

Original Article



Diagnostic performance of cervical cytology in HPV-independent cervical cancer: a comparative analysis with HPV-associated cases

Chi-Son Chang ,¹ Jaewon Na ,² Jun-Hyeong Seo ,² Yoo-Young Lee ,²
Tae-Joong Kim ,² Jeong-Won Lee ,² Byoung-Gie Kim ,² Chel Hun Choi ²

¹Department of Obstetrics and Gynecology, Chung-Ang University Gwangmyeong Hospital, Chung-Ang University College of Medicine, Gwangmyeong, Korea

²Department of Obstetrics and Gynecology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

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Correspondence to

Chel Hun Choi

Department of Obstetrics and Gynecology,
Samsung Medical Center, Sungkyunkwan
University School of Medicine, 81 Irwon-ro,
Gangnam-gu, Seoul 06351, Korea.
Email: chelhun.choi@samsung.com

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ORCID iDs

Chi-Son Chang
<https://orcid.org/0000-0002-0169-2008>
Jaewon Na
<https://orcid.org/0009-0006-1449-7988>
Jun-Hyeong Seo
<https://orcid.org/0000-0002-8044-3084>
Yoo-Young Lee
<https://orcid.org/0000-0001-5902-9877>
Tae-Joong Kim
<https://orcid.org/0000-0002-9693-9164>

ABSTRACT

Objective: This study evaluated the diagnostic accuracy of cervical cytology (Pap test) in human papillomavirus (HPV)-independent (HPVI) cervical cancers compared to that in HPV-associated (HPVA) cancers, and investigated differences in clinical outcomes.

Methods: We retrospectively reviewed the medical records of 515 patients diagnosed with cervical cancer between 2000 and 2021. The patients were categorized as HPVA (n=439) or HPVI (n=76) cervical cancer groups based on pathology and HPV testing. Cytology results were reclassified into 3 clinical categories: negative, low-grade abnormal, and high-grade abnormal. Multivariable logistic regression analyses were performed adjusting for age, stage, tumor size, lymphovascular space invasion, and parametrial invasion. Subgroup analyses were conducted in adenocarcinoma and HPVA cohorts. Survival outcomes were evaluated using Kaplan–Meier analysis and compared using log-rank tests.

Results: HPVI cancers showed a significantly higher rate of false-negative cytology results (39.5%) than HPVA cancers (18.0%, $p<0.001$). High-grade cytological abnormalities were less common in HPVI cases (52.6% vs. 69.2%). Similar trends were observed in adenocarcinoma-only cases, although the differences were not significant (39.5% vs. 22.8%, $p=0.055$).

In multivariable analyses adjusting for clinicopathologic factors, HPVI status remained significantly associated with higher odds of negative cytology (adjusted odds ratio=3.04; 95% confidence interval=1.60–5.78). The Kaplan–Meier analysis demonstrated significantly worse progression-free and overall survival in patients with HPVI cancers ($p<0.001$).

Conclusion: Cervical cytology demonstrated lower sensitivity for detecting HPVI cervical cancers, which are also associated with more aggressive clinical features and poorer outcomes. These findings support the need for tailored screening strategies for this underdetected cancer subtype.

Keywords: Cervical Cancer; HPV-Independent; Cytology; Adenocarcinoma; Pap Test

Jeong-Won Lee 
<https://orcid.org/0000-0002-6110-4909>
 Byoung-Gie Kim 
<https://orcid.org/0000-0002-0572-8450>
 Chel Hun Choi 
<https://orcid.org/0000-0002-0199-6669>

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

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Synopsis

Human papillomavirus (HPV)-independent cervical cancers showed higher false-negative cytology rates and more aggressive clinical features than HPV-associated cancers, particularly in adenocarcinomas. Cytologic abnormalities were less frequent, suggesting that tailored detection strategies may be needed for this underdetected high-risk subtype.

