RESEARCH ARTICLE

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Digital Cervicography by Simply Portable Device as an Alternative Test for Cervical Cancer Screening in Rural Area of Thailand

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Abstract

Objective: Various screening methods for cervical cancer are proved to be effective in reducing such type of cancer. We aims to introduce a new portable device as an alternative method for cervical cancer screening. The performance of device was tested on the assessment of cervical lesions using cervicograph score with the cervical cytology. **Methods:** 325 non-pregnant women were tested from March 2013 to August 2015. The cervical and vaginal cells from the sample were collected for cytology, then all of them received the digital cervicography conducted with our new device and scored using cervicograph score. Small pieces of cervical tissues were also collected for histologic examination. SPSS software version 18.0 was used for the statistical analysis. **Results:** We grouped cytology results and cervicograph scores to 2 subgroups, ≤ ASC-US and ≥ LSIL, and 0-3 points and 4-6 points, respectively. The data then correlated with histology results which sub-grouped to ≤ CIN 1 and ≥ CIN 2. The accuracy, sensitivity, specificity, and positive predictive value (PPV) of cervicograph scores 4-6 points to detect CIN 2+ were 92%, 72.41%, 97%, and 84%, respectively which were not inferior to Pap smear did. **Conclusion:** The digital cervicography device provides similar accuracy to Pap cytology screening and is suitable to use in the area that lacks cytoscreeners. Large scale use and generalization are required for this new device.

Keywords: Alternative test- cervical cancer- screening- cervicography- rural area

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Introduction

Various screening methods for cervical cancer ranging from the conventional method, Pap test, to the latest liquid-based cytology, which detects high-risk human papilloma virus from DNA testing, are proved to be effective in reducing such type of cancer (WHO, 2013). Although there are widely uses of such preventive measures in developing countries, cervical cancer is still the most common type of gynecologic cancer. The incidence of cervical cancer cases in South-East Asia and Thailand reported by Globocan 2012 are 20.5 and 17.8/ 100,000 women/ year, respectively which is slightly increased from previous Globocan reported in year 2008 (Ferlay et al., 2013).

This issue becomes more severe in those who lives in rural area due to the remote inaccessibility of medical services and the lack of medical personnel and cytologist as well as the unawareness of required regular medical check-up. We previously developed an alcohol-based preservative solution, and named this technology as the "Siriraj liquid-based cytology" or "Siriraj-LBC" and reported its significance in year 2008 and 2014 (Laiwejpithaya et al., 2008; Sangkarat et al., 2014). However, it still has limitation of use even it's a low cost LBC technology and was qualified for cervical cancer screening. Despite the limitation of resources, we come up with a new innovative but inexpensive device for cervicography made from USB-pen camera. This portable device can connect with any Android devices in order to both take still photo and record VDO clips anywhere. Such recorded media can be used for further consultation with specialists especially the difficult cases. The device shares the common features to VIA but it possesses the higher magnification (4-15 times) and the capability of video recording on cervical lesions is very useful for further review. Such lesion-amplification function shares the same feature with the colposcopy, the quality of photo taken by our device, however, is still lower than those taken from the expensive colposcopy.

We tested the performance of our device on the assessment of cervical lesions using modified colposcopic index (cervicograph score) with the cervical cytology and patient's medical history. The results show non-inferiority to conventional method, which confirms that the device can be used as an alternative method for cervical cancer

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screening.

The distinct advantages of our devices are that it is user-friendly, portable and cost-efficient tool and there is no waiting time for the screening results compared to the conventional Pap test. Any physicians and other well-trained medical personnel can easily use this device as it is designed to tackle the lack of cyto-technician problem in the remote area. The users, however, are required to have basic skill training on the interpretation of the cervical lesions based on modified colposcopy index.

