Gynecologic Oncology Reports 57 (2025) 101661

Contents lists available at ScienceDirect

Gynecologic Oncology Reports

journal homepage: www.elsevier.com/locate/gynor

Digital cervicography using mobile phones with real-time consultation (DCRC) to improve performance of Visual Inspection with Acetic Acid (VIA) in cervical cancer screening of HIV-infected women. A cross-sectional study☆

P. Tonui [a,*], P. Itsura [a], O. Omenge [a], N. Faiza [a], A. Keter [b], A. Mburu [a], J. Oguda [b], Amina R. Hassan [a], S. Cu-Uvin [c]

[a] Moi University, Eldoret, Kenya
[b] Academic Model Providing Access to Healthcare (AMPATH), Eldoret, Kenya
[c] Brown University, Providence, RI, USA

ARTICLE INFO

Keywords:
Cervical Cancer
Visual Inspection with Acetic Acid
Digital Cervicography Using Mobile Phones with Real-time Consultation

ABSTRACT

Introduction: Visual Inspection with Acetic Acid (VIA) has been adopted for cervical cancer screening in Kenya and other Low-Middle Income Countries despite providing suboptimal results among HIV-infected women. It is mostly performed by nurses in health centers. Innovative ways of improving the performance of VIA in HIV-infected women are desired.

Objective: To establish the feasibility of screening with VIA and Digital Cervicography with Real-time Consultation (VIA-DCRC), and compare its performance to screening with VIA alone among HIV + women.

Methods: This was a cross-sectional analytical study of two hundred HIV + women. There were two groups of women who underwent either VIA or VIA/DCRC cervical cancer screening arms. In the VIA/DCRC arm, a trained nurse did the VIA, captured an image of the cervix, uploaded it, and electronically shared it in real-time with three blinded study consultants (gynecologic oncologists) who separately assessed the digital image and classified it as VIA/DCRC positive or negative. Any two opinions of the gynecologic oncologists that concurred were considered as the final diagnosis.

All participants who screened positive underwent colposcopy and biopsy prior to treatment. Tissues obtained were subjected to histopathological examination. A fraction (15 %) of those who screened negative for VIA and VIA/ DCRC had random cervical biopsies taken at 12 and 6o'clock positions. We estimated the measures of accuracy using the Bayesian method.

Results: The mean age was 39.7 +/- 10.7 years. Average CD4 + count and plasma viral load (log base 10) were 492.2 (SD: 255.3) cells per mm^3, and 2.6 (SD: 0.7) copies per ml respectively. None of the women was a smoker. The median (IQR) time taken for at least one gynecologic oncologist to respond to a digital consultation was 2.0 (IQR 1.0, 4.0) minutes, range: 1.0 – 47.0.

Overall, 60.5 % were diagnosed with cervical pre-malignancies (VIA: 23.1 % (95 % Credible Bounds (CB): 10.1, 37.5), VIA/DCRC: 37.5 % (95 % CB: 26.6, 50.1)).

VIA sensitivity, specificity, positive predictive value and negative predictive value were 28.1 % (95 % CB: 11.2, 6.8), 97.8 % (95 % CB: 93.0, 99.7), 79.8 % (95 % CB: 47.3, 96.8), and 80.4 % (95 % CB: 71.0, 87.5) while that of VIA/DCRC was 69.3 % (95 % CB: 47.8, 89.7), 87.9 % (95 % CB: 76.3, 94.4), 77.6 % (95 % CB: 61.9, 89.3), and 80.3 % (95 % CB: 70.2, 88.9) respectively. Compared to the VIA/DCRC group, there was evidence of better sensitivity, comparable negative predictive value, but poor specificity, RR: 2.46 (95 % CB: 1.06, 6.26), RR: 1.65 (95 % CB: 1.00, 3.50), and RR: 0.90 (95 % CB: 0.78, 0.98) respectively.

☆ This article is part of a special issue entitled: 'Global Gynecologic Oncology' published in Gynecologic Oncology Reports.

* Corresponding author at: Department of Reproductive Health, School of Medicine, Moi University, P.O Box 4606-30100, Eldoret, Kenya.
E-mail address: tonui46@yahoo.co.uk (P. Tonui).

https://doi.org/10.1016/j.gore.2024.101661
Received 18 August 2024; Received in revised form 2 December 2024; Accepted 11 December 2024
Available online 20 December 2024

Conclusions: Cervical cancer screening in HIV + women using VIA/DCRC is feasible and it significantly improves the sensitivity, and comparable negative predictive value of VIA in diagnosing the presence of cervical pre-malignancies by more than double, and 65 % respectively.

