Comparative Study on the Efficacy of High-Definition Electronic Amplification Endoscopy Combined with Image Enhancement Technology and Colposcopy in the Exploration of Cervical and Vaginal Pathologies

Research protocol

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I. Research Background

Colposcopy is currently an essential examination method for detecting cervical and vaginal lesions. However, traditional colposcopy has low magnification and limited field of view, resulting in limited identification of early cervical lesions. According to existing research reports, the diagnostic accuracy of colposcopy for low-grade lesions is only approximately 43.4%, while for high-grade lesions it ranges from 59% to 76%. High-definition magnified electronic endoscopy (100–150x) can clearly visualize microvessels and mucosal structures. In recent years, gastrointestinal magnified endoscopy combined with image enhancement techniques (e.g., NBI/BLI/LCI) has established a mature vascular and epithelial interpretation system for early esophageal squamous cell carcinoma diagnosis. The cervical, vaginal, and esophageal tissues share similar pathological evolution patterns of precancerous lesions and early carcinogenesis due to their stratified squamous epithelium. Theoretically, this technical system can be extended to the exploration of lower genital tract lesions. Preliminary single-center, small-sample studies in Japan suggest that this technology demonstrates superior diagnostic performance for high-grade cervical lesions compared to traditional colposcopy, but high-quality clinical validation remains lacking domestically. Therefore, this study aims to systematically evaluate the diagnostic efficacy of high-definition magnified electronic endoscopy combined with image enhancement techniques versus traditional colposcopy through rigorous paired diagnostic trial design, aiming to

provide clinicians with a more precise examination tool to address the limitations of current methods. The goal is to establish an endoscopic atlas for cervical and vaginal lesions and improve diagnostic accuracy.

II. Research Objective

1. Primary research objective: To compare the diagnostic accuracy of high-definition electronic magnification endoscopy combined with image enhancement technology versus colposcopy in detecting cervical and vaginal lesions.

2. Secondary research objectives: To evaluate and compare the sensitivity, specificity, positive predictive value, and negative predictive value of the two examinations, and to assess differences in imaging characteristics (e.g., lesion boundary clarity and microvascular structure visualization) between the two methods.

3. Research hypothesis: High-definition electronic magnification endoscopy combined with image enhancement technology demonstrates superior diagnostic accuracy for cervical and vaginal lesions compared to traditional colposcopy.

III. Research Content

3.1 Study Design

Study type: Paired diagnostic test design (diagnostic accuracy study with intra-participant comparisons)

Randomization method: sequential randomization

Blind method: Open (blinding of personnel interpreting pathological diagnostic results)

3.2 Multicenter studies (2)

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3.3 Study duration: March 2026 – March 2030

3.4 Sample Size and Calculation Basis

Based on research reports, the diagnostic accuracy of colposcopy for low-grade lesions is only approximately 43.4%, while the diagnostic accuracy for high-grade lesions ranges from 59% to 76%. A domestic multicenter study demonstrated that traditional colposcopy has a specificity of 75.1% and a sensitivity of 70.2% in detecting high-grade cervical lesions. Control group indicators (P0): According to data, traditional colposcopy achieves a diagnostic accuracy of approximately 59-76% for high-grade lesions (HSIL+). The lower limit of 59% is adopted as the calculation benchmark. Experimental group expected indicators (P1): It is hypothesized that high-definition magnified electronic colposcopy can significantly improve detection rates. A 20-percentage-point improvement is required to achieve statistically significant clinical significance, with diagnostic accuracy potentially reaching around 79%. Prevalence in target population: Literature reports indicate that among participants undergoing colposcopy, the proportion of cases ultimately pathologically confirmed as high-grade lesions (HSIL+) ranges from 20% to 40%, with a set threshold of 30%. Statistical power (Power, 1-β): Set at 90%, with $\alpha = 0.05$ (two-tailed).

