2,945) were ≤29 years, 34.1% (1,003/2,945) were 30–39 years, 23.6% (696/2,945) were 40–49 years, 18.2% (536/2,945) were 50–59 years, and 6.8% (199/2,945) were ≥60 years. Only 6.9% (204/2,945) of participants had received HPV vaccination, with 4.3% (127/2,945) having completed the three-dose regimen. Additionally, 50% (1,473/2,945) of participants had a cervical cancer screening history within the past five years.

Among 2,945 participants, 80.6% (2,373/2,945) received HPV combined cytology co-testing screening, while 19.4% (572/2,945) received cytology screening. Overall, 92.6% had abnormal cervical screening results, including cytology ≥atypical squamous cell of undetermined significance (ASC-US) or HPV positive, or both abnormal cytology results and HPV positive. Only 7.4% underwent colposcopic examinations for abnormal symptoms. According to the colposcopic impression, 34.1% (1,004/2,945) of participants were normal/benign, 48.4% (1,426/2,945) were low grade, 16.0% (470/2,945) were high grade, and 1.5% (45/2,945) were cancer. Through biopsy and pathology diagnosis, 80.4% (2,368/2,945) were ≤low grade squamous intraepithelial lesion (LSIL); 537 participants were HSIL, the percentage was 18.2%; 13 participants were AIS, the percentage was 0.4%. Additionally, 27 women (0.9%) were diagnosed with invasive cervical cancer (ICC). The participants with ≥ HSIL totaled 577, the detection rate was 19.6%. Of these 577 participants with ≥HSIL, 471 (81.6%) had HPV combined cytology co-test for cervical cancer screening and 106 (18.4%) had cytology tests for cervical cancer screening (Figure 1).

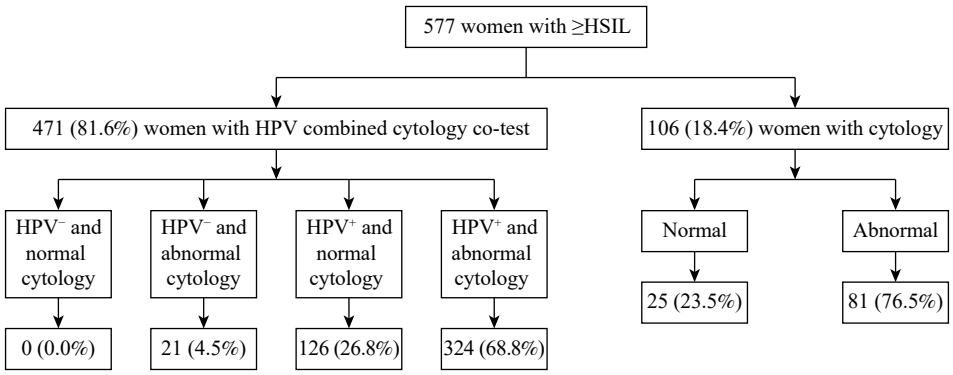

FIGURE 1. Distribution of ≥HSIL with different screening methods (*n*,%) — six provinces, China, June–December 2021.
Abbreviation: HSIL=high-grade squamous intraepithelial lesion; HPV=human papillomavirus.

The results of Table 1 indicated that a lack of cervical cancer screening history within the past 5 years, as well as a positive cervical screening and abnormal colposcopic impression, were independent associated factors of ≥HSIL detection. The results of multivariable logistic regression to evaluate the associations between clinical risk factors and ≥HSIL are presented in Table 2. Positive cervical screening was found to be a risk factor for detecting ≥HSIL (*OR*=1.75, 95% *CI*: 1.07–2.86). Additionally, low grade, high grade, and cancer of colposcopic impression were associated with a higher risk for detecting ≥HSIL (*OR*=2.94, 95% *CI*: 2.13–4.08; *OR*=36.64, 95% *CI*: 26.07–51.48).

DISCUSSION

In our study, the detection rate of ≥HSIL in six hospitals was 19.6%. Having no cervical cancer screening history in the past five years, a positive cervical screening, and an abnormal colposcopic impression were identified as clinical risk factors for detecting ≥HSIL.

Our study showed that the detection rate of ≥HSIL was 19.6%, which is similar to the results of other studies. A study from Chongqing Hospital reported that among 1,055 participants, 211 cases were ≥ Cervical Intraepithelial Neoplasia 2 (CIN2), resulting in a detection rate of 20% (*4*). Previous studies have reported that the detection of CIN and ICC ranged from 4.1 to 6.0 per 1,000 in different age groups with different cervical cancer screening methods in the general population (*5*). In hospitals, most patients had abnormal cervical screening results, making them a high-risk population, thus the detection rate of cervical cancer was much higher than in the general

TABLE 1. Characteristics of participants by detection of ≥HSIL (*n*,%) — six provinces, China, June–December 2021.

