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Clinical Value Analysis of "Internet +" Artificial Intelligence Assisted Diagnosis of Cervical Intraepithelial Lesions

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Abstract: Artificial intelligence (AI) can automatically detect abnormalities in digital cytology images, but its effectiveness in cervical cytology remains to be studied. Our objective was to evaluate the performance and clinical value of "Internet +" AI-assisted cytology in the detection of cervical intraepithelial lesions. A total of 7,225 women were tested for cervical cancer at Qinghai Red Cross Hospital. Cervical epithelial cells were collected with a cervical brush. After fixation, the cervical cell samples were prepared by ThinPrep method in the laboratory and then stained with Feulgen+EA50. After staining, cell images and other data were sent to Ali Cloud by cell scanner. The AI-assisted cytology system in the cloud was used for analysis, and each tested cell was scored. The cell technician first classified the cell samples as negative or positive based on the score of each sample, and then made the diagnosis by reviewing 100% positive samples and 10% negative samples. Each woman with abnormal cytology (including low-grade squamous intraepithelial lesion [LSIL], atypical squamous cells where it was not possible to exclude high grade squamous intraepithelial lesion [ASC-H] and high squamous intraepithelial lesion [HSIL]) identified by either AI or cytologists was refered to colposcopy and biopsy for histological confirmation, and women with atypical squamous cells of undetermined significance (ASC-US) were recommended for an reexamination during 6-12 months. Of these, 698 women underwent colposcopy and histopathology. Results Colposcopy-directed biopsies were performed in 698 women with abnormal cytology diagnoed by either AI or cytologists. The biopsy identified 67 invasive cancer, 64 cervical intraepithelial neoplasia grade 3 (CIN3), 43 cervical intraepithelial neoplasia grade 2 (CIN2), 98 cervical intraepithelial neoplasia grade 1 (CIN1), and 426 cervicitis. By comparing the coincidence rate of cervical cytology and histopathological diagnosis, it could conclude that the detection of CIN2+ among women with HSIL, ASC-H, LSIL, and ASC-US was 92.31%, 77.55%, 32.26% and 7.63%, respectively. If LSIL was used as the positive criterion, the sensitivity of AI in diagnosing CIN1+, CIN2+ and CIN3+ was 69.49%, 82.76% and 83.97%, respectively. In addition, it was found that with the increase of cytological diagnostic level by AI technology, the pathological level of patients also gradually increased. The "Internet+" AI diagnostic technology can assist cytologists in diagnosis, and it has certain clinical value for the early diagnosis of cervical cancer. Further research is needed to apply this technique to more population samples.

1. Introduction

Cervical cancer is one of the frequent common tumors in female. Cervical cytology can detect early cervical cancer changes, timely treatment measures can effectively improve the prognosis of patients. Traditional cytology is diagnosed by pathologists under a microscope, but its sensitivity varies greatly due to the inconsistency of doctors in hospitals and the difficulty of quality control. In the last decade, high-risk HPV tests have been increasingly used in the clinic.

Although cytologist sensitivity has been reported to be lower than that of the HPV technique, the sensitivity is within acceptable ranges and the specificity is good. Cytologists, however, use the traditional method by reading a cell slide manually under a microscope. In the past decade, artificial intelligence (AI) technology based on deep learning algorithm has been developed, and with the rapid development and increasing popularity of information technology, the tide of information has also promoted the innovative development of cytology assisted diagnosis technology. The deep integration of “Internet +”, “artificial intelligence” and medical diagnosis technology can not only fundamentally solve the pain points of grass-roots diagnosis, but also improve the accuracy and diagnosis speed.

Based on years of research and training of millions of cervical specimens, this study used cervical cytopathological AI diagnostic technique in clinical cervical sample detection to explore the performance and clinical value of this technique in cervical intraepithelial lesions (CIN).

2. Materials and Methods

2.1 Source of Specimens

From January 2020 to May 2021, a total of 7225 women aged 16 to 88 years in Qinghai Red Cross Hospital underwent cervical cytology, and cervical cytology samples were collected by conventional method. Specimens were prepared with the liquid-based thin layer, and the kit was provided by Wuhan Landing Medical Intelligence Co., LTD. (Landing Med). After manufacturing flakes, Feulgen+EA50 staining was performed, and then the slides were used to AI-assisted film reading. Of these women, 698 women underwent colposcopy and histopathology..

