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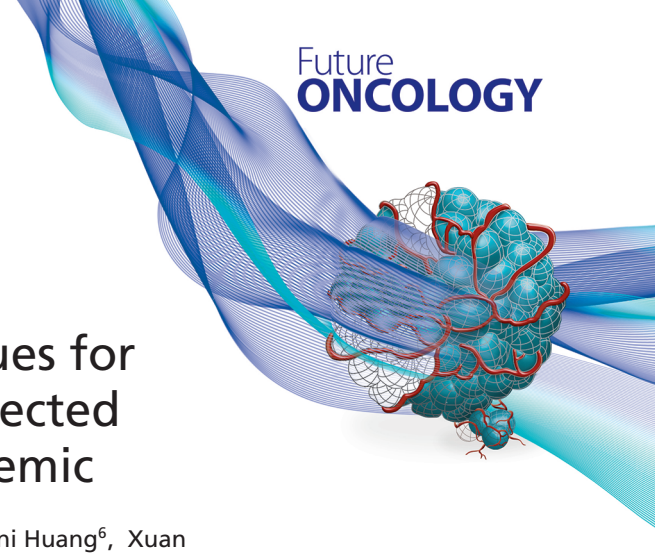

TruScreen detection of cervical tissues for high-risk human papillomavirus-infected women during the COVID-19 pandemic

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Aims: To evaluate the efficacy of TruScreen (TS01) for high-risk human papillomavirus (HR-HPV) women compared with other methods in reducing colposcopy referral rates in hospitals. **Methods:** A single-center, prospective, case–control study was conducted from December 2019 to June 2020. **Results:** Among 139 (46.2%) HR-HPV-positive patients, 58 were CIN1, 52 were CIN2-3 and 29 had cervical cancer (n = 29). The sensitivity and specificity of detecting CIN2+ by TS01, colposcopy and HPV16/18 testing were 96.3% and 46.4%, 85.2% and 40.5% and 59.3% and 74.1%, respectively. The highest sensitivity was 96.3% at HPV16/18 and TS01 (each positive results), and the highest specificity was 83.6% at HPV16/18 and TS01 (both positive) for CIN2+ compared with the other methods. **Conclusion:** TS01 is a noninvasive screening method and can be used to diagnose cervical lesions quickly. It is especially suitable as triage tool for HR-HPV-positive women facing SARS-CoV-2 exposure and infection risks in hospital.

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Keywords: cervical cancer • COVID-19 pandemic • cytology • high-risk HPV • TruScreen

The coronavirus disease 2019 (COVID-19) pandemic, caused by SARS-CoV-2, has radically changed global healthcare and rapidly spread over many countries since late 2019. As of 11 November 11 2020, more than 51 million infection cases and 1,270,930 confirmed deaths had been reported [1]. Each country has initiated measures to reduce the impact on healthcare systems and mitigate the transmission of SARS-CoV-2. Cancer is the leading cause of death in many countries, and its prognosis and burden are highly dependent on disease stage at diagnosis [2]. Thus, major restructuring of organizations and hospitals was needed to adapt resources for oncology care maintenance to ensure the implementation of contingency plans that balance the risks associated with cancer treatment delay or discontinuation versus the risks of COVID-19 exposure and infection in hospitals. SARS-CoV-2 infection rate appeared to be higher in cancer patients than in the general population (1 vs 0.29%). In particular, the risk of developing severe respiratory complications requiring intensive care was higher in cancer patients than in noncancer patients (39 vs 8%; p = 0.0003) [3]. Oncology departments and associations have made new recommendations and therapeutic options for these high-risk patients.

In gynecologic oncology, the diagnostic and therapeutic paradigms have been shifting to maintain critical diseases or gynecological cancers [4–6]. Numerous gynecological groups and societies provided surgical and radiation management recommendations for cervical, endometrial and ovarian cancer in early March 2020 [7,8]. The FRANCOGYN

group proposed recommendations that are similar to the standard of care but emphasized radiochemotherapy as the first-line treatment for cervical cancer instead of immediate surgical treatment during the pandemic [7].

