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Comparison of urine, self-collected vaginal swab, and cervical swab samples for detecting human papillomavirus (HPV) with Roche Cobas HPV, Anyplex II HPV, and RealTime HR-S HPV assay

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ABSTRACT

Background: Human papillomavirus (HPV) is well established as the main cause of cervical cancer. Non-invasive self-collected urine and vaginal sampling have the potential advantage of increasing patient compliance with cervical cancer screening.

Methods: Self-collected vaginal and urine samples and clinician-collected cervical samples were collected from 101 patients, including 84 patients with high grade squamous intraepithelial lesion and 17 patients with benign ovarian disease. Each sample was evaluated with RealTime HR-S HPV, Anyplex™ II HPV, and Cobas® HPV assays. The concordance of urine and of self-collected vaginal samples with cervical samples was assessed using the kappa (*k*) statistic.

Results: In any high-risk HPV (hrHPV), the concordance of self-collected vaginal and urine samples compared to cervical samples was moderate (*k* 0.49–0.58) and fair to moderate (*k* 0.33–0.51), respectively. In HPV 16/18, the concordance of vaginal and urine samples compared to cervical samples was almost perfect (*k* 0.81–0.86) and moderate to substantial (*k* 0.59–0.63), respectively. Among the three methods for HPV detection, RealTime HR-S showed the highest concordance with vaginal (*k*: any hrHPV 0.58, HPV 16/18 0.86) and urine samples (*k*: any hrHPV 0.51, HPV 16/18 0.63) compared to cervical samples.

Conclusion: HPV tests using self-collected vaginal samples and urine showed substantial and moderate agreement compared with cervical samples, respectively, although HPV tests using these samples were still inferior to clinician-collected cervical samples. Further research is needed on the clinical performance of HPV testing using urine and self-collected vaginal samples as the screening method.

1. Introduction

Human papillomavirus (HPV) infection is known to play a crucial role in the development of cervical cancer (Arbyn et al., 2012; Ronco et al., 2014). Although cervical cancer screening is performed by cervical cytology tests, the results are often different depending on the pathologist. Recently, it has been suggested that the HPV test is more accurate than conventional cervical cytology tests in predicting the incidence of cervical cancer. (Arbyn et al., 2012; Committee on Practice, 2012; Ronco et al., 2014).

Cervical cancer is a typical cancer that can be diagnosed early, and systemic screening can reduce incidence and mortality (Iftner and Villa, 2003). However, a major obstacle to controlling cervical cancer is low participation in screening programs. In developed countries, such as the United Kingdom and the United States, 20%–30% of women of screening age have not been screened for the past five years or have never been screened (Bos et al., 2006). In countries without well-developed screening programs, the participation rate was low, and 50%–80% of the women were not screened (Forman et al., 2012). Previous studies have suggested that the HPV test using urine and self-

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collected vaginal samples is sensitive and may increase participation in screening programs (Cuzick et al., 2006; Ronco et al., 2014).

An HPV test using self-collected vaginal samples showed a strong clinical performance in detecting high grade squamous intraepithelial lesions (HSIL), and was considered a good alternative for women wanting to avoid the HPV test using clinician-collected samples or women having difficulty with cervical specimen collection (Arbyn et al., 2014). In addition, since the HPV test using urine samples appears to have good accuracy in detecting HPV, it could be an additional strategy to reach women not participating in the regular screening program (Pathak et al., 2014). However, because processes such as sample collection, storage, and DNA extraction have not been standardized, the clinical performance of the HPV test using urine and self-collected vaginal samples varies widely depending on the studies (Vorsters et al., 2012).

Therefore, the purpose of this study was to compare HPV DNA detection in urine and self-collected vaginal samples with clinician-collected cervical samples, using the Roche Cobas HPV, Anyplex II HPV, and RealTime HR-S HPV assays.

