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Validation of a new HPV self-sampling device for cervical cancer screening: The Cervical and Self-Sample In Screening (CASSIS) study

Mariam El-Zein [a], Sheila Bouten [a], Karolina Louvanto [a,1], Lucy Gilbert [b], Walter Gotlieb [c], Robert Hemmings [d], Marcel A. Behr [e], Eduardo L. Franco [a,*], for the CASSIS Study Group , Victoria Liang [aa], Claudia Martins [ab], Silvy Duarte [ab], Natalia Sarban [ab], Patricia Geddes [ab], Ana Massa [ac], Kathrin Samios [ac], Siham Aboufadl [ad], Sophie Verdon [ae], Cynthia Pereria [ae], Isabelle Lacroix [ae]

[a] Division of Cancer Epidemiology, McGill University, Montreal, Canada
[b] Gynecologic Cancer Service, McGill University Health Centre - Glen Site Cedars Cancer Centre, Montreal, Canada
[c] Division of Gynecologic Oncology and Colposcopy, McGill University - Jewish General Hospital, Montreal, Canada
[d] Department of Obstetrics and Gynecology, McGill University Health Centre - St Mary's Hospital Centre, Montreal, Canada
[e] Department of Microbiology, McGill University Health Centre, Montreal, Canada
[aa] Division of Cancer Epidemiology, McGill University, Montreal, Canada
[ab] Gynecologic Cancer Service, McGill University Health Centre - Glen Site Cedars Cancer Centre, Montreal, Canada
[ac] Division of Gynecologic Oncology and Colposcopy, McGill University - Jewish General Hospital, Montreal, Canada
[ad] Department of Obstetrics and Gynecology, McGill University Health Centre - St Mary's Hospital Centre, Montreal, Canada
[ae] Department of Microbiology, McGill University Health Centre, Montreal, Canada

HIGHLIGHTS

- Self-samples using HerSwab™ are sensitive for detecting high-grade cervical lesions.
- High agreement was found between self- and physician-sampling in detecting HPV.
- Women expressed positive feelings towards using HerSwab™.
- Women preferred self- over physician-sampling.

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ABSTRACT

Objective. We compared the self-sampling performance of the newly designed HerSwab™ device with a physician-collected cervical sample and another self-sample using the cobas® PCR Female swab for the detection of cervical intraepithelial neoplasia (CIN) and cancer.

Methods. Women referred for colposcopy at McGill University affiliated hospital clinics collected two consecutive self-samples, one with HerSwab™ and one with cobas® swab, after receiving instructions. The order of sampling was randomized. The colposcopist then collected a cervical sample and conducted a colposcopic examination. Samples were tested for human papillomavirus (HPV) DNA. Sensitivity and specificity to detect CIN2+ and respective 95% confidence intervals (CI) were calculated to compare sampling approaches. The HPV testing agreement between samples was measured using the Kappa statistic.

Results. Of 1217 women enrolled, 1076 had complete results for HPV and cytology; 148 (13.8%) had CIN1, 147 (13.7%) had CIN2/3, and 5 (0.5%) had cancer. There was very good agreement between methods for HPV detection (HerSwab™ versus physician: kappa = 0.84; cobas® swabs versus physician: kappa = 0.81; HerSwab™ versus cobas® swabs: kappa = 0.87). The sensitivity of HPV detection for CIN2+ was 87.6% (95%CI: 79.8–93.2) with self-sampling using HerSwab™, 88.6% (95%CI: 80.9–94.0) with self-sampling using the cobas® swab, and 92.4% (95%CI: 85.5–96.7) with physician sampling. Corresponding estimates of specificity were 58.1% (95%CI: 54.1–62.1), 55.0% (95%CI: 50.9–59.0) and 58.7% (95%CI: 54.6–62.6). Cytology (ASC-US or more severe) done on the physician-collected specimen was 80.2% (95%CI: 70.8–87.6) sensitive and 61.4% (95%CI: 57.2–65.5) specific for CIN2+.

* Corresponding author at: Division of Cancer Epidemiology, McGill University, 5100 Maisonneuve Blvd West, Suite 720, Montreal, QC H4A 3T2, Canada.
E-mail address: eduardo.franco@mcgill.ca. (E.L. Franco).
[1] Current affiliation: Department of Obstetrics and Gynecology, Turku University Hospital, University of Turku, Finland.

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Conclusions. The HerSwab™ had good agreement with physician sampling in detecting HPV, and adequate performance in detecting high-grade lesions among women referred to colposcopy for abnormal cytology.

1. Introduction

With the advent of testing for human papillomavirus (HPV) nucleic acid in cervical cancer screening there has been growing interest in the introduction of cervicovaginal self-sampling to simplify and increase the coverage of screening programs [1,2], as well as to enable a patient-centered approach to empower women as key actors in the control of gynecologic cancers. Self-sampling is an attractive approach to improve cervical cancer screening coverage in low resource countries and/or to extend coverage to remote areas in middle and high resource countries, where women typically have higher rates of cervical cancer incidence and mortality [3].