2.2 Artificial Intelligence Assisted Diagnosis Technology

In this paper, the artificial intelligence diagnosis method mainly adopted the convolutional neural network obtained by data training, and obtained the abnormal score of a single cell which image diagnosed by the trained convolutional neural network, namely, the analysis results of intelligent diagnosis. The samples were screened in the cervical cancer screening program organized by the Chinese government and training data were extracted from them. After each sample was transformed into digital images through microscanner, the nuclei were identified and labeled by professional cell technicians to build a cytopathological database. The convolutional neural network algorithm was used to mine the characteristics of the tumor cells from the database, that is, the location and contour of each cell, and the tumor cell recognition model was constructed. The model took detected cell images as input and cell malignancy score as output to assist cell doctors in interpreting and improved the efficiency of diagnosis. The model had been deployed on the cloud platform to receive and process samples uploaded by scanning terminals, which realized remote and real-time AI-assisted diagnosis.

2.3 Histopathological Examination

According to WHO pathological criteria, 698 cases were diagnosed as different types of cervicitis, cervical intraepithelial neoplasia grade 1 (CIN1), cervical intraepithelial neoplasia grade 2 (CIN2), cervical intraepithelial neoplasia grade 3 (CIN3) and cervical cancer. CIN2 and CIN3 are high-grade precancerous lesions.

2.4 Diagnosis Process

These women were registered and had cervical cell samples taken at the Qinghai Red Cross Hospital. The samples were placed in cell preservation solution for liquid based procedure with ThinPrep method, which were followed by staining and scanning in the laboratory. Thecell image data were uploaded to the cloud, and then analysed and processed by AI diagnostic system from cloud platform of Landing Med. Cell technicians or doctors reviewed the results diagnosed by AI and made the last diagnosis. Cytological results which were negative were automatically sent to the women and the hospital. If the cytological results were positive, the women required further colposcopy or cervical histological biopsy. Biopsy specimens were histopathologically diagnosed by pathologists. In the case of precancerous lesions (CIN2 or CIN3) or invasive cervical cancer, these women required further treatment at the hospital. In the case of cervicitis or CIN1, cervical cytology was recommended after 1 year.

2.5 Statistical Analysis

To evaluate the performance of the method, histological biopsy results were used as the gold standard. Women were biopsied under a colposcope, so the sensitivity and specificity of the AI diagnostic techniques we calculated were objective. Sensitivity and specificity were calculated according to standard formulas.

3. Results

From January 2020 to May 2021, 7225 women underwent AI-assisted cytology and 698 women with cytological abnormalities underwent colposcopy and histological biopsies. The proportion of AI-assisted cytological abnormalities was 15.43%, among which the proportions of ASC-US, LSIL and ASC-H/HSIL were 9.39%, 4.66% and 1.38%, respectively (Table 1). Among the 698 cases of cervical biopsy, 426 cases were diagnosed as cervicitis, 98 cases were CIN1, 43 cases were CIN2, 64 cases were CIN3 and 67 cases were invasive cancer (Table 2).

Table 1 7225 cytological diagnosis results of cervical samples

TBS diagnosis	The number of cases	Ratio
Normal	6110	84.57%
ASC-US	678	9.39%
LSIL	337	4.66%
ASC-H	58	0.80%
HSIL	42	0.58%
Total	7225	100.00%

Table 2 Comparison of cytological and histological results of 698 cervical biopsy samples

Pathological Diagnosis	AI-TBS Diagnostic Classification			
	ASC-US	LSIL	ASC-H	HSIL
Cervicitis(n=426)	310	103	10	3
CIN1(n=98)	53	44	1	

CIN2(n=43)	9	29	3	2
CIN3(n=64)	7	31	14	12
Cancer(n=67)	14	10	21	22

According to the coincidence rate of cytological diagnosis and histopathological diagnosis calculated by the data from Table 2, the detection of CIN2+ among women with HSIL, ASC-H, LSIL and ASCUS was 92.31 %, 77.55%, 32.26% and 7.63%, respectively (Table 3).