Materials and Methods

The sample for this study are 339 non-pregnant women from Phichit, a province in the northern part of Thailand. Women in the study area had less frequent or no previously cervical cancer screening and the data of National Cancer Institute Thailand 2015 showed highest incidence of new cervical cancer cases in the northern part of Thailand and most of them had stage 3 diseases (32.51%) at diagnosis. These women has no previous diagnosis or treatment of cervical lesions nor hysterectomy record and were random for health check-up. The study took place from March 2013 to August 2015 after the approval by the institutional review board. The cervical and vaginal cells from the sample were collected and smeared on slides, immediately embedded in 95% alcohol and then sent to the local provincial hospital for cytology examination by conventional method. 14 out of 339 were excluded from the study due to the later detected atypical glandular cells or the inadequate specimens. The remaining 325 women also received the digital cervicography conducted with our new device at the gynecologic clinic in Phichit provincial hospital. Cervicographs taken from these women were recorded at 4-15 times magnitudes by the handheld digital cervicography for further review with the so-called cervicograph score, the modified test of Reid colposcopic index (RCI) (Reid and Scalzi, 1985). We, however, omitted the iodine staining procedure and assessed only 3 variables, namely margin, color and vessel due to the various limitations and constraints for such test as indicated in Table 1. All cervicographs of test samples were reviewed and scored twice by 2 physicians for the mutual conclusion. Pictures of handheld digital cervicography camera and cervicographs are showed in Figure 1 and 2.

Small pieces of cervical tissues from test subjects were also collected for histologic examination, which serves as the result diagnosis and accuracy test. The biopsy was performed from the most suspicious area of cervix after applying 3% acetic acid or random biopsy in the case that had no suspected lesion. The test subjects with cervical lesions CIN 2+ would be treated by excisional or destructive procedures depending on the lesion characteristics and individual preference. The correlation between cervical cytology, cervicograph score and histologic results will be analyzed in the next section.

SPSS software version 18.0 was used for the statistical analysis in this study. Demographic data was reported in range, mean, median, standard deviation or percentage as appropriate. Sensitivity, Specificity, Negative predictive value (NPV) and positive predictive value (PPV) were calculated and the correlation was tested using cross tabulation with Chi-square test. Odds ratio and area under the ROC curve (AUC) were used to compare the efficacy of each test, and p-value < 0.05 was statistical significance.

Results

The mean age of the subjects was 46.56 + 11.91 years and most of them, 47.1%, had 2 children (range 0-6). The most common cervical cytology result was negative for intraepithelial lesion or malignancy (NILM), followed by atypical squamous cells of undetermined significance (ASC-US) and low-grade squamous intraepithelial lesion (LSIL) as expected. Cervicographs were recorded by handheld digital cervicography for reviewing and scoring

Figure 1. Handheld Digital Cervicography Camera

Table 1. Modified Colposcopy Index for Assessment of Cervical Lesions (Cervicograph Score*)

Signs	Zero point	One point	Two point
Margin	-Condylomatous or micropaillary -Indistinct acetowhitening -Flocculated or feathered margin -Angular, jagged lesions -Satellite lesions, acetowhitening beyond TZ	-Regular, smooth, straight outlines	-Rolled, peeling edges -Internal demarcation between areas of differing appearance.
Color	-Shiny, snow-white -Indistinct acetowhitening	-Intermediate shiny gray	-Dull, oyster white -Definite punctuation or mosaic
Vessel	-Fine caliber, poorly formed patterns -Condylomatous or micropaillary	-Absent	

*Cervicograph score was modified from Reid colposcopic index (omits the iodine staining procedure); TZ, T-zone

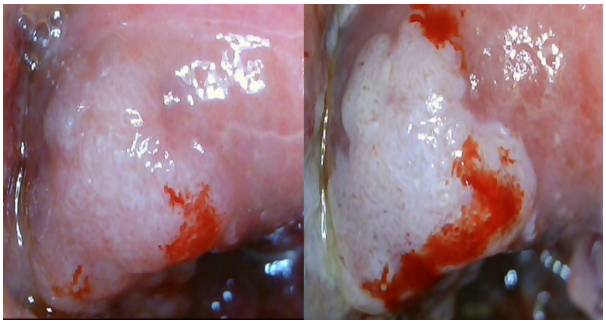

Figure 2. Cervicographs Taken from Handheld Digital Cervicography Camera (Before and after 3% acetic acid application)