1. Introduction

Cervical cancer continues to be the leading cause of cancer-related morbidity and mortality among women. (Bray et al., 2024) The distribution of cases and deaths is heavily weighted towards low- and middle-income countries (LMIC), which have 86 % of the global cases and 88 % of the total deaths. (Jemal et al., 2011) Access to cytology-based or HPV DNA screening, referral for colposcopy, and any form of treatment services is severely limited in these settings owing to the lack of trained manpower, scarcity of financial resources, competing health priorities, and poor awareness of preventive health. (Arbyn et al., 2008) (Sankaranarayanan et al., 2005).

Visual Inspection with Acetic Acid (VIA) has been adopted by several low-middle-income settings as a low-cost alternative to cytology in cervical cancer screening. VIA and conventional pap smears have comparable sensitivity for the detection of high-grade cervical lesions in HIV-uninfected women about 79 – 83 %. (Sankaranarayanan et al., 2005; Mabeya et al., 2012; Zhu et al., 2023) (Maiman et al., 1998; Horo et al., 2012).

New innovative technologies Using a smartphone application, enables the acquisition of consecutive cervical images of VIA. Digital Cervicography using smartphone applications makes it possible to take high-quality pictures for VIA diagnosis. (Wu et al., 2024; IRAN Evaluation of Sensitivity, Specificity, PositITIVE AND NEG PREDICTIVE VALUE OF CERVICOGRAPHY.pdf, n.d.).

Many HIV-infected women may have inflammatory cervical conditions that reduce the sensitivity and specificity of VIA. (Shah et al., 2008) (Gilles et al., 2021) Thus making it a sub-optimal screening tool. Innovative ways of improving the performance of VIA in HIV-infected women are desirable. Data evaluating various techniques aimed at improving the sensitivity/specificity of VIA for the diagnosis of cervical intraepithelial neoplasia 2 or worse (CIN2 +) in HIV-infected women is limited.

Our study compares VIA alone to digital cervicography as an adjunct to VIA with real-time consultation (DCRC). VIA enhanced by digital cervicography (DC) involves digital photography of the cervix to provide a magnified visualization of the surface morphology (Bateman et al., 2015) which is then shared with gynecologic oncologists using smartphones for a telemedicine consult.

Table 1
Demographic and Clinical Characteristics.

Variable	Total	Groups		P-value
	N = 200	VIA/DCRC N = 100	VIA N = 100	
	n (%) or Mean (SD)			
Age (Years), Mean (SD)	39.7 (10.7)	38.9 (9.9)	40.4 (11.4)	0.330[t]
Marital status, n (%)				
Never married	11 (5.5 %)	8 (8.0 %)	3 (3.0 %)	0.125[c]
Married	125 (62.8 %)	54 (54.0 %)	71 (71.7 %)	0.010[c]
Divorced/Separated/ Widowed	63 (31.7 %)	38 (38.0 %)	25 (25.3 %)	0.053[c]
Education level, n (%)				
None/Primary	123 (61.5 %)	61 (61.0 %)	62 (62.0 %)	0.884[c]
Secondary	62 (31.0 %)	33 (33.0 %)	29 (29.0 %)	0.541[c]
College/University	15 (7.5 %)	6 (6.0 %)	9 (9.0 %)	0.421[c]
Occupation, n (%)				
Housewife	76 (38.0 %)	38 (38.0 %)	38 (38.0 %)	>0.999[c]
Self-employed	99 (49.5 %)	52 (52.0 %)	47 (47.0 %)	0.479[c]
Employed	25 (12.5 %)	10 (10.0 %)	15 (15.0 %)	0.285[c]
Years living with HIV, Mean (SD)	6.8 (4.0)	6.9 (3.7)	6.6 (4.3)	0.588[t]
On ARV, n (%)	192 (96.0 %)	97 (97.0 %)	95 (95.0 %)	0.721[f]
CD4 cell count per mm^3, Mean (SD)	492.2 (255.3)	455.5 (219.8)	532.6 (285.9)	0.095[t]
CD4 < 500 cells per mm^3, n (%)	74 (58.7 %)	42 (63.6 %)	32 (53.3 %)	0.241[c]
Detectable viral load, n (%)	50 (34.5 %)	23 (31.1 %)	27 (38.0 %)	0.379[c]
[†]Viral load copies per ml, Mean (SD)	2.6 (0.7)	2.4 (0.5)	2.8 (0.9)	0.093[t]
WHO clinical stage, n (%)				
Stage 1 or 2	105 (69.1 %)	52 (69.3 %)	53 (68.8 %)	
Stage 3 or 4	47 (30.9 %)	23 (30.7 %)	24 (31.2 %)	0.947[c]

[†] Log base 10.
[c] Pearson's Chi Square test.
[f] Fisher's exact test.
[t] Independent samples *t*-test.