INTRODUCTION

Cervical cancer remains a significant global health concern and is the fourth most common cancer in women [1]. Most cervical cancers are caused by persistent infection with high-risk human papillomavirus (HPV) [2,3], and screening strategies based on HPV test results and cervical cytology have contributed substantially to the decline in the incidence and mortality of cervical cancer in many countries [4].

However, HPV-independent (HPVI) cervical cancers, which account for approximately 5%–15% of cases, represent a distinct clinical and pathological entity [5]. They tend to occur in older women, are often diagnosed at more advanced stages, and have a significantly worse prognosis than HPV-associated (HPVA) tumors [6].

Despite these differences, current cervical cancer screening programs rely primarily on HPV testing and cytology [7-10]. Although cytological examination is useful in reducing the cervical cancer burden, it has lower sensitivity for glandular lesions and is particularly limited in detecting HPVI cancers [11,12]. Moreover, given that HPVI cervical cancers lack detectable HPV DNA, increasing the adoption of primary HPV screening may exacerbate the diagnostic gap for these tumors [13].

HPVI cervical cancers often present with subtle or non-specific cytological abnormalities and may yield negative results in both Pap tests and HPV assays [14]. Recent studies have highlighted the potential of false-negative cytology in detecting these tumors, emphasizing the limitations of the current screening modalities [12,15]. These diagnostic limitations highlight the need to evaluate the performance of cytological examination in HPVI cervical cancers and explore potential approaches for improving early detection.

We aimed to evaluate the diagnostic accuracy of cervical cytology in HPVI cervical cancers compared to that in HPVA cancers. We analyzed cytological classifications, HPV test results, histological subtypes, and clinical outcomes to highlight potential blind spots in current screening strategies and reinforce the need for tailored approaches to detect HPVI tumors.

MATERIALS AND METHODS

1. Study population

We retrospectively reviewed the medical records of patients with cervical cancer who underwent primary treatment at a single tertiary academic cancer center between January 2000 and November 2021. Tumors were categorized as HPVA or HPVI based on the histologic subtype, in accordance with the International Endocervical Adenocarcinoma Criteria and

Classification (IECC) and the 2020 World Health Organization (WHO) Female Genital Tumor classification [16,17].

Demographic and clinical characteristics, including age at diagnosis, tumor size, stage according to the 2018 International Federation of Gynecology and Obstetrics (FIGO) staging system, and initial levels of squamous cell carcinoma (SCC) antigen, cancer antigen (CA) 125, and CA 19-9, were collected from electronic medical records. The treatment modality and histopathological features such as stromal invasion depth, lymphovascular space invasion (LVSI), and lymph node metastasis were also recorded.

Patients were treated according to standard protocols based on the clinical stage, including surgery with or without adjuvant therapy, primary chemoradiotherapy, or chemotherapy. After treatment, patients were followed up every 3 months for 2 years, every 6 months for the next 3 years, and annually thereafter. Progression-free survival (PFS) was defined as the time from the initial treatment to recurrence or the last follow-up, and overall survival (OS) as the time to death or last contact. This study was approved by the Institutional Review Board (IRB No. SMC 2023-08-102-001) Samsung Medical Center, and the requirement for informed consent was waived because of the retrospective nature of the study.

2. Comparison of cervical cytology and histopathology results

All patients underwent at least 1 cervical cytology test within 6 months prior to cancer diagnosis. Patients were excluded if they had not undergone cervical cytology testing prior to diagnosis or if the cytology results were unsatisfactory or unclassifiable. Cytology results were categorized into a 3-tier classification system according to the 2019 American Society for Colposcopy and Cervical Pathology (ASCCP) guidelines [10]. Negative cytology included results reported as negative for intraepithelial lesion or malignancy (NILM). Low-grade abnormal results included atypical squamous cells of undetermined significance (ASCUS) or low-grade squamous intraepithelial lesion (LSIL). High-grade abnormal cytology included high-grade squamous intraepithelial lesion (HSIL), atypical squamous cells—cannot exclude HSIL (ASC-H), atypical glandular cells (AGC), adenocarcinoma in situ (AIS), or malignant cytology. HPV test results were obtained within the same diagnostic period when available and were investigated and recorded.