Cervical cancer is one of the most easily preventable malignant tumors, but it is the main cause of death of women all over the world. In recent decades, the Pap test has become a standard method for reducing the incidence and mortality of cervical cancer in many countries. However, the limitations of Pap test and cytology are the sensitivity (~50%) and a significant proportion of inadequate specimens [9]. The most important cause of cervical cancer is persistent human papillomavirus (HPV) infection. The development of cervical cancer is slow in most patients, particularly the development from precancer to invasive cancer [10]. High-grade cervical intraepithelial neoplasia (CIN2 and CIN3) can develop within 3–5 years after high-risk HPV (HR-HPV) infection, and progression to invasive cancer may take 20–30 years [11]. HR-HPV testing has been used for cervical cancer primary screening in many countries [12–14]. The sensitivity and specificity of HR-HPV versus cytology for detection of CIN2+ were 86.4% and 71.0%, versus 53.2% and 83.0% in the ATHENA HPV study (n = 34,254) [15]. HR-HPV testing was substantially more sensitive in detecting CIN2 than cytology (96.1% vs 53.0%) but less specific (90.7% vs 96.3%) in the overview of the European and North American studies [16]. The high sensitivity of HR-HPV screening can prevent missed diagnosis in women with cervical lesions. Due to lower specificity, especially in young women, efforts should be made to optimize triage strategies to prevent unnecessary intervention in colposcopy. Due to the low specificity of HPV testing, especially in young women, efforts should be made to optimize triage strategy to prevent unnecessary intervention and referral of women with transient HPV infection to colposcopy [15]. The high sensitivity but less specific HPV tests may lead to overreferral rate for colposcopy, patient panic, overtreatment and too many hospital visits. In nonpregnant patients with histologic high-grade squamous intraepithelial lesion (CIN2 and CIN3), treatment is recommended unless the patient has concerns about the effect of treatment on future pregnancy that outweigh her concerns about cancer [12–14].

Consensus or recommendations on cervical cancer prevention focus on increasing the proportion of patients without screening, the risk of missed or delayed cancer diagnosis and precancer treatment and management. The long-term development characteristics of precancerous cervical lesions also provide many management and follow-up options compared with that for other cancers during the COVID-19 pandemic. The first expert consensus for colposcopy and outpatient surgery of the lower genital tract during the COVID-19 pandemic was announced by the Italian Society for Colposcopy and Cervico-Vaginal Pathology on 5 April 2020 [17]. The European Federation for Colposcopy and European Society of Gynecological Oncology suggested the action of HPV vaccination, screening programs, colposcopy and surgery during and after the COVID-19 pandemic at the end of May 2020 [18]. The American Society of Colposcopy and Cervical Pathology (ASCCP) interim guidance for timing and treatment procedures for patients with abnormal cervical screening tests were announced on 26 May 2020 [19].

The development of multiple medical digital technologies, including the Internet, big data and artificial intelligence, has been widely applied in medical fields such as cytology, histopathology, imaging and point-of-care instruments in the past decade. Currently, the COVID-19 outbreak offers an opportunity to use these technologies [20]. TruScreen (TS01) is a portable instrument that uses optical and electrical signals to analyze cervical tissues with a built-in algorithm in real time [21,22]. The operation process of TS01 takes approximately 1–2 min, during which the operator places the tip of the hand piece on the cervix and pushes a button to obtain the result. This method is suitable in regions where colposcopy and cytology are unavailable, patient follow-up is difficult or situations in which reducing the waiting time for results is crucial. The possible advantages of TS01 are decreased specimen contact during cytology and HPV diagnosis, reduced patient and medical staff contact in outpatient and colposcopy departments and adequate cervical cancer screening and follow-up rate during the COVID-19 pandemic.

This study aimed to evaluate the positivity rate, sensitivity and specificity of TS01 for HR-HPV-positive women in our hospital in November 2019. The study was halted from mid-January to March 2020. In addition, this study proposed a flowchart to reduce colposcopy referral rate and a flowchart specific to the COVID-19 pandemic.

Materials & methods

Patient recruitment

A total of 1344 women who visited the gynecology clinics were invited to participate in the study in the outpatient department of The First Affiliated Hospital of the University of South China from December 2019 to June 2020. The study was approved by the Institutional Review Board of The First Affiliated Hospital (no. FA-193-01). Informed consent forms were signed by all participants. The inclusion criteria were as follows: sexually active

women who voluntarily participated and provided informed consent. The exclusion criterion was as follows: patients who were pregnant and had a history of cervical cancer and precancerous surgery. All cervical specimens for HPV testing were collected using the Hybribio sampling kit (Hybribio Co., Guangdong, China), which contained an endocervical collection brush and a tube with specimen transport medium. All specimens were processed for HPV DNA testing and stored at -20°C. After HR-HPV testing, all HR-HPV-positive patients were transferred to a colposcopic room for TS01 testing and colposcopic impression.

HPV DNA testing

HBRT-H14, 14-high-risk HPV with 16/18 genotyping real-time PCR kit (Hybribio Co.) was used for HR-HPV genotyping. HPV16 subtype, HPV18 subtype, and 12 other HR-HPV subtypes were tested once each for each specimen. HBRT-H14 showed a high coincidence rate with the WHO HPV DNA proficiency panel reported by the international HPV genotyping proficiency study of the WHO global HPV Laboratory Network (LabNet). HPV DNA testing showed HR-HPV, HPV16 subtype, HPV18 subtype and non-HPV16/18 HR-HPV.