2. Methods

2.1. Study site and setting

The AMPATH Cervical Cancer Screening Program runs seven outreach clinics which are located in regional government hospitals and the clinics are manned by trained cervical cancer screening nurses who work 8 h a day from Monday to Thursday. These nurses screen for cervical cancer using VIA. One of the six dedicated gynecologic oncologists visit each of these clinics weekly to offer mentorship, colposcopy, and LEEP services.

Webuye Clinic is located at Webuye County Hospital which is about 72.4 km away from the tertiary center of Moi Teaching and Referral Hospital (MTRH) where the study gynecologic oncologists are situated. The clinic is run by two nurses and a research assistant and they screen about 200 women a month, about 25 % of whom are HIV-infected.

Chulaimbo clinic is located in the Chulaimbo sub-county hospital which is about 126 km from MTRH and is run by two cervical cancer screening nurses and a research assistant they screen an average of 180 women in a month with approximately 25 % being HIV-infected.

The two sites were chosen because they are rural clinics approximately 80 to 150 km away from MTRH and therefore are not easily accessible by program gynecologic oncologists. For this reason, the nurses manning these clinics would stand to benefit from real-time electronic consultations with the gynecologic oncologists.

Each of the two clinics was provided with smart Cellular Phones with the appropriate data plan which was used to take cervical photos and send the data to the gynecologic oncologists. There is excellent cellular phone service in both rural and urban Kenya. The data was transmitted from the nurses in the field to the gynecologic oncologists through a secure mobile application secured by encrypted password logins for the providers on both ends.

2.2. Study population

All HIV-infected women seeking cervical cancer screening services in Webuye and Chulaimbo clinics between June 2015 and May 2016

Table 2
Gynecological Characteristics.

Variable	Total	Groups		P-value
		VIA/ DCRC	VIA	
	N = 200	N = 100	N = 100	
	n (%) or Median (IQR) or Mean (SD)			
Parity, Mean (SD)	3.6 (2.1)	3.3 (2.0)	3.8 (2.1)	0.097[t]
Currently using contraceptives, n (%)	100 (51.0 %)	50 (50.5 %)	50 (51.5 %)	0.884[c]
Types of contraceptives				
Condoms, n (%)	45 (45.0 %)	24 (48.0 %)	21 (42.0 %)	0.360[c]
Coil/IUCD, n (%)	3 (3.0 %)	1 (2.0 %)	2 (4.0 %)	>0.999[f]
Bilateral tubal ligation, n (%)	3 (3.0 %)	2 (4.0 %)	1 (2.0 %)	>0.999[f]
Implant, n (%)	3 (3.0 %)	3 (6.0 %)	0 (0.0 %)	0.242[f]
Pills, n (%)	4 (4.0 %)	4 (8.0 %)	0 (0.0 %)	0.117[f]
Norplant, n (%)	11 (11.0 %)	4 (8.0 %)	7 (14.0 %)	0.338[c]
Jadelle, n (%)	11 (11.0 %)	2 (4.0 %)	9 (18.0 %)	0.025[c]
Depo Provera, n (%)	33 (33.0 %)	19 (38.0 %)	14 (28.0 %)	0.288[c]
Class of the contraceptives				
Non-Hormonal, n (%)	62 (62.0 %)	32 (64.0 %)	30 (60.0 %)	0.680[c]
Hormonal, n (%)	50 (50.0 %)	26 (52.0 %)	24 (48.0 %)	0.689[c]
Experiencing inter-menstrual bleeding, n (%)	38 (19.2 %)	19 (19.0 %)	19 (19.4 %)	0.945[c]
Experiencing contact/post-coital bleeding, n (%)	11 (5.6 %)	9 (9.0 %)	2 (2.0 %)	0.033[c]
Currently experiencing abnormal vaginal discharge, n (%)	35 (17.8 %)	16 (16.2 %)	19 (19.4 %)	0.554[c]
Foul-smelling discharge, n (%)	23 (67.6 %)	8 (53.3 %)	15 (78.9 %)	0.151[f]
Previously had cervical cancer screening, n (%)	118 (60.2 %)	58 (58.6 %)	60 (61.9 %)	0.640[c]
Number of times, n (%)				
Once	92 (79.3 %)	46 (80.7 %)	46 (78.0 %)	
More than once	24 (20.7 %)	11 (19.3 %)	13 (22.0 %)	0.716[c]
Results of previous screens, n (%)				
Negative	112 (95.7 %)	56 (96.6 %)	56 (94.9 %)	0.662[c]
Positive	5 (4.3 %)	2 (3.4 %)	3 (5.1 %)	

[c] Pearson's Chi Square test.
[f] Fisher's exact test.
[t] Independent samples *t*-test.

constituted the study population. Those who met the eligibility criteria and gave consent were enrolled into the study.