2. Materials & methods

2.1. Clinical specimens

Three bio-specimens each (clinician-collected cervical sample, self-collected vaginal, and urine samples) were collected from women admitted to four medical centers in Korea for surgical treatment of HSIL or ovarian disease between September 2017 and January 2018. The ages of the patients enrolled in this study were between 20 and 50 years. Exclusion criteria were as follows: previous treatment for cervical disease (including the loop electrosurgical excision procedure, cold knife conization, cryotherapy, and laser therapy), previous hysterectomy, prior chemotherapy, or radiation treatment for cervical neoplasia or another concurrent cancer, HIV infection or AIDS, or pregnant at the time of the study. The study was approved by the relevant Institutional Review Boards, and all women provided informed consent to participate in the study (KUGH17222).

2.2. Sample collection and preparation

Study participants were provided a self-collection kit consisting of a urine collection cup (BD Vacutainer, manufactured by BD Diagnostics, Franklin Lakes, NJ, USA), a plastic brush (Flocked Swab, manufactured by Noble Biosciences, Inc., Gyeonggi-Do, South Korea), PreservCyt Solution (ThinPrep, manufactured by Hologic, Marlborough, Massachusetts, USA), and illustrated instructions. On the day before surgery, participants self-collected a vaginal sample by inserting a plastic brush one inch into the vagina, rotating the swab for 15 s, and then removing it. The brush was subsequently suspended in 5 ml of ThinPrep, PreservCyt Solution. Participants then underwent a pelvic exam during which the clinician collected a cervical sample using a cervical brush (Cervical Brush, manufactured by Noble Biosciences, Inc., Gyeonggi-Do, South Korea). This brush was also suspended in 5 ml of ThinPrep, PreservCyt Solution. On the morning of surgery, women were instructed to collect initial flow of urine (first-void) samples (approximately 30 mL) with a urine collection cup. The cervical samples were used as a reference sample for HPV DNA detection. Cervical, vaginal, and urine samples were stored at 4 °C, and processed within a week (Nilyanimit et al., 2017).

2.3. DNA extraction

For the cervical and vaginal samples, the PreservCyt Solution samples were thoroughly mixed, and three 0.5-ml aliquots were transferred into 1.5-ml microcentrifuge tubes. The cells were pelleted by centrifugation at 15,000 x *g* for 15 min and the supernatant solution was discarded. Cells were resuspended in 600 µl phosphate-buffered saline (PBS). Urine samples were placed into a 50 ml tube (20–40 ml) and centrifuged at 3000 x *g* for 10 min, and the supernatant solution was discarded. Cells were resuspended in 400 µl phosphate buffer saline buffer (PBS) and transferred into 1.5-ml microcentrifuge tubes.

DNA was extracted from 200 µl of sample using the QIAamp DNA blood minikit (manufactured by Qiagen, Hilden, Germany). The extracted DNA was eluted in 100 µl of buffer AE into a clean sterile microfuge tube and stored at −20 °C for about 2 weeks until testing (Gonzalez et al., 2012; Qin et al., 2016; Sahasrabuddhe et al., 2014). RealTime HR-S HPV and Anyplex™ II HPV 28 assays were performed at the Korea University Guro Hospital, and the Cobas 4800 HPV assay at Green Cross Reference Laboratory.

2.4. HPV DNA genotyping

HPV genotyping was done via three different methods.

2.4.1. Anyplex™ II HPV 28

Twenty-five microliters of the eluted DNA was used in the Anyplex II HPV kit assay (Seegene, Seoul, South Korea) (Estrade and Sahli, 2014). This real-time PCR test simultaneously detects 19 high-risk HPVs (16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58,59, 66, 68, 69, 73, 82) and 9 low-risk HPVs (6, 11, 40, 42, 43,44, 54, 61, 70), using dual priming oligonucleotides (DPO™, Seegene) and a melting curve analysis method of tagging oligonucleotide cleavage and extension (TOCE™, Seegene) (Cho et al., 2013). TOCE predicted the melting temperature of the Catcher duplex and supported real-time PCR for HPV 28 using a predetermined target sequence. The L1 gene and human β-globin gene were amplified concurrently, and we measured the fluorescence continuously with increasing temperature. The inclusion of an internal control allowed the checking of the entire process from DNA extraction to PCR amplification. A negative control and three positive controls provided by the manufacturer were included in each PCR run as requested. Data recording and interpretation were automated with Seegene viewer software according to the manufacturer's instructions.