The benefits of HPV self-sampling are twofold. HPV testing on self-collected samples is reported to have equivalent or better sensitivity than cytology to detect cervical precancerous lesions [4–6], and offering women a simple and convenient means of self-testing increases cervical screening participation [7,8]. Conceivably, although there is some loss of sensitivity and specificity in screening for cervical cancer in a specimen that is not directly collected from the ecto- and endo-cervix, the overall accuracy of the self-collected HPV test results remains superior to that of physician-collected Pap smears in identifying the presence of cervical precancerous lesions [9–11].

Canada is gradually transitioning from cytology to HPV testing in its provincial cervical cancer screening programs [12]. Given the size of its territory, low population density, and size of its aboriginal populations, Canada is ideally suited for large-scale implementation of self-sampling to augment its forthcoming provincial, HPV-based cervical cancer screening programs. In this context, we sought to validate a new collection device, the HerSwab™ (referred to hereafter as HerSwab) self-collection system, designed by a Canadian company (Eve Medical, Toronto, ON). The HerSwab device was designed to be anatomically comfortable in allowing women to collect a self-sample of exfoliated cervicovaginal cells.

2. Methods

2.1. Study design and population

The Cervical And Self-Sample In Screening (CASSIS) study was designed to compare the diagnostic performance of HPV testing in self-collected samples with standard physician-collected samples for the detection of cervical intraepithelial neoplasia grade 2 or worse (CIN2+) and cervical cancer among women referred for colposcopy. The performance of HerSwab was also compared with that of a second self-sample via the cobas® PCR Female swab (referred to as cobas swab). Women collected both self-samples, but the order of sampling was determined by randomization. We hypothesized that the HerSwab sample would yield sensitivity and specificity that are no worse than those with the physician-collected sample, while providing results that are better than or equivalent to those with the self-sample based on the cobas swab. As a performance benchmark, we used cytology results from physician-collected conventional Pap smears in the same patients. As a secondary objective, we measured and compared patient satisfaction with the three sampling approaches.

CASSIS is a 3-arm study carried out from June 22, 2015 through April 15, 2016 in colposcopy clinics at three McGill University affiliated hospitals in Montreal, Canada. Women aged 21–74 were eligible to participate if they had been referred to the participating colposcopy clinic because of an abnormal cervical cancer screening result or for initial treatment of a cervical lesion. We excluded women referred for follow-up post-treatment of a cervical lesion. The study was approved by the McGill University and respective study hospitals' Institutional Review Boards. It was registered in clinicaltrials.gov (NCT02397252).

2.2. Study procedures and data collection

Depending on the study site, a trained study nurse or research assistant approached women attending the colposcopy clinic to explain the study and distribute information leaflets. After receiving written informed consent, each participant was verbally instructed on how to perform the cervicovaginal self-sampling techniques using bilingual, illustrated instructions (Supplemental Fig. 1). These were also posted in designated areas (restroom, changing area or examination room) in which the unsupervised self-sampling was performed. The study representative indicated to the participant the sequence of the two self-sampling methods, depending on results from a priori computer-generated randomization. Women were given a two-section tray, numbered to indicate which self-sample to perform first. Once both self-samples were collected, the woman was then seen by the attending colposcopist for a physician-collected cervical sample and colposcopy following the standard of care at each clinic. The physician-collected sample was always obtained after the two self-samples to ensure that the use of a speculum would not interfere with exfoliation of the vaginal canal.

Cytology was based on the actual colposcopy visit sample if performed at that time; otherwise, it was based on the referral cytology report. Cytology results, based on the actual CASSIS visit or referral cytology, were interpreted according to the Bethesda classification as NILM: Negative for Intraepithelial Lesion or Malignancy; ASC-US: Atypical Squamous Cells- of Undetermined Significance; ASC-H Atypical Squamous Cells- cannot exclude HSIL; LSIL: Low Squamous Intraepithelial Lesion; HSIL: High Squamous Intraepithelial Lesion; AGC: Atypical Glandular Cells; and cancer [13]. Colposcopy protocol followed clinical practice guidelines by the Society of Canadian Colposcopists. Biopsies were taken from all areas on the cervix that appeared abnormal and were histologically assessed and classified as normal, CIN1, CIN2, CIN3, or invasive cancer, based on the most severe histology grading. Respecting local clinical practice norms, we did not require that blind biopsies be taken if the cervix had no visible lesional tissue on colposcopic examination. Endocervical curettage was performed when the transformation zone could not be visualized. Negative colposcopy results with no biopsies but with visualization of the transformation zone were considered in one set of analyses to indicate no disease. Since colposcopy was performed a few minutes after the collection of samples, colposcopists were obviously blinded to the results of self- and physician-collected screening tests. Pathologists assessing study outcomes were blinded to HPV test results. Colposcopical and histopathological biopsy examinations were conducted by senior McGill gynecologists and pathologists, respectively.

After specimen collection, participants completed a short survey about their experience with HerSwab relative to the other two sampling methods. It consisted of 10 questions on the ease of use, comfort, embarrassment, and clarity of instructions when using HerSwab and the cobas swab as compared to the physician-collected sample. The questionnaire has been previously used in evaluating HerSwab for other medical conditions [14].

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