2.3. Study design

This is a cross-sectional analytical study of a group of HIV-infected women seeking screening services at the two peripheral AMPATH cervical cancer screening clinics.

2.4. Sampling and recruitment

Nurses identified HIV-infected patients undergoing routine cervical cancer screening and who met the eligibility criteria. This included women above the age of 18 years, non-pregnant or within 3 months of pregnancy by self-report, with no obvious invasive disease, no history of hysterectomy or current anticoagulant therapy, and deemed healthy enough to undergo a pelvic examination (as assessed by the nurse enrolling for the study and defined as patients who were not bedridden or physically incapacitated).

The enrolling nurse then counseled and invited these women to participate in the study. Informed written consent was obtained from all participants, and a nurse-administered questionnaire was used to collect socio-demographic data. Informed consent was obtained in Kiswahili or English language, as appropriate to the patient, using forms at the appropriate literacy level in a setting that ensured privacy and confidentiality.

2.5. Sampling technique and sampling size

The differences in detection rates of both malignant lesions and pre-invasive disease among the two tests i.e., VIA alone and VIA/DCRC was unknown as this was the primary study testing this screening tool in this area. Therefore, this precluded sample size and power calculations. The proportion of discordant pairs as diagnosed by the two screening tests (VIA and VIA/DCRC) in our HIV population was also unknown. The study therefore enrolled 200 consecutive, HIV-infected women.

2.6. Study procedure

Relevant socio-demographic data collected included age, marital status, occupation, and education level. A full medical history (CD4 counts, plasma viral load if available, WHO Disease stage, antiretroviral therapy/adherence, sexual history, STD history, other medical co-morbidities, contraception, gravidity/parity, smoking, substance abuse including alcohol, age at first sexual activity) was also obtained.

Half of the study participants (100) underwent cervical cancer screening by VIA and the other half had VIA with Digital Cervicography and Real-time Consultation (VIA/DCRC) done by the screening nurse. Allocations of clients to either the VIA-only arm or VIA/DCRC arm was done by random number digital allocation. The nurse documented his/her findings as either VIA positive or VIA negative and management of either finding proceeded as per Ampath CCSP protocols. For the study participants who were screened by VIA/DCRC, the nurse did VIA and then took a photograph of the cervix using the provided cell phone, uploaded it, and electronically shared it in real-time with the three-study consultant gynecologic oncologists who independently provided an assessment of the digital image as VIA/DCRC negative or VIA/DCRC positive (low grade or high grade) and texted back their opinion to the concerned study nurse. Data (digital image of the cervix) was transmitted from the nurses in the field to clinicians through a mobile phone. No patient identifiers were included in the data transmitted electronically thus ensuring patient confidentiality.

The consultant gynecologic oncologists were blinded to the assessment of the nurse and to the assessment of the other oncologists. Any two opinions of the consultants that concurred were, in this study, taken as the final result of the VIA/DCRC screening. All participants who screened VIA or VIA/DCRC positive underwent colposcopy and biopsy which was scheduled in a return visit in two to three weeks and was

Table 3
Screening results.

Variable	N	n (%) or Median (IQR)
VIA		
Negative	100	93 (93.0 %)
Positive	100	7 (7.0 %)
VIA/DCRC		
Negative		67 (67.0 %)
Positive	100	33 (33.0 %)
Time taken to relay the results by the consultants (Minutes)		2.0 (1.0, 4.0)
Range (Min. – Max.)		1.0 – 47.0

Table 4
Biopsy and Histological Findings.

Variable	N	n (%)
Cervical biopsies for histological examination		
VIA Negative	93	16 (17.2 %)
VIA/DCRC Negative	67	10 (14.9 %)
Positive for VIA | VIA/DCRC	40	40 (100.0 %)
Total biopsied	200	66 (33.0 %)
Histology results among all the participants who were biopsied		
CIN 1		20 (30.3 %)
CIN 2		17 (25.8 %)
CIN 3	66	10 (15.2 %)
Micro invasive carcinoma		3 (4.5 %)
Normal (No Epithelial Abnormality)		16 (24.2 %)
CIN2+	66	30 (45.5 %)

Table 5
Biopsy Results by Screening Arm.

Verified Groups	Biopsy Results (CIN2 +)		Total
	No	Yes	
VIA Negative	14 (87.5 %)	2 (12.5 %)	16 (24.2 %)
VIA/DCRC Negative	7 (70.0 %)	3 (30.0 %)	10 (15.2 %)
Positive for VIA | VIA/DCRC	15 (37.5 %)	25 (62.5 %)	40 (60.6 %)
Total	36 (54.5 %)	30 (45.5 %)	66 (100.0 %)

done by Ampath CCSP study gynecologic oncologists. Patients who were eligible for cryotherapy or LEEP as per Ampath CCSP standard of care were triaged to colposcopy and biopsy first before treatment and 15 % of those who screened VIA or VIA/ DCRC negative from each group had random cervical biopsies taken at 12 and 6o'clock positions. Treatment followed the standard of care of AMPATH CCSP.