2.4.2. Cobas 4800 HPV

The Cobas 4800 system (Roche Molecular Diagnostics, Pleasanton, CA, USA) features fully automated sample preparation combined with real-time PCR technology. The test is designed to extract, amplify and detect a broad spectrum of hrHPV genotypes, as well as to co-amplify the human cellular globin gene. In this study, only real-time PCR was performed, because DNA extraction was already performed. A sample of 50 µl of eluted DNA was diluted with 100 µl of buffer AE, and used in the Cobas HPV kit assay (Lim et al., 2017). PCR amplification and detection occurred in a single tube, where probes with four different reporter dyes were used to track the different targets in the multiplex reaction. Reporter dye 1 was used to track the hrHPV pool with 12 HR targets (HPV-31, -33, -35, -39, -45, -51, -52, -56, -58, -59, -66 and -68); dyes 2 and 3 were used to track HPV-16 and HPV-18, respectively; and dye 4 was used to target β-globin to provide a control for cell number adequacy, extraction, and amplification.

2.4.3. RealTime HR-S HPV

A 25-µl sample of the eluted DNA was used in the RealTime HR-S HPV assay (Sejong Medical Co., Ltd., Paju, South Korea), which was performed as recommended by the manufacturer. This product is a qualitative in vitro diagnostic reagent for detecting 14 kinds of high-risk human papillomaviruses (HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) in cervical liquid-based cytology specimens and cervical swabs, using real-time PCR. This test can simultaneously amplify and detect the target nucleic acids of high risk HPV 16, HPV 18, and internal control (IC). When using PCR, the detection efficiency may be inhibited by the inhibitory substances present in the clinical specimen. The IC of this product is an endogenous whole process control

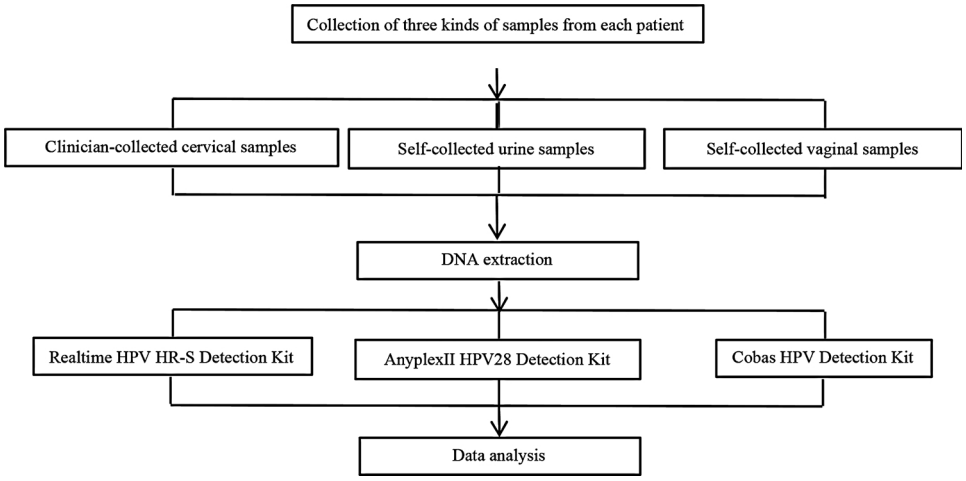

Fig. 1. Study scheme.

used to monitor the entire process from sample collection, nucleic acid extraction, and PCR inhibition, and it is amplified simultaneously with the gene of the pathogen in one PCR tube.

This test is composed of two processes: (1) sample pretreatment for simultaneous extraction of HPV and cellular DNA; and (2) PCR amplification of target DNA using complementary primers specific for HPV and hemoglobin, and detection of 14 double–fluorescent-labeled HPV types and hemoglobin nucleic acid by cleavage of oligonucleotide detection probes. In this test, the entire process is monitored through extraction, amplification, and detection of hemoglobin. During amplification with primers specific for 14 HPV types and hemoglobin DNA, amplified DNA is detected using secondary oligonucleotide probes labeled with four different fluorescence dyes. Signals amplified from 12 high-risk HPV types (High risk HPV Other type; 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68), HPV 16 and HPV 18 are detected using different fluorescence dyes, and the signal of hemoglobin is also detected by another unique fluorescence dye.