The pathologic diagnosis of cervical cancer was based on colposcopy-directed biopsy, cervical conization, or hysterectomy specimens, all of which reviewed by the pathology department of our institution [18]. Histological subtypes were determined in accordance with the IECC [16] and 2020 WHO classification system [17]. HPV A tumors include SCC, adenosquamous cell carcinoma, adenocarcinomas of usual type, mucinous type-not otherwise specified, mucinous type-intestinal, mucinous type-invasive stratified mucin-producing (ISMP), and mucinous type-signet-ring cell. HPV I adenocarcinomas included gastric, clear cell, mesonephric, endometrioid, and serous types.

3. Statistical analysis

Clinical and pathological variables were compared between patients with HPV A and HPV I cervical cancers. Continuous variables were analyzed using Student's *t* test or the Mann–Whitney *U* test, and categorical variables were compared using the Pearson χ^2 test or Fisher exact test, as appropriate. To evaluate whether baseline clinicopathologic differences influenced the association between HPV status and negative cytology, multivariable logistic regression analyses were performed. Covariates included age, stage, tumor size, LVSI, and

parametrial invasion. Histologic subtype was not included in the multivariable model due to substantial overlap with HPV status, as all HPV+ tumors in this cohort were adenocarcinomas. To further account for histologic differences, additional subgroup analyses were conducted in adenocarcinoma cases and within the HPV+ cohort. Survival distributions were estimated using the Kaplan–Meier method and compared using the log-rank test. All statistical tests were 2-sided, with p-values <0.05 considered statistically significant. All analyses were conducted using R version 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria; <http://www.R-project.org/>).

RESULTS

1. Baseline characteristics and clinical features

Among the 515 patients, 439 (85.2%) and 76 (14.8%) patients had HPV+ and HPV- cervical cancers, respectively. Compared to HPV+, those with HPV- tumors were older (median 50.5 vs. 48.0 years), had significantly larger tumors (3.6 cm vs. 1.4 cm, $p<0.001$), and showed more frequent parametrial invasion (38.8% vs. 12.6%, $p<0.001$), LVSI (55.2% vs. 30.9%, $p<0.001$), and nodal metastasis (pelvic: 40.3% vs. 16.6%; paraaortic: 9.0% vs. 0.7%, both $p<0.001$). Recurrence and mortality rates were significantly higher in HPV- cases (35.5% and 23.7%, respectively) than those in HPV+ cases (9.8% and 1.1%, respectively; both $p<0.001$) (**Table 1**).

Similar trends were also observed in the adenocarcinoma subgroup ($n=177$). Patients with HPV- adenocarcinoma ($n=76$) were significantly older (50.5 vs. 43.0 years, $p<0.001$) and had more aggressive features including deeper invasion, more frequent nodal metastases, and poorer outcomes, with 35.5% recurrence and 23.7% mortality compared to 11.9% and 2.0% in HPV+ adenocarcinomas, respectively ($p<0.001$) (**Table S1**).

The detailed histological subtypes of the adenocarcinoma are shown in **Fig. 1**. In the HPV+ group ($n=101$), usual-type adenocarcinoma was predominant (80.2%), followed by the intestinal (9.9%) and ISMP (7.9%) subtypes. In contrast, the HPV- group ($n=76$) mainly consisted of gastric-type (72.4%) and clear-cell (13.2%) adenocarcinomas (**Fig. 1**).