TruScreen examination

The TS01 examination was performed by gynecologists who were blinded to the HR-HPV and gynecological results. TS01 diagnosis was performed before performing colposcopic examinations. The women were asked to lie down in the lithotomy position. After inserting a speculum, the operator inserted the handpiece mounted with a single-use sensor into the vagina. Following the probing pattern set in the operation manual, the surface of the cervix was probed using the tip of the handpiece, point-by-point. The TS01 result was printed after the whole cervix was detected, and the touchscreen of the handpiece was pressed. TS01 was tested once for patients reported to have normal or abnormal results.

The TS01test was performed without colposcopic visualization to be consistent with the routine used in the primary care setting. For the purpose of this study, the result was encrypted using a predetermined coding protocol to prevent the clinician from decoding the result and to eliminate possible verification bias associated with prior knowledge of the TS01 result while performing colposcopy and at the time of decision-making regarding the biopsy site.

Colposcopy & histology

All enrolled patients underwent colposcopy performed by the investigators at the hospital, and the standardized colposcopic examination of the cervix was performed by qualified gynecologists. Each examination was performed with 3–5% acetic acid and Schiller test. Lesions were described in terms of color, margin, vessels and iodine-staining characteristics. Colposcopy showed absence of intraepithelial lesion (NILM), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion and cancer. Specimens for colposcopy-directed biopsies were obtained at targeting areas with acetowhitening metaplasia or higher abnormalities from distinct acetowhite lesions on the Schiller test. Two randomized biopsies with endocervical curetting (for transformation zone III finding) was performed when no abnormal finding was noted during colposcopy. The biopsied specimens were reviewed and interpreted by two pathologists according to standard hospital procedures.

Statistical analysis

All data, including basic information and HPV genotyping, TS01, colposcopy and histological examination results, were recorded and evaluated. The chi-square and Fisher's exact tests (two-sided) were used to analyze the status of tests completed individually or in combination. Fisher's exact test is considered to be more accurate than the chi-squared test in sample sizes smaller than five. SPSS version 22 (IBM Corp, Armonk, NY, USA) was used for data analysis. The sensitivity and specificity for CIN1+, CIN2+ and CIN3+; odds ratio; p-value (two-sided); and 95% CI of all tests were evaluated. Categorical variables were expressed as numbers and percentages, whereas continuous data were expressed as means with standard deviation.

Results

Patient characteristics & colposcopy biopsy results

A total of 22.4% HR-HPV-positive patients (n = 301) of the 1344 women were enrolled in the gynecology clinics in the study (Figure 1 & Table 1). The average age of the HR-HPV patients was 40.8 years (range: 16–81 years), of which 53.8% had pathology confirmed normal cervixes (n = 162; HR-HPV = 301), 19.3% (n = 58) had CIN1,

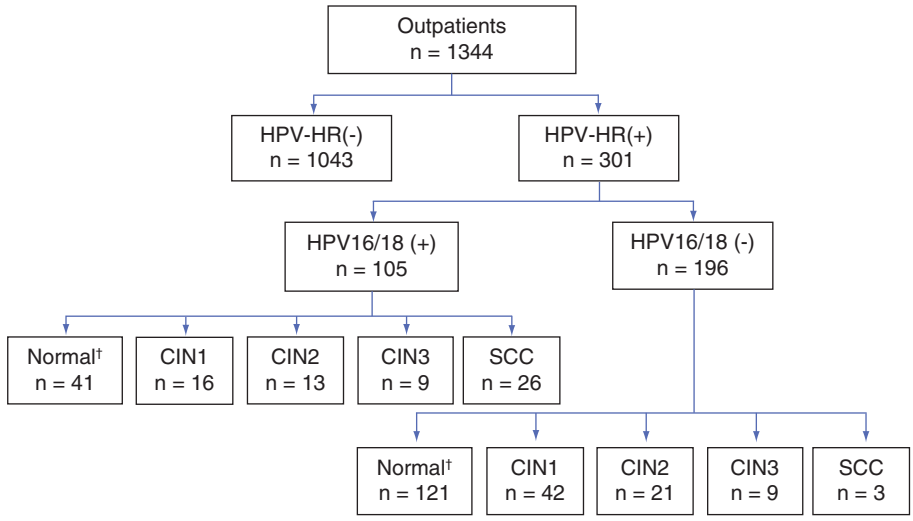

Figure 1. Enrollment and outcome of the study (November 2019–June 2020).
†No intraepithelial lesion was found in biopsy.

