Comparison of mobile colposcopic impression to cytology and HPV results in a high-risk US population

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Background: The mobile and online-connected EVA System colposcope allows providers to capture and annotate colposcopic images, connect for a live consultation, or observe beginning colposcopists remotely for quality assurance. An analysis was done on a high-risk patient population in California to explore if visualization using EVA at screening can improve patient management. **Methods**: Colposcopy exam results recorded on the EVA System app from N=327 patients were analyzed retrospectively. The specific parameters of interest included colposcopic impression, latest cytology and HPV test results, and other patient data including age and HIV status. These data were compared against histopathology results, obtained from patients' medical records. **Results**: For CIN 2+ histopathology, both HPV testing and cytology (ASCUS threshold) had an NPV of 1.00; cytology (LSIL threshold) had an NPV of 0.94, and visualization had an NPV of 0.89. In terms of PPV, visualization had the highest value of the various tests (0.45); the remaining tests ranged between 0.17-0.29. Similar results were found for CIN 3 histopathology, where visual colposcopic impression had a PPV of 0.146, higher than all other tests, which ranged between 0.04-0.09. In terms of test inadequacy rates, visualization failed to yield a result in <1% of cases. HPV, cytology, and histopathology had inadequacy rates of 20%, 4%, and 5%, respectively. **Conclusion**: Visualization had a higher PPV and much lower inadequacy rates than HPV testing and cytology. This suggests it may have a role to play in triage of HPV+ patients. Further analysis on a screening population is needed.

Introduction

The ubiquity of digital cameras and smartphones are changing the role of visualization within cervical cancer care. Digital cervicography efforts in Zambia [1] developed a screening program based on visualization. Mobile colposcopes have also become commercially available, making colposcopy more accessible even in remote locations. MobileODT's mobile colposcope [2] also includes secure storage of images for remote consultation, telecolposcopy and quality assurance. Yet despite all these tools now available, there has not been rigorous analyses on a US population comparing visual methods, primarily used in low resource settings, with HPV testing and cytology.

In this study, we compared cervical images with traditional screening tests in a California clinic addressing a high risk population. In this retrospective study, cervical decisions based on digital images were compared with cytology and HPV testing, with cervical intraepithelial neoplasia (CIN) 2 and CIN 3 pathology as endpoints.

Our objective was to determine whether capturing colposcopic impressions during primary cervical cancer screening can improve the accuracy (sensitivity and specificity) of the screening test and provide information that could be useful in patient management.

The current screening paradigm of HPV testing with cytology as a triage test lacks a test with a high positive predictive value (PPV), leading to overtreatment. As a first step, we examined visualization on a colposcopy population which has a higher prevalence of disease, comparing it to HPV testing and cytology (both ASCUS and LSIL thresholds), measured against histopathology. Our hypothesis was that visualization will improve management because it yields an immediate result.

Methods

A retrospective study was conducted on colposcopy patients examined using MobileODT's mobile colposcope – the Enhanced Visual Assessment (EVA) System (Fig. 1) – which was built around a smartphone platform. The EVA System is ran by an app that collects basic patient information and stores it together with colposcopy images on a HIPAA-compliant cloud-based image portal. We compared information stored on the EVA System to the recent medical history. Patient demographics and medical history are shown in Fig. 2A-C. This study was covered by the Institutional Review Board approval of the National Cancer Institute, USA (18-NCI-00695).

Fig 1: The EVA System's Mobile Colposcope.

Patient information was collected through the patients' electronic medical records. Specifically, HPV and cytology history, other STD history, gravida, parity, and contraceptive information was recorded. In parallel, information was also retrieved from the EVA System web portal, which contains clinical decisions recorded on a job aid (Fig. 3) at the point of care (PoC).

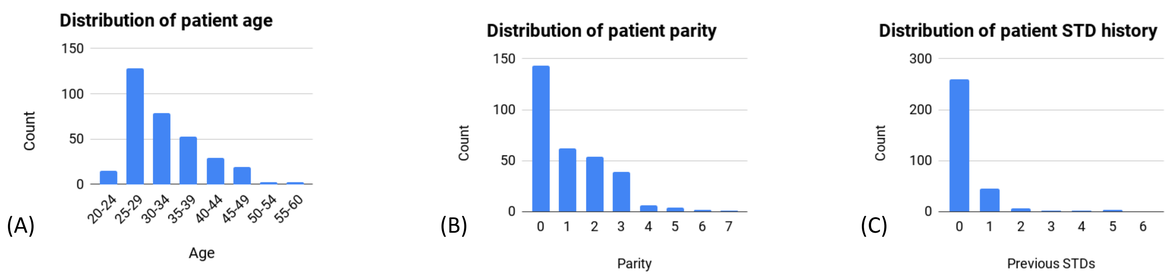

Fig 2: Distribution of patient age (A), parity (B), and STD history (C). Information available on EVA app

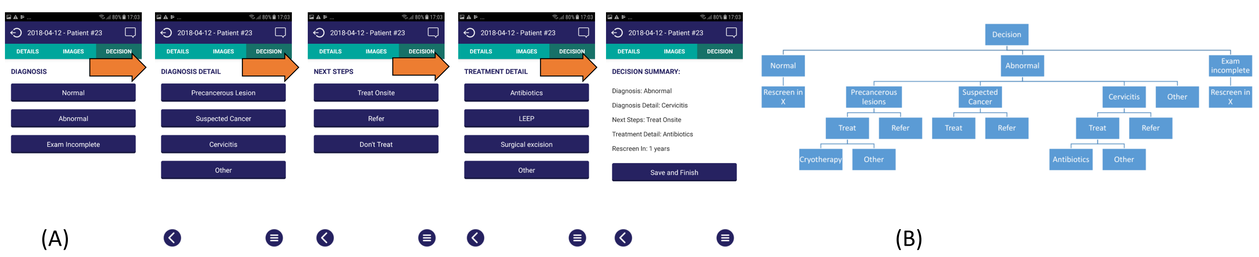

Fig 3: Decision Support Job Aid on the EVA System app. (A) Screenshots of the key steps. (B) Full decision tree backbone.