2.7. Statistical data analysis

Categorical variables such as marital status, education level, and occupation were summarized using frequencies and the corresponding percentages. Continuous variables were summarized using mean and the corresponding standard deviation if Gaussian assumptions were holding. If Gaussian assumptions were violated, they were summarized using the median and the corresponding interquartile range (IQR). Gaussian assumptions were assessed using the Shapiro-Wilk test and histograms.

Categorical variables were compared using Pearson's Chi-square test. Mean between groups was compared using independent samples *t*-test while median values were compared using two samples Wilcoxon ranks sum test. Data analysis was done using R: A language and environment for statistical computing.

The estimates for the sensitivity and specificity of a test that is only based on verified subjects suffer from verification bias. Hence in this analysis, we utilized Bayesian analysis implemented using the Gibbs sampler algorithm to estimate the sensitivity, specificity, and positive predictive and negative predictive values. (Martinez et al., 2006) The estimates so obtained will not be subject to verification bias. We reported the estimates and the corresponding 95 % credible bounds.

3. Results

A total of 200 consecutive, HIV-infected women were enrolled in the study. Half of these women were screened for cervical cancer using VIA and the remaining half by VIA/DCRC. The demographic and clinical characteristics of the women in each arm are shown in Table 1 and two groups were found comparable.

The mean age of the study population was 39.7 years with the majority of whom being married and with primary school being the highest level of education. On average, the women had lived with HIV disease for close to 7 years and 96 % were on HAART.

Table 2 shows the gynecological characteristics of the study participants. The mean parity was 3.6 with 60.2 % having undergone cervical cancer screening at least once in the past and 4.2 % of whom had a previous abnormal screen. The two groups maintained comparability in their gynecologic characteristics.

Table 3 summarizes the screening results of the two screening methods and also shows that the median (IQR) time taken by the doctors to respond to a real-time consultation was 2.0 (IQR: 1.0, 4.0) minutes, range (1.0 – 47.0).(See Tables 4–8).

The gynecologic oncologists reported a VIA/DCRC positivity rate of 33 % while nurses reported a VIA positivity rate of 7 %.

Among the 66 women who underwent cervical biopsy and histopathological examination, 30 (45.5 %) had CIN2+ (CIN2, CIN3, and micro-invasive carcinoma).

Sixty-six participants had cervical biopsies. Of this number 16 (24.2 %), and 10 (15.2 %) were VIA negative and VIA/DCRC negative respectively. The rest (60.6 %) were screen positives by either VIA or VIA/DCRC.

The sensitivity, specificity, positive predictive value, and negative predictive value for VIA were 28.1 % (95 % CB: 11.2, 6.8), 97.8 % (95 % CB: 93.0, 99.7), 79.8 % (95 % CB: 47.3, 96.8), and 80.4 % (95 % CB: 71.0, 87.5) respectively. Similarly, the sensitivity, specificity, positive predictive value, and negative predictive value for VIA/DCRC were 69.3 % (95 % CB: 47.8, 89.7), 87.9 % (95 % CB: 76.3, 94.4), 77.6 % (95 % CB: 61.9, 89.3), and 80.3 % (95 % CB: 70.2, 88.9) respectively. Comparison of VIA/DCRC to VIA alone showed evidence of better sensitivity, and comparable negative predictive value for VIA/DCRC, RR: 2.46 (95 % CB: 1.06, 6.26), and RR: 1.65 (95 % CB: 1.00, 3.50) respectively. Specificity was significantly lower among the VIA/DCRC group compared to the VIA alone group, RR: 0.90 (95 % CB: 0.78, 0.98). There was no evidence of a difference in positive predictive values between the two groups, 1.00 (95 % CB: 0.84, 1.17).

Upon comparing the performance of VIA/DCRC to that of the VIA specifically among women whose cervixes were assessed by both methods, the findings correcting for verification bias reveal that VIA/DCRC would correctly identify CIN2 + for 87.8 % (95 % CB: 70.0, 98.2) of the women with CIN2 + compared to VIA which identified 34.7 % (95 % CB: 18.1, 55.3) of the women with CIN2 + correctly. This demonstrates an increase in sensitivity of 2.5 times when VIA/DCRC is used

Table 6
Absolute frequencies for the cross-tabulation of the test results and histology findings in the VIA arm and the VIA/DCRC arm.