Table 1. Basic information and colposcopy, biopsy, TruScreen diagnosis method and HPV16/18 results of high-risk human papillomavirus subjects.

Index	n (%)
HR-HPV patients	301
Age, years, mean (range)	40.8 (16–81)
Pathology	
SCC	29 (9.6)
CIN 3	18 (6.0)
CIN 2	34 (11.3)
CIN1	58 (19.3)
Normal	162 (53.8)
Colposcopy impression	
SCC	21 (7.0)
HSIL	27 (9.0)
LSIL	152 (50.5)
No lesion found†	101 (33.6)
HPV16/18	105 (34.9)
TS01 positive	196 (65.1)

†No lesion found in the cervical area by colposcopy. This may indicate normal screen, inflammation, cyst, polyp, condyloma, erosion and tumor.
CIN: Cervical intraepithelial neoplasia; HR-HPV: High-risk human papillomavirus; HSIL: High-grade squamous intraepithelial lesion; LSIL: Low-grade squamous intraepithelial lesion; SCC: Squamous cell carcinoma; TS01: TruScreen diagnosis method.

11.3% (n = 34) had CIN2, 6.0% (n = 18) had CIN3 and 9.6% (n = 29) had cervical cancer. The positive rates of HPV16/18, TS01 and colposcopy (≥LSIL) were 34.9%, 65.1% and 66.5%, respectively (Table 1). The positive rate of TS01 was 65.1%, including normal (46.9%), CIN1 (72.4%), CIN2 (94.1%), CIN3 (94.4%) and cancer (100%), respectively. Of the 26.9% (81/301) patients who were pathologically diagnosed with CIN2+, 96.3% (78/81) were positive detected by TS01, 59.3% (48/81) by HPV 16/18 testing and 85.2% (69/81) by colposcopy (Table 2).

Sensitivity & specificity tests for CIN2+ by analysis of each test

The sensitivity and specificity of each diagnostic test for CIN2+ are summarized in Table 3. The sensitivity and

Table 2. Positive rate of different diagnosis.

Testing	Pathology				
	Normal, n (%)	CIN1, n (%)	CIN2, n (%)	CIN3, n (%)	SCC, n (%)
Subjects	162 (100)	58 (100)	34 (100)	18 (100)	29 (100)
HPV16/18	41 (25.3)	16 (27.6)	13 (38.2)	9 (50.0)	26 (89.7)
TS01(+)	76 (46.9)	42 (72.4)	32 (94.1)	17 (94.4)	29 (100)
Colposcopy (≥LSIL)	82 (50.6)	49 (84.5)	27 (79.4)	17 (94.4)	25 (86.2)
HPV16/18 and TS01(+)	23 (14.2)	13 (22.4)	13 (38.2)	9 (50.0)	26 (89.7)
HPV16/18 or TS01(+)	94 (58.0)	45 (77.6)	32 (94.1)	17 (94.4)	29 (100)

CIN: Cervical intraepithelial neoplasia; LSIL: Low-grade squamous intraepithelial lesion; HR-HPV: High-risk human papillomavirus; SCC: Squamous cell carcinoma; TS01: TruScreen diagnosis method.

Table 3. Performance of three diagnosis tests for identifying women with CIN2+ of cervix.

Diagnosis	Sensitivity (95% CI)	Specificity (95% CI)	Odds ratio (95% CI)	p-value
HPV 16/18+	59.3% (47.8–69.9)	74.1% (67.7–79.6)	4.16 (2.43–7.11)	<0.001
TS01+	96.3% (88.8–99.0)	46.4% (39.7–53.2)	22.48 (6.88–73.37)	<0.001
Colposcopy (≥LSIL)	85.2% (75.2–91.8)	40.5% (34.0–47.3)	3.91 (2.00–7.63)	<0.001
TS01+ or 16/18+‡	96.3% (88.8–99.0)	36.8% (30.5–43.6)	15.15 (4.63–49.57)	<0.001
TS01+ and 16/18+†	59.3% (47.8–69.9)	83.6% (77.9–88.1)	7.43 (4.21–13.14)	<0.001

†The 'and' rule, in which the diagnosis is positive only if both A and B are positive. Either A or B can be negative for the diagnosis to be negative, trust negative.
‡The 'or' rule, in which the diagnosis is positive if either A or B is positive. Both A and B must be negative for the diagnosis to be negative, trust positive.
CIN: Cervical intraepithelial neoplasia; LSIL: Low-grade squamous intraepithelial lesion; TS01: TruScreen diagnosis method.