Table 2. Cervical Cytology Results

Cytology result	n	%
NILM	156	48
ASC-US	57	17.54
LSIL	52	16
ASC-H	13	4
HSIL	45	13.84
Cancer	2	0.62

NILM, negative for intraepithelial lesion or malignancy; ASC-US, atypical squamous cells of undetermined significance; LSIL, low-grade squamous intraepithelial lesion; ASC-H, atypical squamous cells, cannot exclude high-grade lesion; HSIL, high-grade squamous intraepithelial lesion

by 2 physicians, 210/325 (64.61%) had T-zone type 1, 48/325 (14.77%) had T-zone type 2 and the remaining 20.62% had T-zone type 3. The percentage of cervical cytology result and cervicograph scores which assessed by modified colposcopic index were showed in Table 2 and 3.

All subjects who had cervical biopsy results CIN 2+ would be received appropriate treatments thereafter depended on the lesion characteristics and individual preference. The data of this part was not shown in this study.

We grouped cervical cytology results and cervicograph scores to 2 subgroups, ≤ ASC-US and ≥ LSIL, and 0-3 points and 4-6 points, respectively. The data then correlated with histology results which sub-grouped to ≤ CIN 1 which required no further treatment and ≥ CIN 2. When we grouped the data like this, the histologic results in each subgroup had significant differences ($p < 0.0001$). Odds ratio of cytology ≥ LSIL to detect cervical lesions CIN2+ was 11.67 (95% CI 5.83-23.36) compared with

Table 3. Cervicograph Scores Determined by Modified Colposcopic Index

Cervicograph score	n	%
0	84	25.85
1	107	32.92
2	57	17.54
3	27	8.31
4	18	5.54
5	22	6.77
6	10	3.07

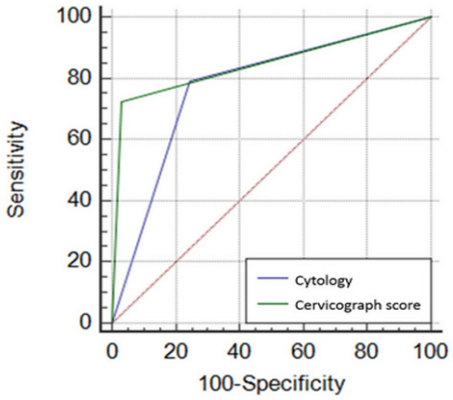

Figure 3. ROC Curves of Cytologic Results and Cervicograph Scores to Detect CIN 2+ lesions

cytology ≤ ASC-US and 84.98 (95% CI 34.23-210.95) for cervicograph scores 4-6 points compared with 0-3 points. Accuracy, sensitivity, specificity, PPV, and NPV of cytologic results ≥ LSIL to detect CIN 2+ lesions in this study were 76%, 79.31%, 75.28%, 41.07% and 94.36% and cervicograph scores 4-6 points to detect CIN 2+ lesions were 92%, 72.41%, 97%, 84%, and 94.18%, respectively. Figure 3 showed ROC curves of cytology and cervicograph score, AUC of the first one was 0.773 (95% CI 0.723-0.817) compared with 0.847 (95% CI 0.803-0.884) in the later.

Discussion

Cervicography is an alternative test for cervical cancer screening which provides accuracy, sensitivity, specificity, and positive predictive value (PPV) non-inferiority to Pap smear and has been considered in some areas in which traditional methods are limited. From this study, we used newly invented tool; the portable digital cervicography, and the results of this device on the detection of CIN2+ lesions compared with Pap smear are showed.