2.5. Sample size calculation

A formula proposed by Tang et al was used to calculate the sample size to address the hypothesis of equivalence of test performance in studies with a matched-pair design (multiple tests applied on the same participants) (Tang et al., 2003). In this study, the sensitivity and specificity of the HPV test were assumed to be 96% and 89%, respectively (Arbyn et al., 2015). Under a worst-case assumption for an HPV assay on urine or self-collected vaginal sample that 5% of CIN2+ cases are positive on clinician samples but negative on self-samples and accepting a confidence level of 95% and a power of 80%, the required sample size was 83 CIN2+ cases (Arbyn and Castle, 2015; Stanczuk et al., 2016). HPV prevalence is considered to be 86%, and if all 83 individuals are positive for HPV, 17 are required as negative controls to confirm the specificity of each test method for HPV infection (Guan et al., 2012).

2.6. Statistical analysis

The primary endpoint was the concordance of HPV detection using vaginal and urine samples compared to cervical samples as a gold standard. The HPV concordance between paired samples (vaginal vs cervical samples, urine vs cervical samples) was the percentage of paired samples with the any high-risk HPV group or specific types (HPV 16/18). In addition, concordance between tests was assessed using the kappa statistic (Cohen's kappa, k) and defined as "poor" ($k = 0$), "slight" ($0.01 < k < 0.20$), "fair" ($0.21 < k < 0.40$), "moderate" ($0.41 < k < 0.60$), "substantial" ($0.61 < k < 0.80$), "almost perfect" ($0.81 < k < 1$) or "perfect" ($k = 1$). McNemar's test is a statistical test used to evaluate paired nominal data. McNemar's test can be used to compare the proportions of hrHPV positive results between self-collected vaginal/urine samples and clinician-collected cervical samples while accounting for the correlation of multiple samples within subjects (Stanczuk et al., 2016). This analysis has been used previously in HPV research assessing the concordance of self-collected vaginal samples versus clinician-collected cervical samples (Durkalski et al., 2003). Anyplex™ II HPV 28 detects 19 high-risk HPV (16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 69, 73, and 82), while RealTime HR-S and Cobas 4800 HPV detect 14 high-risk HPV (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68). Only 14 HPV (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68) were considered high risk HPV in this study. Confidence intervals were calculated, and the significance level was set at 0.05. The statistical analyses were performed using SPSS™ (24.0, IBM Corp, Armonk, NY, USA) and MedCalc Software©.

3. Results

Clinician-collected cervical samples and self-collected vaginal and urine samples were collected from 101 participants: 84 diagnosed with cervical HSIL and 17 diagnosed with ovarian disease. The median age of

Table 1
Prevalence of HPV infection by cervical, vaginal and urine sampling method according to HPV type and three different HPV tests.

	HPV genotype	Cervical samples		Vaginal samples		Urine samples	
		+ (%)	– (%)	+ (%)	– (%)	+ (%)	– (%)
RealTime HR-S	HPV 16/18	31 (30.7)	70 (69.3)	32 (31.7)	69 (68.3)	26 (25.7)	75 (74.3)
	All hrHPV	87 (86.1)	14 (13.9)	84 (83.2)	17 (16.8)	75 (74.3)	26 (25.7)
Anyplex II	HPV 16/18	28 (27.7)	73 (72.3)	30 (29.7)	71 (70.3)	19 (18.8)	82 (81.2)
	All hrHPV	89 (88.1)	12 (11.9)	81 (80.2)	20 (19.8)	72 (71.3)	29 (28.7)
Cobas	HPV 16/18	37 (36.6)	64 (63.4)	36 (35.6)	65 (64.4)	26 (25.7)	75 (74.3)
	All hrHPV	89 (88.1)	12 (11.9)	79 (78.2)	22 (21.8)	64 (63.4)	37 (36.6)