Table 4. The colposcopy referral rate by test.

Test items	Colposcopy (%†)	Noncolposcopy (%†)	CIN3+ missed	Number not referred to colposcopy
HPV16/18	105 (34.9%)	196 (65.1%)	12	NILM = 121, CIN1 = 42, CIN2 = 21, CIN3 = 9, Ca = 3
TS01	196 (65.1%)	105 (34.9%)	1	NILM = 86, CIN1 = 16, CIN2 = 2, CIN3 = 1, Ca = 0
TS01 or HPV16/18	217 (72.1%)	84 (27.9%)	1	NILM = 68, CIN1 = 13, CIN2 = 2, CIN3 = 1, Ca = 0
TS01 and HPV16/18	84 (27.9%)	217 (72.1%)	12	NILM = 139, CIN1 = 45, CIN2 = 21, CIN3 = 9, Ca = 3

†Target numbers divided by numbers of HR-HPV+ women.
Ca: Cancer; CIN: Cervical intraepithelial neoplasia; NILM: No intraepithelial lesion was found; TS01: TruScreen diagnosis method.

specificity of TS01 were 96.3% and 46.4%, respectively, compared with 59.3% and 74.1% for HPV16/18 testing and 85.2% and 40.5% for colposcopy, respectively. On comparing the three types of diagnostic methods, the odds ratio of TS01 22.48 (6.88–73.37) was higher than that of HPV16/18 testing and colposcopy ($p < 0.0001$) for HR-HPV-positive women. Combined HPV16/18 and TS01 (one of the positive) had the highest sensitivity compared with the other methods at (96.3%). Additionally, combined HPV16/18 and TS01 (both positive) had the highest specificity among the methods (83.6%). The new concept is to screen initially with HR-HPV testing plus genotyping for HPV 16 and HPV 18. To refer all women who were HPV 16/HPV 18 positive to colposcopy and reflex testing by TS01 those HR-HPV-positive but not positive for HPV 16/HPV 18 (Figure 2). For gynecologists, the decision point to use TS01 instead of direct colposcopy is for patients with HPV16/18 positive at follow-up but with normal cervix in previous colposcopy.

Recommendation of the cervical cancer flowchart during the COVID-19 pandemic

Cytology testing was postponed during the COVID-19 pandemic at our hospital. We proposed a rapid, opportunistic hospital cervical cancer screening flowchart using HR-HPV as the primary test and TS01 diagnosis as a triage method during the COVID-19 pandemic (Figure 3). To reflex all HR-HPV-positive women with TS01, referring to colposcopy only those with TS01 positive result, whereas those with negativeTS01 had follow-up in 12 months. The HR-HPV with TS01(-), normal, or LSIL patients were followed up after 6–12 months. The follow-up period was in accordance with the policy of COVID-19 grading and cases. The noncolposcopy rate in Figures 2 & 3 was 27.9% and 34.9% in Table 4.