Methods: Sample size estimation was performed using the sample size calculation formula for paired design diagnostic tests (McNemar test). A minimum of 212 study participants with complete paired data and valid gold standard results were required, accounting for a dropout rate of 10%-20%. The final planned total sample size was 270 cases.

Continuous enrollment was employed to include all eligible participants who met the inclusion criteria and consented to participate in the study until the target sample size was achieved. To balance potential biases arising from examination

sequence, a simple randomization method was used to assign participants to two distinct examination sequences (Sequence A group: initial observation and image acquisition using a conventional optical colposcope (magnification 7.5-15x), followed by endoscopy (preset magnification 90-120x); Sequence B group: initial examination using an endoscope, followed by colposcopy).

3.5 Inclusion and exclusion criteria, withdrawal/termination criteria

Inclusion criteria: ① Age 18-65 years with indications for colposcopy (HPV16/18 positive; HPV non-16/18 positive with LCT ≥ ASCUS; HPV negative with LCT ≥ LSIL; persistent HPV infection ≥ 1 year). ② Voluntary signing of informed consent form.

Exclusion criteria: ① Pregnant or lactating women. ② Acute genital tract infections or severe coagulation disorders. ③ History of radiotherapy for malignant tumors or severe mental disorders in study participants. ④ Minors.

Exit criteria: ① Requested withdrawal by study participants. ② Occurrence of serious adverse events (e.g., major bleeding, allergic reactions).

3.6 Methods and Procedures

The same study participant was randomly assigned to groups A and B according to sequence randomization, with examination sequences conducted in two groups.

Procedure for Evaluation Method 1 (Colposcopy): Study participants were placed in the lithotomy position. After routine disinfection and draping, a speculum was inserted. Traditional colposcopy was performed at designated time points (after saline administration, 1 minute and 2 minutes post-acetic acid test, and post-iodine test). The colposcopy specialist interpreted imaging features, recorded proposed diagnostic opinions, and marked suspected lesion sites (denoted as Point Y). The cervical surface was conceptualized as a clock face centered on the cervical os, with

the 12 o'clock position representing the top of the cervix. For example, Y6 indicates suspected cervical lesion at the 6 o'clock position under colposcopy.

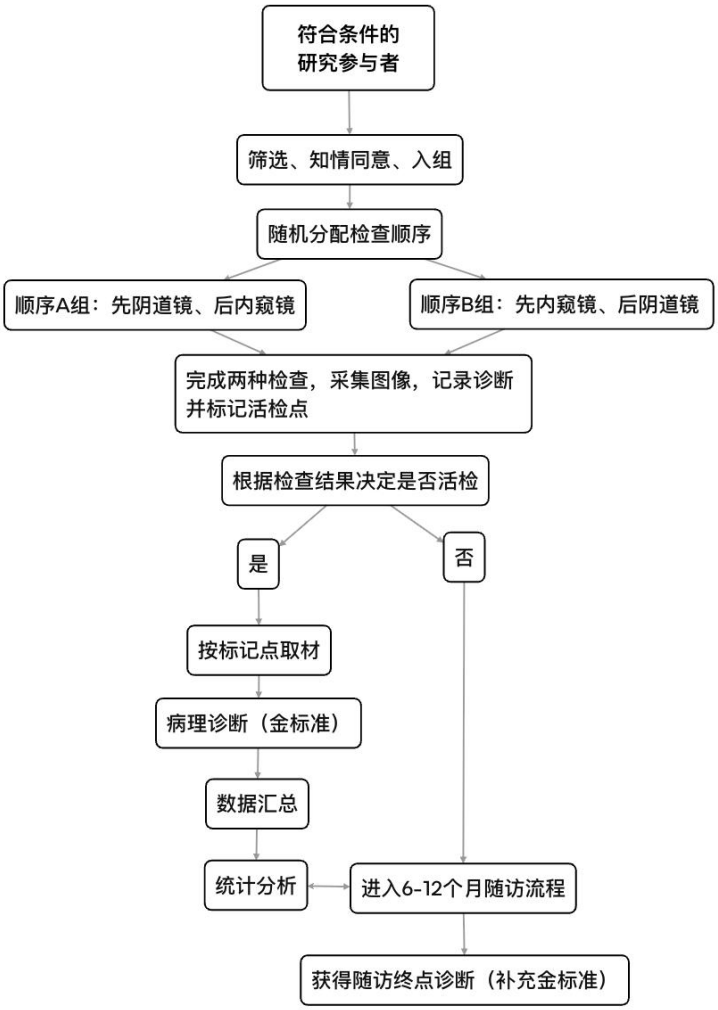
Evaluation of Probe Method 2 (High-Definition Electronic Magnification Endoscopy + Image Enhancement Technology): Procedure Flow: In the same study participants, high-definition electronic magnification endoscopy combined with image enhancement technology was used to observe the cervix and vagina and acquire images at specified time points (after saline administration, 1 minute after acetic acid test, 2 minutes after acetic acid test, and after iodine test). The endoscopist interpreted the images based on characteristic features, recorded proposed diagnostic opinions, and marked suspicious lesion sites on the schematic diagram (denoted as N-point, e.g., N3 indicates suspected cervical lesion at point 3 under endoscopic evaluation; lesions simultaneously identified as suspicious by colposcopy and endoscopy are labeled as T-point, e.g., T9 indicates suspected cervical lesion at point 9 according to both examinations).