Table 3 Coincidence rate between cytology diagnosis and histopathological biopsy diagnosis (%)

AI-TBS Diagnostic Classification	Histopathology		
	Cervicitis	CIN1	CIN2 and above
ASC-US	78.88%	13.49%	7.63%
LSIL	47.47%	20.28%	32.26%
ASC-H	20.41%	2.04%	77.55%
HSIL	7.69%	-	92.31%

LSIL was used as the positive criterion, the sensitivity of AI in diagnosing CIN1+, CIN2+ and CIN3+ was calculated, and the results were shown in Table 4.

Table 4 Sensitivity and Specificity of Ai-Assisted Diagnosis for Cervical Intraepithelial Neoplasia (%)

	Sensitivity	Specificity
CIN1+	69.49%	72.77%
CIN2+	82.76%	69.27%
CIN3+	83.97%	65.61%

Note: Since no women with negative cytology were biopsied, the specificity calculated in Table 4 was for reference only.

987 samples were randomly selected and reviewed under the microscope by experienced pathologists. Of 809 AI-assisted negative diagnoses, 808 cases were manually negative, with a 99.9% coincidence rate (Table 5).

Table 5 987 Cervical cancer screening data reviewed under microscope

Category	AI	Manual Review					
		Normal	ASC-US	ASC-H	LSIL	HSIL	Total
Normal	809	808			1		809
ASC-US	113	13	94	2	3	1	113
ASC-H	2			2			2
LSIL	55	7	1		46	1	55
HSIL	8					8	8
Total	987	828	95	4	50	10	987

4. Discussion

Histopathological diagnosis was used as the gold standard to evaluate the level of AI cell diagnosis technology. In this study, HSIL and ASC-H were cytologically diagnosed, and the histopathological findings were 92.31% and 77.55% CIN2+, respectively. 20.28% of LSIL cases were CIN1, and 32.26% were CIN2+. This result was consistent with the results of several published articles and even had a higher coincidence rate. Only about 7.63% of ASCUS cases were CIN2+, which were not completely consistent with that of most published articles, but most of them were within 10%.

ASCUS percentage and ASC:SIL ratio are also used to measure the level of cellular diagnosis. A recent survey in more than 1500 hospitals of different levels in China found that ASC:SIL ratio was 1.3-2.1. The results showed that the ASC:SIL ratio was 1.6:1. Among 7225 patients with negative medical records, 809 were randomly selected for microscopic review, 808 were normal and 1 was LSIL. The coincidence rate between AI diagnosis and microscopic diagnosis was 99.9%. It indicated that AI diagnosis was less misdiagnosed in discriminating negative samples.

It takes 1 to 2 years to train a qualified cytology technician abroad, while cytopathologists need more time. However, the diagnosis level among cell technicians and cytopathologists is inconsistent due to different experience and mental state, resulting in strong subjectivity and great difference in diagnosis. Cellular AI diagnosis technology overcomes the disadvantages of manual subjective factors and long time personnel training, making the diagnosis level more consistent, and can work 24 hours a day, reducing the labor intensity and time of technicians and doctors.

The cell technicians who participated in the detection only had 2 to 3 months of cytology training, and they made positive or negative judgments based on the AI score of each sample and their own experience. Hologic launched ThinPrep Imaging System, which can also be used for cervical cancer screening. In this system, suspicious cells are picked out after scanning, and cell technicians observe suspicious cells under the microscope to make a judgment. Technicians using the AI system in this paper do not need to judge under the microscope, but directly judge the image, so that the work efficiency of cell technicians is significantly improved.

5. Conclusion

In conclusion, our results showed that AI-assisted cytology system had considerable accuracy in the diagnosis of histological CIN2+, and had high clinical value in the early diagnosis of cervical cancer. The data confirmed that “Internet +” AI diagnostic technology could achieve a high level of cell diagnosis, while reducing the labor intensity of doctors and technicians and improving their work efficiency.

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