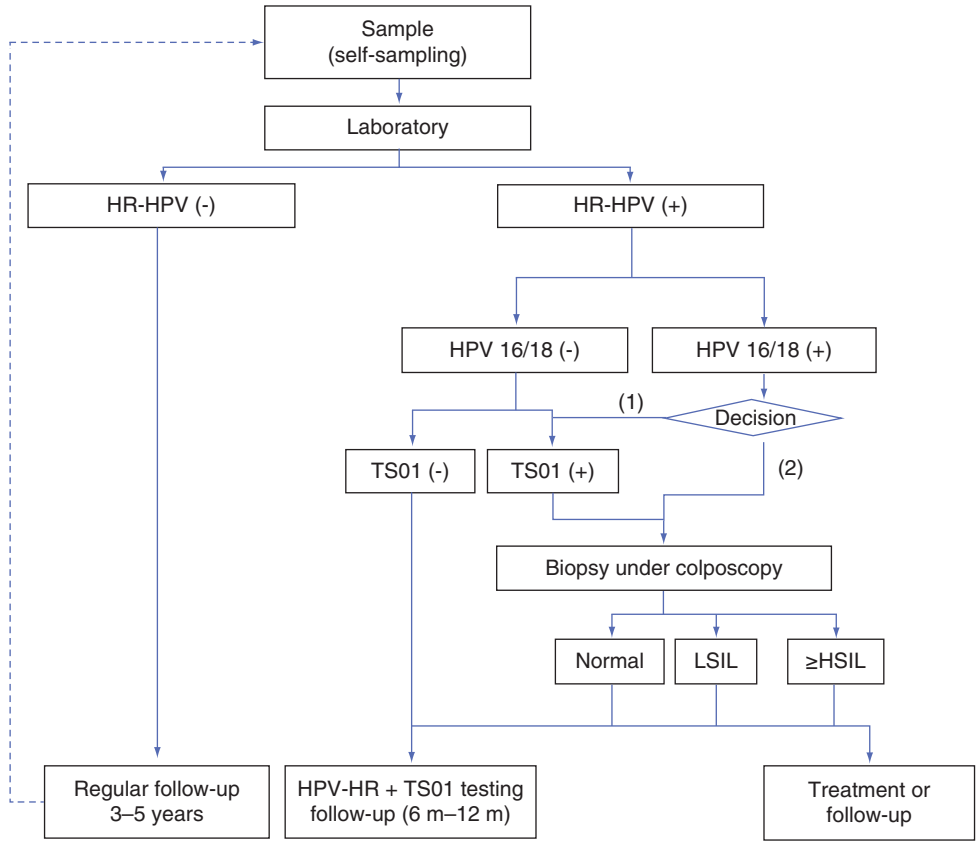

Figure 2. Recommendation process for cervical cancer screening management in hospitals, especially in regions where cytology and colposcopy are not readily available.
HSIL: High-grade squamous intraepithelial lesion; LSIL: Low-grade squamous intraepithelial lesion; TS01: TruScreen diagnosis method.

Discussion

Currently, primary prevention (HPV vaccines) and secondary prevention (HPV tests) methods by screening using HPV tests include self-collected samples for women to reach underscreened populations. The prevention strategy promoted WHO's call to eliminate the possibility of cervical cancer [23,24]. The primary goal of cervical cancer screening is to detect high-grade precancers (CIN2, CIN3 and adenocarcinoma *in situ*) that are likely to progress to invasive cancer. Cytology (Pap smear) is a valuable cervical cancer screening method that reduces the incidence, mortality rate and treatment-related morbidity in many developed countries. However, recent trend analyses indicate that cervical cancer incidence rates have stopped decreasing or are actually increasing even in countries with well-organized cytology facilities [25,26]. This phenomenon might be explained by the limitations of cytology-based screening methods because of their increased exposure to HR-HPV and low screening coverage rates, particularly among young women [27]. Additionally, patients usually have poor awareness regarding routine screening or follow-up. Furthermore, in developing countries, experienced cytologists and cytology-based facilities are scarce and insufficient.

Cervical cancer screening primarily consists of cytological tests, HPV DNA tests and visual inspection. Randomized population-based trials have demonstrated that HPV-based screening is more effective in protecting against incident cervical precancer and cancer than cytology. Although HPV infections and CIN are common, they rarely lead to cervical cancer [28,29]. However, HR-HPV testing cannot distinguish clinically relevant lesions, and many women are extremely worried about HPV infection. WHO has recommended visual inspection as the cervical cancer screening method of choice in low-resource areas [30]. Unfortunately, quality control is difficult to implement in visual inspection, with variations in sensitivity (56.1–93.9%) and specificity (74.2–93.8%) [31]. Therefore, a simple, accurate and less time-consuming instrument or method is needed.

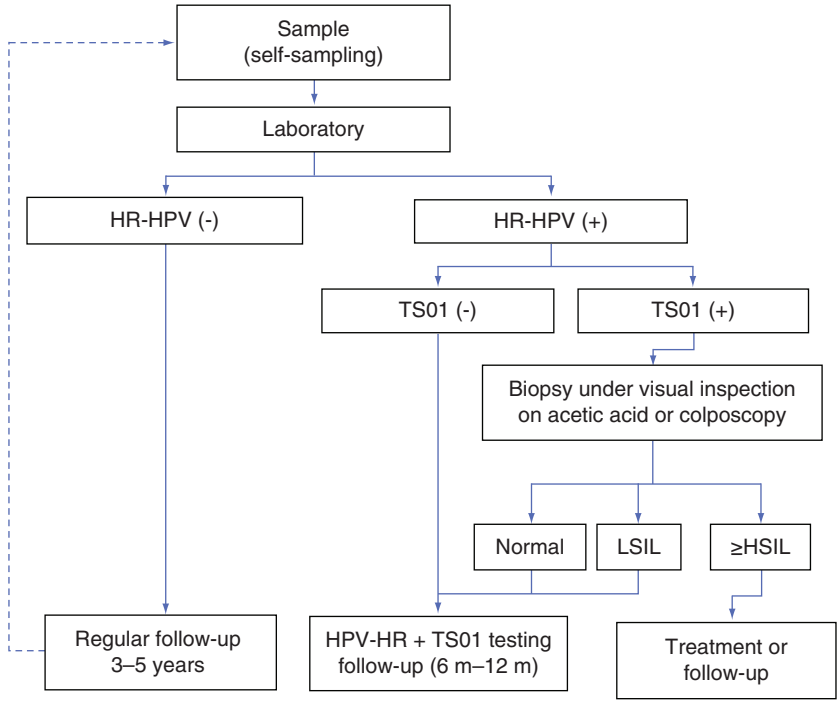

Figure 3. Recommendation of a rapid process for cervical cancer screening management in hospitals during the COVID-19 pandemic.
HSIL: High-grade squamous intraepithelial lesion; LSIL: Low-grade squamous intraepithelial lesion; TS01: TruScreen diagnosis method.