2. Cervical cytology results based on HPV status and histology

Among patients with available cytology data, negative Pap test results (false-negatives) were significantly more frequent in HPV- cancers than in HPV+ cancers (39.5% vs. 18.0%, $p<0.001$). High-grade abnormalities were less frequent in patients with HPV- cancers (52.6%) than those with HPV+ cancers (69.2%) (**Table 2**). In the adenocarcinoma subgroup, 39.5% of

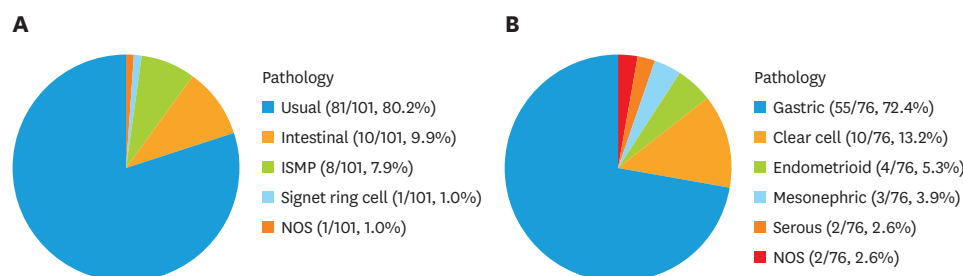


Fig. 1. Detailed histology of (A) HPV-associated adenocarcinoma and (B) HPV-independent adenocarcinoma. HPV, human papillomavirus; ISMP, invasive stratified mucin-producing; NOS, not otherwise specified.

Table 1. Baseline characteristics of patients

Characteristics	HPV-associated (n=439)	HPV-independent (n=76)	p-value
Age (yr)	48.0 (39.0–58.0)	50.5 (44.0–56.0)	0.061
Histology			-
Squamous cell carcinoma	331 (75.4)	-	
Adenosquamous carcinoma	7 (1.6)	-	
Adenocarcinoma	101 (23.0)	76 (100.0)	
SCC	1.2 (0.8–4.0)	0.8 (0.4–1.1)	<0.001
CA 125	7.8 (4.8–16.2)	12.5 (6.8–27.1)	0.003
CA 19-9	10.5 (3.6–26.6)	18.2 (4.8–136.3)	0.077
FIGO stage			0.026
I	232 (52.8)	41 (53.9)	
II	48 (10.9)	12 (15.8)	
III	140 (31.9)	15 (19.7)	
IV	19 (4.3)	8 (10.5)	
Initial treatment			<0.001
OP only	183 (41.7)	10 (13.2)	
OP + RT/CCRT	114 (26.0)	56 (73.7)	
CCRT	130 (29.6)	9 (11.8)	
Others	12 (2.7)	1 (1.3)	
Tumor size	1.4 (0.0–3.1)	3.6 (2.2–5.0)	<0.001
Parametrial invasion			<0.001
Negative	264 (87.4)	41 (61.2)	
Positive	38 (12.6)	26 (38.8)	
LVSI			<0.001
Negative	208 (69.1)	30 (44.8)	
Positive	93 (30.9)	37 (55.2)	
PLN			<0.001
Negative	252 (83.4)	40 (59.7)	
Positive	50 (16.6)	27 (40.3)	
PALN			<0.001
Negative	300 (99.3)	61 (91.0)	
Positive	2 (0.7)	6 (9.0)	
Recur	43 (9.8)	27 (35.5)	<0.001
Death	5 (1.1)	18 (23.7)	<0.001

Data are presented as number (%) or median (range).

CA, cancer antigen; FIGO, International Federation of Gynecology and Obstetrics; HPV, human papillomavirus; LVSI, lymphovascular space invasion; OP, operation; PALN, paraaortic lymph node; PLN, pelvic lymph node; RT, radiotherapy; SCC, squamous cell carcinoma.

Table 2. Cervical cytology test results for HPVA and HPV-I cervical cancer

Cytology test result	HPVA (n=439)	HPVI (n=76)	p-value
			<0.001
Normal (false-negative)	79 (18.0)	30 (39.5)	
Low-risk abnormal	56 (12.8)	6 (7.9)	
ASCUS	49 (11.2)	6 (7.9)	
LSIL	7 (1.6)	0 (0.0)	
High-risk abnormal	304 (69.2)	40 (52.6)	
AGC	29 (6.6)	18 (23.7)	
ASC-H	50 (11.4)	0 (0.0)	
HSIL/AIS	124 (28.2)	10 (13.2)	
Malignancy	101 (23.0)	12 (15.8)	

Values are presented as number (%).