		Biopsy Verified			Unverified by Biopsy	Total
		CIN2+		Total		
		Yes	No			
VIA	Positive	4	3	7	0	7
	Negative	2	14	16	77	93
	Total	6	17	23	77	100
VIA/ DCRC	Positive	21	12	33	0	33
	Negative	3	7	10	57	67
	Total	24	19	43	57	100

Table 7
Measures of Accuracy of VIA and VIA/DCRC Among Participants with Histologically Confirmed CIN2+.

Measure of accuracy	VIA % (95 % CB)	VIA/DCRC % (95 % CB)	RR (95 % CB)
Sensitivity	28.1 (11.2, 96.8)	69.3 (47.8, 89.7)	2.46 (1.06, 6.26)
Specificity	97.8 (93.0, 99.7)	87.9 (76.3, 94.4)	0.90 (0.78, 0.98)
Positive predictive value	79.8 (47.3, 96.8)	77.6 (61.9, 89.3)	1.00 (0.84, 1.17)
Negative predictive value	80.4 (71.0, 87.5)	80.3 (70.2, 88.9)	1.65 (1.00, 3.50)

CB – Credible bounds.

Table 8
Comparison of Measures of Accuracy of VIA by Nurses and VIA/DCRC by Consultants for the Detection of CIN2 + Among Same Women Evaluated Directly by the Two Groups.

		VIA by Nurses % (95 % CB)	VIA/DCRC by Consultants % (95 % CB)	RR (95 % CB)
Excluding unverified women	Se	34.3 (18.1, 53.7)	85.4 (69.0, 95.5)	2.47 (1.52, 4.73)
	Sp	95.3 (89.0, 98.6)	83.6 (74.4, 90.7)	0.88 (0.79, 0.98)
	PPV	41.0 (29.6, 47.3)	38.4 (31.6, 43.7)	0.94 (0.73, 1.33)
	NPV	45.1 (42.3, 47.1)	48.6 (46.8, 49.6)	1.08 (1.02, 1.15)
	Prev	24.3 (16.8, 33.2)	24.4 (16.8, 33.4)	1.00 (0.61, 1.62)
Assuming unverified women were all negative	Se	34.3 (18.1, 53.3)	85.5 (68.9, 95.5)	2.47 (1.52, 4.73)
	Sp	82.0 (62.5, 94.2)	37.7 (19.0, 59.3)	0.47 (0.23, 0.78)
	PPV	41.4 (30.1, 47.4)	38.8 (31.7, 43.9)	0.94 (0.73, 1.31)
	NPV	33.2 (24.7, 40.0)	40.3 (27.9, 47.1)	1.21 (0.81, 1.69)
	Prev	55.7 (40.9, 69.7)	55.7 (41.0, 69.4)	1.00 (0.68, 1.46)
Correcting for verification bias	Se	34.7 (18.1, 55.3)	87.8 (70.0, 98.2)	2.50 (1.50, 4.84)
	Sp	83.2 (63.6, 94.6)	36.9 (17.2, 59.4)	0.45 (0.21, 0.76)
	PPV	28.4 (15.1, 41.2)	23.5 (16.5, 31.1)	0.83 (0.49, 1.66)
	NPV	44.4 (41.0, 46.8)	47.5 (42.2, 49.7)	1.07 (0.94, 1.17)
	Prev	24.2 (16.5, 33.1)	24.2 (16.6, 33.0)	1.00 (0.61, 1.64)

CB – Credible bounds, Se – Sensitivity, Sp – Specificity, PPV – Positive predictive value, NPV – Negative predictive value, Prev – Prevalence, RR – Rate Ratio.

for cervical cancer screening in HIV + women (95 % CB: 1.50, 4.84). However, more often the VIA/DCRC would misclassify most of the women without CIN2 + as having CIN2+, specificity: 36.9 % (95 % CB: 17.2, 59.4) vs. 83.2 % (95 % CB: 63.6, 94.6), RR: 0.45 (95 % CB: 0.21, 0.76).

4. Discussion

The selection of an appropriate screening test is reliant on its accuracy, based on its sensitivity, and specificity, and even more profoundly its safety profile and simplicity in terms of execution. HIV-infected individuals are uniquely situated to rapidly progressive disease once exposed to the HPV virus and thus require the availability of accessible screening methods. (Shah et al., 2008; Perez-Guzman et al., 2020) (Gichangi et al., 2003) VIA has been used in LMICs due to its comparable sensitivity to cytology however the test can be improved upon to increase its accuracy.

The analyses from this study show that screening with VIA with the addition of digital cervicography with real-time consultation allows the detection of the presence of cervical cancer and its precursors with an accuracy as good or even better than VIA alone. When a head-to-head comparison of the performance of VIA and VIA/DCRC on the detection of CIN2 + for women who underwent the two tests in this study, it was found that VIA/DCRC improved the sensitivity of VIA by 2.5 times. This makes VIA/DCRC an attractive tool during screening. In low-middle-income countries, digital cervicography is a useful screening method for cervical cancer prevention. (IRAN Evaluation of Sensitivity, Specificity, PositITIVE AND NEG PREDICTIVE VALUE OF CERVICOGRAPHY.pdf, n.d.).