Clinical risk factor	≤LSIL*, *n* (%)	≥HSIL*, *n* (%)	χ^2	*P*
Age (years)			5.38	>0.05
≤29	405 (79.3)	106 (20.7)		
30–39	792 (79.0)	215 (21.0)		
40–49	572 (82.2)	124 (17.8)		
50–59	443 (82.6)	93 (17.4)		
≥60	156 (77.9)	43 (22.1)		
HPV vaccination			4.93	>0.05
Yes	163 (79.9)	41 (20.1)		
No	2,205 (80.4)	536 (19.6)		
Cervical cancer screening history in 5 years			32.82	<0.001
Yes	1,137 (82.7)	217 (17.3)		
No	1,158 (78.1)	320 (21.9)		
Unknown	73 (64.5)	40 (35.4)		
Cervical cancer screening method			0.51	>0.05
Cytology	466 (81.5)	106 (18.5)		
HPV combined cytology co-test	1,902 (80.2)	471 (19.8)		
Cervical cancer screening results this time			13.10	<0.001
Abnormal	2,018（79.4）	525 (20.6)		
Normal	350（87.1）	52 (12.9)		
Colposcopic impression†			759.68	<0.001
Normal/benign	953 (94.9)	51 (5.1)		
Low grade	1,237 (86.7)	189 (13.3)		
High grade	177 (37.7)	293 (62.3)		
Cancer	1 (2.2)	44 (97.8)		

Abbreviation: HSIL=high-grade squamous intraepithelial lesion; LSIL=low grade squamous intraepithelial lesion; HPV=human papillomavirus.

* ≤LSIL includes normal cervix and LSIL; ≥HSIL included HSIL and ICC.

† The Fisher exact test was used due to the small sample size of one cell (<5).

TABLE 2. Multiple logistic regression analysis of related clinical factors on detection of ≥HSIL — six provinces, China, June–December 2021.

Risk factor	Detection of ≥HSIL		
	*OR**	95% *CI*	*P*
Cervical cancer screening results			
Normal	Ref.		
Abnormal	1.75	1.07–2.86	<0.050
Colposcopic impression			
normal/benign	Ref.		
low grade	2.94	2.13–4.08	<0.001
High-grade and malignant cancers	36.64	26.07–51.48	<0.001

Abbreviation: HSIL=high-grade squamous intraepithelial lesion; *OR*=odds ratio.
* Adjusted for age, HPV vaccination, and cervical cancer screening history in the past 5 years.

population.

Our study also indicated that without screening in 5 years and abnormal screening results had a negative association with the detection of ≥HSIL, especially abnormal screening results would increase the risk of detection by 75% compared with normal screening results. Cervical cancer screening history was a risk factor of advanced stage of cervical cancer; a study from Denmark found that the less advanced invasive cervical cancer stage (stage I) was 3.14 times higher given adequate attendance to cervical cancer screening programs, with 61.6% of patients having deficient screening histories (*6*). An American research also indicated that 60% of women aged 21 years and older who were diagnosed with invasive cervical cancer had no cervical cancer history among 367 participants (*7*). Cervical cancer screening programs have been conducted by the Chinese Government since 2009, but only half of the participants attended screening in the last 5 years in our study. The percentage of deficient screening histories in our study was slightly lower than those of previous studies (*6*–*7*), which may be related to the different age range and observation indicators. The study reported that abnormal cervical cancer screening results were a risk factor of the detection rate of HSIL and ICC (*OR*=1.75). A woman who has cervical cancer screening just one time in her life after 35 years old, her risk of dying from cervical cancer would decrease by 70%. If she is screened every 5 years, her risk of dying from cervical cancer drops by more than 85% (*8*). Therefore, cervical cancer screening is an efficient secondary preventable measure; it is not only about screening on time, but also a long-term management strategy for controlling cervical precancers and cancer. According to the report about cervical cancer screening coverage estimates of 202 countries, 1.6 billion (67%) of 2.3 billion women aged 20–70 years had never been screened for cervical cancer (*9*). In China, the population-based screening rate is lower (*10*). It is necessary to conduct more extensive health education to enhance awareness of cervical cancer among the target population, and then to increase the initiative screening rate.

Colposcopy examination is a key method for diagnosing cervical precancer as a second step, and it requires a more professional and trained doctor. According to the quality control manual of cervical screening, the high-grade coincidence rate between colposcopy impression and biopsy should be ≥60% (*11*). The coincidence rate in our study was 62.3% (HSIL), meeting the quality control requirement. The doctors in the six study hospitals have received training, which has enabled them to provide high-quality colposcopy examinations and improve the detection rate of cervical precancer.

HPV vaccination is an important primary prevention method; however, due to the low vaccine coverage rate, it has not been a significant factor in our study. Most women were screened by HPV combined cytology co-test, but the detection rate of cervical precancers did not differ significantly between different screening methods. The detection rate was mainly influenced by the quality of colposcopy and the screening results. There were several limitations to our study. Firstly, we focused mainly on clinical factors affecting the detection rate of cervical precancers in medical facilities, not including social factors. Secondly, most participants underwent colposcopy examination due to abnormal cervical cancer screening results, and few participants underwent colposcopy examination for abnormal symptoms; however, we did not collect more detailed information on abnormal

symptoms. Finally, in this study, we only collected data from participants who underwent colposcopy examination, and the cervical cancer screening results may have come from different health facilities or different screening methods, so we could not compare the relationship between screening quality and detection of ≥HSIL. Therefore, further research with larger populations, higher quality, and multiple sites is needed in the future.

The World Health Organization's cervical cancer elimination campaign must increase both screening coverage and treatment of detected cervical precancers (*9*). Our study indicated that cervical cancer screening and colposcopy impression were the main clinical influencing factors in health facilities. To achieve elimination goals, it is essential to disseminate health knowledge to improve public awareness of cervical cancer prevention and to enhance capacity building of professional staff to improve the quality of cervical cancer screening.

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