Biopsy specimens from suspicious sites (2-4 mm per tissue block, totaling 2-4 tissue blocks) were submitted for examination. Endoscopists and colposcopists were unaware of each other's interpretation results. Pathologists conducted microscopic examination of the biopsy specimens and issued pathological diagnosis results (pathologists were unaware of the grouping and proposed microscopic diagnosis results).

For study participants who showed no suspicious lesions on conventional colposcopy or endoscopy, informed consent was obtained to voluntarily opt for biopsy. Those who chose biopsy had their pathological results compared with the proposed microscopic diagnosis using the gold standard. Participants opting against biopsy underwent 6-12 month follow-up HPV and TCT testing. Those with negative follow-up HPV/TCT results, abnormal HPV/TCT findings, or persistent negative results after colposcopy evaluation or colposcopic biopsy pathology were classified

as true negatives (suboptimal microscopic diagnosis negative with follow-up gold standard confirmation). Participants with ≥CINII or VAINII findings after 6-12 month colposcopic biopsy were categorized as false negatives (no suspicious lesions detected microscopically but confirmed high-grade lesions by follow-up gold standard). Image feature analysis was performed between experimental and control groups, with accuracy validated through pathological or follow-up results. Adverse events were recorded 24 hours post-examination (when vaginal swabs were removed after biopsy) for participants undergoing both instrument-based examinations.

technology roadmap ：



3.7 Evaluation indicators:

Primary outcome measure: accuracy rates of the two examinations, with histopathological results or follow-up outcomes serving as the gold standard.

Secondary outcome indicators: sensitivity, specificity, positive predictive value, negative predictive value, AUC, and lesion recognition rate (referring to the ability to identify suspicious lesions through high-definition magnified endoscopy in cases that are difficult to detect with conventional colposcopy).

Efficacy indicators: clarity of lesion margins and visualization capability of microvascular structures (including resolution of point-like, clustered, and spiral patterns), assessed using a 4-point Likert scale: 1=poor, 2=average, 3=good, 4=excellent.

Safety indicators: Examination-related adverse event incidence rate (e.g., bleeding, infection, mucosal injury or perforation during the procedure), postoperative complication rate within 24 hours (e.g., lower abdominal discomfort, vaginal bleeding, fever), and examination tolerance (assessing the proportion of study participants who discontinued the examination midway or requested termination of the procedure).