Technological advances in cervical cancer screening have developed rapidly over time. TS01, with similar principles with cytology and pathology, is a sensor device for the optical and electrical analysis of cervical tissues to detect precancerous lesions and cancer [22]. The cervical epithelium can be detected by the special frequency of light and can also be transferred to cervical tissues to detect changes in the blood vessels of the subcutaneous layer of the cervix. Many studies have reported that TS01 is noninvasive and simple to operate and provides quick results; thus, it is easy to use for opportunistic screening, follow-up and cervical cancer screening, especially in low-resource areas. According to a meta-analysis, the pooled sensitivity and pooled specificity of TS01 were 76% and 69%, respectively, with an AUC of 0.7859 [32]. Compared with the meta-analysis of TS, in this study, TS01 had higher sensitivity (96.3%), lower specificity (46.4%) and a highly positive detection rate (96.3% [78/81]) for pathologically diagnosed CIN 2+ for HR-HPV triage. A new finding in the present study is the TS01 and/or HPV16/18 combination methods. The low specificity of TS01 [32] and TS01 was improved by the new version of TS01 equipment, and HPV16/18 results are shown in Table 2. Two cases of CIN2 (5.9%; 49 and 53 years old with 12 other types of HPV and Type III transformation zone by colposcopy), one case of CIN3 (5.6%; 51 years old with HPV33 and Type III transformation zone by colposcopy) and no case of cervical cancer was detected by HPV16/18 and TS01 combination tests. TS01 had higher sensitivity and specificity than colposcopy for pathological CIN (sensitivity [specificity] of TS01 vs. colposcopy) than for CIN1 (86.3% [53.1%] vs 88.5% [42.0%]), CIN2 (96.3% [46.4%] vs 85.2% [40.5%]) and CIN3 (97.9% [40.9%] vs 89.4% [37.8%]) (Table 3). These results show that TS01 has the potential to replace colposcopy as the standard method in the future because of its accuracy, as shown in this study. However, additional data are needed to analyze and verify the validity of this finding.

In early 2015, the Society of Gynecologic Oncology and the ASCCP jointly issued interim clinical guidance regarding the use of HR-HPV as a primary testing method for cervical cancer screening, triaging positive HR-HPV tests with genotyping for 16/18 and reflex cytology for women positive for the 12 other HR-HPV genotypes [33]. The 2020 Cervical Cancer Screening guideline update from the American Cancer Society recommends that individuals initiate cervical cancer screening at age 25 years and undergo primary HR-HPV testing every 5 years through age 65 years [34]. According to the screening guidelines, HR-HPV testing has replaced cytology as the primary screening

method for cervical cancer in many countries. This cervical cancer screening study was conducted in gynecological outpatients using HR-HPV genotyping as primary tests. In all HR-HPV-positive women, HPV16/18 genotyping, TS01 and colposcopy were used to evaluate the accuracy of the test and the colposcopy referral rate. Figure 2 provides a flowchart for cervical cancer screening in hospitals, especially in regions with low-accuracy cytology and colposcopy. Without reducing the detection rate of cervical cancer, the advantage of the method is that it does not require experienced cytology experts, maintains the examination of women with high-risk HPV16/18 infection, reduces colposcopy referral rates and quickly provides diagnostic results.

Liang *et al.* reported that cancer patients with COVID-19 have a 3.5-fold higher risk of requiring mechanical ventilation and ICU admission or death compared with patients without cancer [35]. In addition, the cancer diagnosis rate has decreased because of the COVID-19 pandemic [36], and cervical cancer prevention activities have been disrupted worldwide. The recommendations for cervical cancer prevention were made to balance the risks associated with treatment delay or discontinuation versus the risks of SARS-CoV-2 exposure and infection [18,19]. Compared with the contact time and the number of personnel in cytology and colposcopy, TS01 has a shorter inspection time and a positive rate of 94% CIN2+, which is a more suitable hospital inspection method during the COVID-19 pandemic [37]. These opportunities helped minimize the risk of patient exposure to the SARS-CoV-2 virus and decrease the demand for healthcare services. Figure 3 shows a recommendation flow chart of hospital opportunistic screening for low- and middle-risk area during the COVID-19 pandemic. The advantages of the new concept are that it can quickly screen a large number of women whose screening has been delayed due to the pandemic, promptly obtain diagnostic results and maintain the quantity and quality of screening.