In Lusaka, Zambia, clinical performance of digital cervicography and cytology to detect cervical intraepithelial neoplasia grade 2 or worse was estimated. Sensitivity and specificity of cervicography were 84 % (95 % CI: 72–91 %) and 58 % (95 % CI: 52–64 %). At high-grade squamous intraepithelial lesions or worse cut off for cytology, sensitivity, and specificity were 61 % (95 % CI: 48–72 %) and 58 % (95 % CI: 52–64 %). In this study, cervicography with real-time consultation appears to have comparable efficacy as cytology in screening HIV-infected women. (13).

The sensitivity, specificity, and positive predictive value (PPV) of cervicography in the detection of CIN 2 + were 72.41 %, 97 %, and 84 %, respectively in a study in Thailand, which were not inferior to Pap smear. (Singhakum et al., 2018).

Firnhaber C et al demonstrated a 65.4 % sensitivity for the detection of CIN2 + in HIV-infected women by VIA and this sensitivity was increased to 76 % with physician quality assurance review of digital cervicographs. (Firnhaber et al., 2013; Jeronimo and Tsu, 2015).

For many LMICs with low screening participation, implementing successful and affordable screening programs in low-resource settings is crucial. Additional research is needed to validate the clinical performance of digital cervicography, and these programs can be scaled up using practical, cost-effective methods. (IRAN Evaluation of Sensitivity, Specificity, PositITIVE AND NEG PREDICTIVE VALUE OF CERVICOGRAPHY.pdf, n.d.).

The difference between the previous studies and our study is the aim to do real-time consultation with gynecologic oncologists by texting cervical images by phone and giving immediate feedback to clinical nurses. The rapid response rate by the gynecologic oncologist of 2.0 min ensures the feasibility of conducting real-time consultation in a low-resource setting without an on-site gynecologic oncologist. This will improve care and service delivery to the patients by providing prompt and appropriate management. It further determines that the reliability and accuracy of VIA is improved by the use of digital cervicography in addition to real-time consultation in these settings where VIA is the only available screening modality. Cervical cancer screening centers can be linked to gynecologic oncologists by readily available mobile phones for telemedical consultation. This will decrease the number of patients referred to the main hospital for colposcopy.

The primary limitation of this study was the absence of an adequate sample size and power calculations. At the time of the study, logistical and resource constraints made it challenging to recruit a larger group. We selected 200 women to ensure that we could manage the study within these constraints while still obtaining meaningful data. Other limitations of the study include the scheduling of women for follow-up exams 2 to 3 weeks after the initial visit rather than employing a screen-and-treat approach. Additionally, biopsies were performed using 2-quadrant position sampling instead of the more comprehensive 4-quadrant position sampling, which would have increased the likelihood of detecting diseased regions of the cervix.

5. Conclusions

Our clinical performance point estimates suggest that VIA/DCRC is comparable to VIA alone and significantly improves the performance of

VIA screening in identifying cervical lesions in our population of HIV-infected women. The additional use of telemedical consultation boosts the sensitivity of VIA and based on the response time from this study, there would be minimal delay for patients being screened in peripheral centers.

5.1. Recommendations

There is a need to integrate and implement VIA-DCRC into cervical cancer screening protocols for HIV-infected women which could improve early detection and diagnosis. Additionally, training nurses and other healthcare professionals on the use of digital cervicography and VIA-DCRC could improve screening accuracy and diagnostic capabilities, particularly in settings with limited resources. Furthermore, to ensure wider applicability and comprehension of the advantages and limitations of VIA-DCRC, more research with bigger sample sizes and diverse populations is advised to validate and build upon these findings.

CRediT authorship contribution statement

P. Tonui: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Investigation, Formal analysis, Data curation, Conceptualization. **P. Itsura:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Conceptualization. **O. Omenge:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Conceptualization. **N. Faiza:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Conceptualization. **A. Keter:** Validation, Software, Methodology, Formal analysis, Data curation. **A. Mburu:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Conceptualization. **J. Oguda:** Validation, Software, Methodology, Formal analysis, Data curation. **Amina R. Hassan:** Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Conceptualization. **S. Cu-Uvin:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Resources, Project administration, Methodology, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

The authors would like to thank the AMPATH Cervical Cancer Screening Program team at MTRH, Webuye and Chulaimbo.