3.8 Data Management and Statistical Analysis

Data collection: Structured electronic case report forms were designed and implemented for data acquisition, covering baseline characteristics, imaging features and proposed diagnoses of the two examinations, biopsy information and pathological results, follow-up records, and adverse event profiles.

Data entry and verification: Independent entry by two individuals, employing logical consistency checks and scope verification, with disputed data corrected based on original records.

When baseline measurement data conform to normal distribution, mean ± standard deviation is used for description, and independent samples t-test is

employed for intergroup comparisons. If normal distribution is not met, median (interquartile range) is used for description, and Mann-Whitney U test is applied for intergroup comparisons. For baseline categorical data, case count (percentage) is used for description, and chi-square test or Fisher's exact test is utilized for intergroup comparisons.

Primary outcome measures: The accuracy rates of both examinations were calculated separately as (true positives + true negatives) / total cases. The difference in accuracy rates between the two examinations was compared using a paired chi-square test to determine statistical significance, with the calculated difference and its 95% confidence interval (CI) reported. Sensitivity and specificity were assessed using the McNemar test. For secondary outcome measures, count data comparisons between groups were performed using chi-square tests, with rate differences and their 95% CIs reported. When data followed a normal distribution, independent samples t-tests were used for intergroup comparisons. For non-normally distributed metric data, Mann-Whitney U tests were employed for intergroup comparisons.

The incidence rate of adverse events was calculated as the total incidence rate and the incidence rates of various events, with chi-square test or Fisher's exact test used to compare intergroup differences.

Subgroup analysis was performed to evaluate the stability of the results, with all findings presented as two-sided. A p-value <0.05 was considered statistically significant.

4、Alternative diagnostic and therapeutic methods available

Study participants may opt out of this research without any adverse impact on their access to conventional treatments. For this condition, standard therapeutic approaches include: performing only traditional colposcopy, with biopsy taken when necessary based on endoscopic findings to guide subsequent management plans. If

biopsy is not required, regular follow-up examinations are recommended. Traditional colposcopy has a long history and is performed by highly skilled practitioners, but its imaging quality is suboptimal, resulting in poor visualization of the cervical canal. This may lead to unnecessary biopsies and endocervical curettage (ECC).

5、Data Management and Information Confidentiality

During the study period, personal information such as the names and genders of study participants will be replaced with codes or numbers and strictly confidential. Only the relevant physicians will be aware of their data, ensuring robust protection of participants' privacy rights. Study findings may be published in academic journals, but no personal information of study participants will be disclosed.

If study participants consent to participate in this study, all their medical records will be reviewed by relevant personnel from the research institution initiating this study and relevant authoritative agencies, or by an independent ethics committee, to assess the appropriateness of study procedures.

6、Adverse Event Management

Study participants required the insertion of specula and application of acetic acid or iodine tincture to the cervical and vaginal mucosa. Biopsy may be necessary when indicated. Mild pain, mucosal trauma, or slight vaginal bleeding are considered normal phenomena. If major vaginal bleeding, allergic reactions, or infections occur during or within 24 hours post-procedure (before follow-up completion) and cannot be ruled out as unrelated to the procedure, they shall be classified as adverse events. The procedure must be immediately discontinued, and the research team will provide prompt medical intervention to participants while reporting the incident within 24 hours.

VII. Ethical Principles and Requirements for Life Sciences and Medical Research

This clinical study will comply with relevant regulations including the Declaration of Helsinki issued by the World Medical Assembly and the Ethical Review Guidelines for Life Science and Medical Research Involving Human Subjects. Prior to enrollment, each study participant must sign an informed consent form. Investigators are required to provide written explanations detailing the study's objectives, nature, procedures, potential benefits, and risks in a comprehensive manner, while ensuring participants are aware of their right to withdraw at any time. All participants are fully informed prior to enrollment and given sufficient time to consider participation. Participation is voluntary, and only those who have signed the informed consent form will be included in the study.

VIII. Main References

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