Here, we performed a feasibility assessment and analyzed the clinical practice data of TS01 diagnosis in HR-HPV-positive patients, the real practices in our hospital during the pandemic. A higher CIN2+ percentage was observed in the study. This phenomenon shows that it is important and meaningful for women who will go to the hospital for gynecological examination after the COVID-19 pandemic to be defined as high-risk and requiring opportunistic cervical cancer screening.

There are some limitations associated with this study. Only women with HR-HPV-positive results were referred to colposcopy, and women with negative results were not referred; biopsies were performed on the basis of these results. This procedure created a bias that reduces potential false-negative results from primary screening (higher sensitivity) from the final pathology. Second, the data for 301 HR-HPV-positive women from 1433 patients included in the study were incomplete. Furthermore, the cross-sectional study with no four-quadrant biopsy for normal observation women without follow-up for pathological results was incomplete, and the power of clinical performance assessment was limited compared with that for a longitudinal study. Therefore, further evaluation and large population studies are needed to establish firmly the clinical utility of TS01 in the Chinese population.

Conclusion & future perspective

TS01 is a noninvasive and easy triage instrument for cervical lesion diagnosis in HR-HPV-positive women. We recommend an opportunistic screening flowchart for cervical cancer for hospitals in regions where cytology and colposcopy are not readily available. Rapid opportunistic cervical cancer screening flowcharts for hospitals are particularly recommended during the COVID-19 pandemic. We propose that the suggested approach would be useful in outpatient departments of hospitals in highly populated countries where cytology as a primary screening tool is not readily accessible through community-based settings.

Author contributions

Z Wang, Y Zhang, YN Kang, and Y Ma Y contributed to the conception and design of the study. Z Wang and Y Ma coordinated the clinical trial. YG Tang, FR Yu, X Zhou contributed the clinical data collection, analysis and evaluation. FR Yu contributed the colposcopies. YN Kang, FH Zhong and K Huang conducted clinical data review. YL Liou contributed to the manuscript writing. All authors read the final version of manuscript and approved of the submitted version.

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Financial and competing interests disclosure

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No writing assistance was utilized in the production of this manuscript.

Summary points

- Technological advances in cervical cancer screening have developed rapidly over time. TruScreen (TS01), which uses a similar principle to that of cytology and pathology, is a sensor device for the optical and electrical analysis of cervical tissues to detect precancerous lesions and cancer. The positive rates of TS01 in normal, CIN1, CIN2 and CIN3 lesions and cancer were 46.9%, 72.4%, 94.1% and 100.0%, respectively.
- Compared with the clinical data for TS01, the new generation of TS01 has higher sensitivity (96.3%), lower specificity (46.4%) and higher positive detection rate (96.3% [78/81]) for pathologically diagnosed CIN 2+ for high-risk human papilloma virus (HR-HPV) triage. Combined HPV16/18 and TS01 (each positive) had the highest sensitivity compared with the other methods (96.3% for CIN2+). Additionally, combined HPV16/18 and TS01 (both positive) had the highest specificity among the methods (83.6% for CIN2+).
- We recommend a flowchart for opportunistic hospital screening for cervical cancer in regions where cytology and colposcopy are not readily available (Figure 2). The new concept initially screens with a panel of HR-HPV plus genotyping for HPV 16 and 18 to refer all women who are HPV16/18-positive to colposcopy and reflex testing by TS01 for those who are HR-HPV-positive but not HPV16/18-positive. For gynecologists, the decision point to use TS01 instead of direct colposcopy is for patients with HPV16/18 positivity at follow-up but with a normal cervix in previous colposcopy.
- TS01 is a portable instrument that can be used to reduce SARS-CoV-2 infections by reducing contact time and ensuring the safety of patients and healthcare professionals with high performance. A rapid opportunistic hospital cervical cancer screening flowchart is recommended for use during the COVID-19 pandemic (Figure 3). To reflex all HR-HPV-positive women with TS01, only TS01 positive results are refer to colposcopy, whereas those with TS01 negative results have follow-up in 12 months. The HR-HPV with TS01(-), normal or low-grade squamous intraepithelial lesion patients were followed up after 6–12 months.
- We believe that the proposed approach is useful in outpatient departments of hospitals in highly populated countries where cytology as primary screening is not readily accessible through community-based settings.

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