References

Arbyn, M., Sankaranarayanan, R., Muwonge, R., Keita, N., Dolo, A., Mbalawa, C.G., et al., 2008. Pooled analysis of the accuracy of five cervical cancer screening tests assessed in eleven studies in Africa and India. Int. J. Cancer 123 (1), 153–160.

Bateman AC, Parham GP, Sahasrabuddhe V V, Mwanahamuntu MH, Kapambwe S, Katundu K, et al. NIH Public Access. 2015;67(2):212–5.

Bray, F., Laversanne, M., Sung, H., Ferlay, J., Siegel, R.L., Soerjomataram, I., et al., 2024. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J. Clin. 74 (3), 229–263.

Firnhaber, C., Mayisela, N., Mao, L., Williams, S., Swarts, A., Faesen, M., et al., 2013. Validation of cervical cancer screening methods in HIV positive women from Johannesburg South Africa. PLoS One 8 (1), 2–9.

Gichangi, P.B., Bwayo, J., Estambale, B., De Vuyst, H., Ojwang, S., Rogo, K., et al., 2003. Impact of HIV infection on invasive cervical cancer in Kenyan women. AIDS 17 (13), 1963–1968.

Gilles C, Velghe-lenelle M, Manigart Y, Konopnicki D, Rozenberg S. Should the management of high-grade cervical squamous intraepithelial lesions (HSIL) be different in HIV-positive women? AIDS Res Ther [Internet]. 2021;18(1):1–11. Available from: https://doi.org/10.1186/s12981-021-00371-x.

Horo, A., Jaquet, A., Ekouevi, D., Toure, B., Coffie, P.A., Effi, B., et al., 2012. Cervical cancer screening by visual inspection in Cte d'Ivoire, operational and clinical aspects according to HIV status. BMC Public Health 12 (1).

IRAN Evaluation of Sensitivity, Specificity, PositITIVE AND NEG PREDICTIVE VALUE OF CERVICOGRAPHY.pdf.

Jemal, A., Bray, F., Center, M.M., Ferlay, J., Ward, E., Forman, D., 2011. Global cancer statistics. CA Cancer J. Clin. 61 (2), 69–90.

Jeronimo, J., Tsu, V., 2015. Correspondence to "Evaluation of a cervicography-based program to ensure the quality of visual inspection of the cervix in HIV-infected women in Johannesburg, South Africa. J. Low. Genit. Tract Dis. 19 (2), e46.

Mabeya H, Khozaim K, Liu T, Orango O, Chumba D, Pisharodi L, et al. Virus Y Infected Women in Western Kenya. 2012;16(2):92–7.

Maiman, M., Fruchter, R.G., Sedlis, A., Feldman, J., Chen, P., Burk, R.D., et al., 1998. Prevalence, risk factors, and accuracy of cytologic screening for cervical intraepithelial neoplasia in women with the human immunodeficiency virus. Gynecol. Oncol. 68 (3), 233–239.

Martinez, E.Z., Alberto Achcar, J., Louzada-Neto, F., 2006. Estimators of sensitivity and specificity in the presence of verification bias: a Bayesian approach. Comput. Stat. Data Anal. 51 (2), 601–611.

Perez-Guzman, P.N., Chung, M.H., De Vuyst, H., Dalal, S., Mutai, K.K., Muthoni, K., et al., 2020. The impact of scaling up cervical cancer screening and treatment services among women living with HIV in Kenya: a modeling study. BMJ Glob. Heal. 5 (3), 3–12.

Sankaranarayanan, R., Gaffikin, L., Jacob, M., Sellors, J., Robles, S., 2005. A critical assessment of screening methods for cervical neoplasia. Int. J. Gynecol. Obstet. 89 (SUPPL. 2), 4–12.

Shah, S., Montgomery, H., Crow, J.C., Smith, C.J., Moore, A., Sabin, C.A., et al., 2008. Cervical intraepithelial neoplasia treatment in Human Immunodeficiency Virus-positive women. J. Obstet. Gynaecol. (Lahore) 28 (3), 327–332.

Singhakum, N., Laiwejpithaya, S., Chaopotong, P., 2018. Digital cervicography by simply a portable device as an alternative test for cervical cancer screening in rural areas of Thailand. Asian Pac. J. Cancer Prev. 19 (4), 1145–1149.

Wu T, Lucas E, Zhao F, Basu P, Qiao Y. Artificial intelligence strengthens cervical cancer screening - present and future. Cancer Biol Med [Internet]. 2024; Available from: http://www.ncbi.nlm.nih.gov/pubmed/39297572.

Zhu Y, Feldman S, Leung SOA, Creer MH, Warrick J, Williams N, et al. AACC Guidance Document on Cervical Cancer Detection: Screening, Surveillance, and Diagnosis. J Appl Lab Med [Internet]. 2023;8(2):382–40Available from: https://doi.org/10.1093/jalm/jfac142.