References

[1] Parham, Groesbeck P., et al. "Population-level scale-up of cervical cancer prevention services in a low-resource setting: development, implementation, and evaluation of the cervical cancer prevention program in Zambia." PLoS One 10.4 (2015): e0122169.
[2] Peterson, Curtis W., et al. "Real-time monitoring and evaluation of a visual-based cervical cancer screening program using a decision support job aid." Diagnostics 6.2 (2016): 20.

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Results

A comparison of HPV testing, visual colposcopic impression, and cytology (ASCUS and LSIL thresholds) against histopathology, with a CIN 2 endpoint is shown in Tables 1-4, respectively. Using a similar analysis, the PPV and NPV with a CIN 3 endpoint are given in Table 5. A comparison of inadequacy rates for the various tests is shown in Fig. 4.

Table 1: HPV testing versus histopathology, CIN 2 endpoint.

	HPV +	HPV -	HPV Unknown
Histo +	41	0	9
Histo -	189	17	56
Histo Unknown	10	2	3

Sens: 1.000 PPV: 0.178
Spec: 0.083 NPV: 1.000

Table 2: Visual colposcopic impression versus histopathology, CIN 2 endpoint.

	Vis +	Vis -	Vis Unknown
Histo +	22	28	0
Histo -	26	233	3
Histo Unknown	3	12	0

Sens: 0.440 PPV: 0.458
Spec: 0.900 NPV: 0.892

Table 3: Cytology (ASCUS threshold) versus histopathology, CIN 2 endpoint.

	Cyt +	Cyt -	Pap Unknown
Histo +	49	0	1
Histo -	240	12	10
Histo Unknown	11	3	1

Sens: 1.000 PPV: 0.170
Spec: 0.048 NPV: 1.000

Table 4: Cytology (LSIL threshold) versus histopathology, CIN 2endpoint.

	Cyt +	Cyt -	Pap Unknown
Histo +	39	10	1
Histo -	97	155	10
Histo Unknown	11	3	1

Sens: 0.796 PPV: 0.289
Spec: 0.618 NPV: 0.939

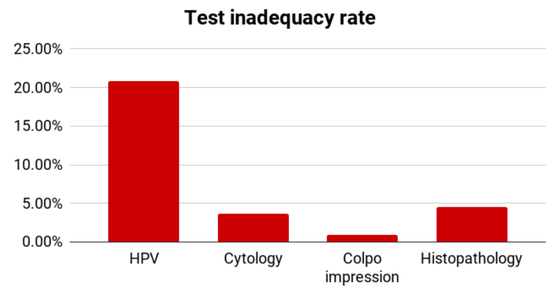

Fig 4: Comparison of inadequacy rates for the 4 tests used in the study. A rate of 2% is considered acceptable.

Table 5: A comparison of PPV and NPV for 4 tests, with a *CIN 3 endpoint*.

	PPV	NPV
HPV	0.048	1.000
Cytology / ASCUS	0.042	1.000
Cytology / LSIL	0.089	1.000
Vis colpo. impression	0.146	0.981

Discussion and Conclusion

In this retrospective study, we sought to determine whether visualization of the cervix during screening can provide information that can improve patient management. We compared the colposcopic impression to HPV testing and cytology, using CIN 2 histopathology of the colposcopic biopsy as an endpoint. Our results showed that the PPV of colposcopic visualization (46%) was higher than those of both HPV testing (18%) and cytology (ASCUS threshold at 17%, LSIL threshold at 29%). Similar trends were observed when looking at high grade lesions (CIN 3). At the time of screening, NPV is more important the PPV. However, as a triage test, the higher PPV of visualization for both CIN 2 and CIN 3 suggests that it could potentially have a role to play.

In our study, both HPV testing and cytology (ASCUS threshold) performed perfectly in terms of NPV and sensitivity. The performance of cytology was indeed surprising, as it was much better than values reported in the literature. Moreover, a preliminary analysis of confounding factors showed STD history correlated with advanced disease more than gravida, parity, and age (data not shown).

One of the surprising results of the current study is the high inadequacy rates of the standard of care tests. The main benefit of colposcopic impression was that the provider was only unable to make a decision at the PoC in <1% of cases. This was much lower than the comparative tests. HPV testing surprisingly had an inadequacy rate of 20%, which is problematic for a primary screening test used at a US clinic. Cytology had an inadequacy rate of 4%, which is still lower than the 2% inadequacy rate expected of cytopathology services. Histopathology had an inadequacy rate of 5%.

The benefit of an immediate result offered by visualization can be substantial on those patients on a non-negligible portion of the population.

The main limitation of the present study was that it was based on a colposcopy population, which could have potentially biased the colposcopic impression. What made the current study possible was the ability to record colposcopic impression on the colposcope at the PoC, a feature that is currently only available on the EVA System. Follow up studies will have a prospective design and would enable examining a screening population, which would circumvent such a bias from the colposcopic impression and provide a more reliable assessment of how visualization at screening can affect patient management.