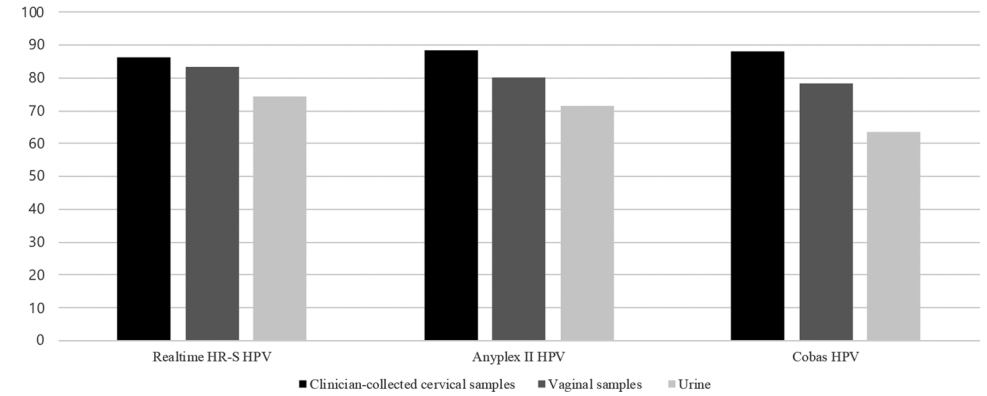

Fig. 2. The positive rate of HPV by sampling method (cervical, vaginal, urine) and HPV test methods (Sejong-Medical RealTime HR-S HPV test, the Seegene Anyplex II HPV 28 test and the Roche Cobas 4800 HPV).

the participants was 41 ± 21.3 years (Fig. 1).

Table 1 and Fig. 2 show the positive rates of the HPV tests using clinician-collected cervical samples and self-collected vaginal and urine samples. The overall hrHPV positive rate was highest in clinician-collected cervical samples (87–89/101), followed by self-collected vaginal (79–84/101) and urine samples (64–75/101). There was no significant difference of hrHPV positivity between HPV assays.

Table 2 shows the agreement in HPV detection using self-collected vaginal/urine samples compared to clinician-collected cervical samples. In HPV 16/18, the concordance of the HPV test using vaginal samples compared with cervical samples was almost perfect (91.1–94.1%, k 0.81–0.86). In all hrHPV, HPV tests using vaginal samples versus cervical samples showed a substantial agreement (73.3–89.1%, k 0.49–0.58). In HPV 16/18, the concordance of the urine HPV test compared with the clinician-collected cervical samples HPV test was substantial (83.2–85.1%, k 0.59–0.63). In all hrHPV, the HPV test using urine versus clinician-collected cervical samples showed a fair to moderate agreement (81.2–86.1%, k 0.33–0.51).

The McNemar's analysis showed that there was no statistically significant difference in HPV 16/18 (RealTime HR-S $P = 1.000$, Anyplex $P = 0.690$, Cobas $P = 1.000$) and all hrHPV (RealTime HR-S $P = 0.550$, Anyplex $P = 0.060$) detection using self-collected vaginal samples compared to clinician-collected cervical samples, while there was a significant difference in Cobas HPV ($P = 0.010$) for detecting all hrHPV using self-collected vaginal samples compared to clinician-collected cervical samples. Only the RealTime HR-S HPV assay using urine to detect HPV 16/18 was not statistically significant compared to clinician-collected cervical samples, while the Anyplex and Cobas HPV assays using urine compared with clinician-collected cervical samples were significantly different in detection of both HPV 16/18 and all hrHPV.