In the area, in which there are still the high incidence of cervical cancer such as Thailand and many developing countries, cervical cancer screening is useful to detect preinvasive lesions. The early treatment can be then required before the lesions progress further to become cancer. Different traditional methods are used to detect preinvasive cervical diseases for example; cervical cytology, VIA and HPV DNA detection. Each of these techniques, however, still has major limitations such as low sensitivity, complex and prolonged screening process, long waiting time, and expensive cost.

The studies yield the good results using cervicography as a single screening method for detecting CIN lesions (Ferris, 1994; Fallala and Mash, 2015) and those women who were the sample could receive immediate treatment in the same visit (single-visit approach). This approach technique can significantly reduce the referral and loss to follow up rates (Fallala and Mash, 2015).

Several studies showed better detection rates for CIN lesions when cervicography is used as an adjunctive test to cervical cytology with high sensitivity and predictive

value (Greenberg et al., 1993; Ferris, 1994; De Sutter et al., 1998; Gasperin et al., 2012). As Bomfim-Hyppolito (2006) reported an improved sensitivity, specificity and PPV when cervicography is used as an adjunctive test to VIA. Moreover, the study from Korea compared the three different combination of adjunctive tests among Pap smear, HPV DNA testing, and cervicography. Trivially, the triple-combined test was the most sensitive test while the double-combined test with Pap test and cervicography performed better than the combination between Pap test and HPV DNA testing (98.1% and 92.3%, respectively) (Kim et al., 2013).

Previous study used cervicography for triage of women with mild abnormal cervical cytology (ASC-US/ LSIL) and concluded that cervicography functioned moderately well at detecting CIN2-3 lesions, especially in young women (Ferris et al., 2001). Several studies also supported the use of cervicography in abnormal Pap test population (Cecchini et al., 1992; Chen et al., 2008). However, cervicography for evaluation of high-grade lesion did not yield higher sensitivity than cytology and specificity was also reduced. Moreover, the result interpretations also highly depends on doctor's experience (De Sutter et al., 1998; van Niekerk et al., 1998). Cervicography may be suitable in the remote area where Pap screening or cytologist is not available (van Niekerk et al., 1998). Baldauf (1997) reported high false positive rate of cervicography relative to Pap smear, and did not support cervicography over Pap smear.

This study showed highly agreement between high-cervicograph score group (4-6 points) and cervical histology CIN2+ concordant with one study from Korea (Bae et al., 2012). Our new device for cervical cancer screening showed non-inferiority to Pap test for detecting CIN2+ lesions. Therefore, this device is suitable for the area that Pap test is not available or lack of cytologists. Although we omitted iodine staining procedure during cervicography which is in line with many US clinicians, there are little or no possible effect in the interpretation of the results. Previous studies are also used a modified RCI or the abbreviated Reid colposcopic index ranging from 0 to 6 as in this study (Ferris and Litaker, 2006; Boonlikit, 2016). Basic interpretation of cervicograph is in line with VIA and colposcopy, thus physicians even who are not gynecologists and medical personnel who have received basic VIA or colposcopy training can easily use this device. In Thailand, we have regularly basic and advance training courses for VIA and colposcopy for physicians, nurses and other medical personnel who interested in health promotion and disease prevention which supported by the government. Since this new device can record both still photo and VDO file, it could be used as telemedicine for learning and consulting with the specialists. In additional, this device can save the cost of original cervicography films that used in the study of Kim et al., (2016) in Korea.

The distinct advantage of this study is the reliable data and solid research methodology, including cervical histologic results from every test subjects. In addition, a single same physician performed the cervicoscopy in all samples in order to ensure the accuracy of the results. The main challenge, however, is this new device is still new to the market and not widely used in the country but due to its ease of use and cost effectiveness, the learning curve is rather low for any medical personnel. In conclusion, this new device is suitable to use in the area that lack of Pap smear or cytologists but provides the similar accuracy to those tests. Its capability to store taken cervicogram in digital format, can be transfered instantly without any further cost as well as recorded in the database for further review. Large scale use and generalization, however, are required for this digital cervicography device.

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Statement conflict of interest

All authors declared no potential conflict of interest relevant to this article.

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