4. Discussion

In this study, HPV tests using self-collected vaginal samples and urine showed substantial and moderate agreement compared with clinician-collected cervical samples, respectively. We found that HPV tests using vaginal samples rather than urine specimens were more consistent with cervical samples. In particular, HPV 16/18 detection using vaginal samples showed an almost perfect agreement (k > 0.8) with the HPV test using cervical samples. In addition, there was no statistically significant difference between the positive rates of cervical samples and vaginal specimens for all hrHPV detection as well as HPV 16/18. These results are consistent with previous studies (Gupta et al., 2018; Reisner et al., 2018). Systematic reviews and meta-analysis in 2005–2007 showed fair to good agreement (k 0.24-0.96) between cervical and vaginal samples, while recent studies have shown excellent performance of HPV detection on vaginal samples (concordance 91.2–96.8%, k 0.66–0.88) (Asciutto et al., 2017; Dijkstra et al., 2012; Gupta et al., 2018).

In this study, the urine HPV test showed a moderate agreement with cervical samples, and there was a statistically significant difference in HPV positivity compared to cervical samples with the exception of the RealTime HR-S HPV assay using urine to detect HPV 16/18. The result of our study was disappointing compared to previous publications (Asciutto et al., 2017; Dijkstra et al., 2012; Petignat et al., 2007). Although the concordance rate for the HPV test using urine samples compared with cervical samples varied across studies (75%–100% concordance, k = 0.41–0.93), some recent studies reported a good agreement (k = 0.688–0.792) between paired samples (Enerly et al., 2013; Hagihara et al., 2016; Van Keer et al., 2018).

Differences in the results between studies might occur depending on the sampling, storage, DNA extraction from the samples, and study population (Vorsters et al., 2014). First, there could be a large difference in results depending on the collection device between cervical sampling (cone-shaped brush, cytobrush, Dacron swab), vaginal sampling (swab, brush, tampon or lavage), and urine (collection device) (Dijkstra et al., 2012). For collecting vaginal and urine samples, it is important to obtain enough exfoliated cervical cells, particularly with the collection device for urine, for which it is useful to include the first stream (Chen et al., 2009; Vorsters et al., 2014). In addition, care should be taken to prevent DNA degradation during storage and

Table 2
Concordance between HPV detection tests using cervical, vaginal and urine samples.

	HPV genotype	Vaginal/cervical samples			Urine/cervical samples		
		Concordance	Kappa (95% CI)	Two-tailed McNemar's *P* value	Concordance	Kappa (95% CI)	Two-tailed McNemar's *P* value
RealTime HR-S	HPV 16/18	93.1%	0.86 (0.72-0.95)	1.000	85.1%	0.63 (0.47-0.80)	0.300
	All hrHPV	89.1%	0.58 (0.36-0.80)	0.550	84.2%	0.51 (0.31-0.71)	< 0.001
Anyplex II	HPV 16/18	94.1%	0.86 (0.74-0.97)	0.690	85.1%	0.59 (0.41-0.77)	0.040
	All hrHPV	86.1%	0.49 (0.26-0.71)	0.060	81.2%	0.44 (0.25-0.64)	< 0.001
Cobas	HPV 16/18	91.1%	0.81 (0.69-0.93)	1.000	83.2%	0.61 (0.45-0.77)	0.010
	All hrHPV	73.3%	0.51 (0.30-0.73)	< 0.001	86.1%	0.33 (0.16-0.50)	< 0.001

extraction. In this study, a specified device was not used for urine collection, and occasionally the storage was extended for a week after DNA extraction. This might have reduced the concordance of the HPV test in this study. Second, the HPV positive rate of our study was high, because most of the patients in this study were already diagnosed with HSIL. The kappa value might have been calculated lower in this study, because the kappa value is calculated to be highest when the ratio of positive to negative is 1:1 (Chen et al., 2009). In order to obtain qualified self-collected vaginal and urine specimens efficiently, patients who were admitted to surgery for HSIL or ovarian tumors were included in this study. The HPV prevalence was higher than in previous studies, because the study was conducted on a selected group of women, most of whom were diagnosed with HSIL (Asciutto et al., 2018; Bernal et al., 2014; Enerly et al., 2013).

The positive rate of the HPV test was highest in cervical samples, followed by vaginal samples and urine. In addition, compared with cervical samples, the concordance rate of the HPV test using vaginal samples was higher than that of urine samples. The reason for this result may be that self-collected vaginal or urine samples did not contain enough exfoliated cervical cells for detection (Vorsters et al., 2012). In a previous meta-analysis, although the HPV test using the self-sampled vaginal samples was comparable to the cervical specimen, the HPV test using vaginal samples was less sensitive and accurate than the cervical samples (Arbyn et al., 2014). In addition, HPV detection using cervical samples was superior to urine, and the HPV DNA yield was higher for cervical samples, although HPV can be successfully detected in urine and urine-based tests. (Lim et al., 2017; Mendez et al., 2014; Sahasrabuddhe et al., 2014).

In this study, there are differences in concordance among the three HPV detection methods as in the sampling methods. There was no difference between the three tests in HPV 16/18 detection, while the Real-time HR-S HPV assay using self-collected vaginal and urine samples had the highest concordance compared to the HPV test using cervical samples in all hrHPV detection. In a comparison between the three HPV tests, the real-time HR-S HPV assay had a high concordance with the Anyplex HPV assay, but a low concordance with the Cobas HPV assay. There are several possible reasons for these variations among the three HPV assays. First, the enzymes, target regions, primer sequences, probe sequences, and reference sequences used vary across the HPV detection methods (Enerly et al., 2013). Second, since three HPV assays were performed from only one sample in the study, the amount of that sample might not have been sufficient. Finally, there may have been differences in the applications of the systems. The Cobas HPV assay is highly automated and it is adapted for primary specimens, while the real-time HR-S and Anyplex HPV assays use extracted DNA (Sahasrabuddhe et al., 2014). Therefore, only the real-time PCR of the Cobas system was performed by skipping the DNA extraction and preparation process. This difference may have affected the outcome.

This study has several limitations. First, this study showed only the concordance rates between sampling methods. In order for HPV tests using urine and self-collected vaginal samples to be clinically applied, further investigation will be required to measure the clinical performance of HPV tests using these samples to detect precancerous cervical neoplasia and cancer. Second, because our study was conducted in a specific population diagnosed with HSIL, it is difficult to apply this result to the general population for screening or patients diagnosed with LSIL. Therefore, further studies on these women are needed. Third, the study did not use a chelating agent to collect cell-free DNA, which may have been associated with low concordance in the urine samples (Vorsters et al., 2012). Previous studies have detected a substantial amount of non-cell-associated DNA and a chelating agent can be used to avoid degradation of cell-free DNA (Vorsters et al., 2014). Forth, in this study, urine and self-collected vaginal samples taken from a single person were divided for three different HPV tests. Therefore, the reliability of HPV test may deteriorate due to insufficient sample amount used to these tests. However, almost all samples in the present study have interpretable results as internal control was valid in Roche Cobas HPV, Anyplex II HPV, and RealTime HR-S HPV assay. Only 4% of urine samples had invalid result as internal control was not detected in Anyplex II HPV. Fifth, there was a difference in sample processing between vaginal samples and urine. The vaginal samples were centrifuged at 13,000 *g* for 15 min with preservative, while the urine samples were centrifuged only at 3000 *g* for 10 min without preservative. Finally, this study has a relatively small sample size. However, a unique strength of our study was the concurrent characterization of the agreement of non-invasive sampling methods with clinician-collected cervical samples in patients with HSIL. In addition, this study performed three kinds of HPV assays concurrently to provide a comparative analysis.

5. Conclusion

HPV tests using self-collected vaginal samples and urine showed substantial and moderate agreement compared with cervical samples, respectively, although HPV tests using these samples were still inferior to clinician-collected cervical samples. The RealTime HR-S HPV assay using self-collected vaginal and urine samples had the highest concordance with the HPV test using cervical samples for all hrHPV detection among the three HPV detection methods. Further research is needed on the clinical performance of HPV testing using urine and self-collected vaginal samples as the screening method and on the optimization, detection, and extraction of urine and vaginal samples by HPV DNA detection.

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Disclosure

The authors from Sejong Medical CO. are employees of and/or shareholders of the company, which developed the RealTime HR-S HPV assay. The remaining authors declare no competing financial interests.

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