AGC, atypical glandular cells; AIS, adenocarcinoma in situ; ASC-H, atypical squamous cells—cannot exclude HSIL; ASCUS, atypical squamous cells of undetermined significance; HPVA, human papillomavirus-associated; HPV-I, human papillomavirus-independent; HSIL, high grade squamous intraepithelial lesion; LSIL, low grade squamous intraepithelial lesion.

the HPV-I cases had false-negative cytology results compared with 22.8% of the HPVA cases ($p=0.055$). High-grade abnormalities were more frequently observed in HPVA (66.3%) than in HPV-I (52.6%) adenocarcinomas (**Table S2**).

Among patients with HPVA cancers, cytological performance was also compared between patients with SCC and adenocarcinoma/adenosquamous carcinoma (AC/ASC). False-negative results were slightly more common in AC/ASC (23.1%) than in SCC (16.3%); however, the difference was not statistically significant ($p=0.224$) (**Table S3**).

HPV test results were consistent with the histological classifications of HPVA and HPVI tumors. Among the entire cohort, HPV test results were available for 226 patients (43.9%). Additionally, HPV-negative results were significantly more frequent in HPVI cancers (75.0%) than in HPVA cancers (1.4%; $p<0.001$). In the adenocarcinoma subgroup, 65 patients (36.7%) had available HPV test results. Furthermore, HPV-negative results were observed in 75.0% of HPVI adenocarcinomas and in none of the HPVA adenocarcinomas ($p<0.001$). In the HPVA cohort, 214 patients (48.7%) had valid HPV test results. HPV positivity was similarly high in both SCC (98.1%) and AC/ASC (100.0%) cases, with no significant difference ($p=0.718$).

3. Multivariable analysis

To account for potential baseline differences between HPVA and HPVI tumors, multivariable logistic regression analyses were performed adjusting for age, stage, tumor size, LVSI, and parametrial invasion (**Table 3**). After adjustment, HPVI status remained significantly associated with higher odds of negative cytology (adjusted odds ratio [OR]=3.04; 95% confidence interval [CI]=1.60–5.78; $p=0.001$). Stage, tumor size, LVSI, and parametrial invasion were not independently associated with negative cytology.

In analyses in adenocarcinoma cases, HPVI tumors demonstrated higher odds of negative cytology compared with HPVA adenocarcinomas (adjusted OR=1.93; 95% CI=0.88–4.25), although statistical significance was not reached (**Table S4**). Within the HPVA cohort, AC/ASC was independently associated with higher odds of negative cytology compared with SCC (adjusted OR=2.18; 95% CI=1.10–4.32; $p=0.026$) (**Table S5**). Tumor size was also independently associated with negative cytology in this subgroup, with larger tumors showing higher odds of negative cytology (adjusted OR=1.26; 95% CI=1.03–1.54; $p=0.025$), whereas stage, parametrial invasion, and LVSI were not.

4. Survival analysis

The Kaplan–Meier analysis demonstrated that HPVI cervical cancers had significantly worse PFS and OS than HPVA cancers ($p<0.001$ for both). The 3-year PFS rates were 59.0% in HPVI cases and 84.1% in HPVA cases (**Fig. 2A**), whereas the 3-year OS rates were 74.0% and 95.6%, respectively (**Fig. 2B**).

Similar patterns were observed in the adenocarcinoma subgroup: 3-year PFS and OS rates were 59.0% and 74.0% in HPVI adenocarcinomas, compared to 79.9% and 88.9% in

Table 3. Multivariable logistic regression analysis of factors associated with negative cytology

Variable	Adjusted OR (95% CI)	p-value
HPV-independent (vs. HPV-associated)	3.04 (1.60–5.78)	0.001
Age	0.99 (0.96–1.01)	0.273
Stage (III–IV vs. I–II)	1.50 (0.76–2.95)	0.246
Tumor size (cm)	1.15 (0.98–1.35)	0.084
Parametrial invasion	1.13 (0.55–2.32)	0.747
LVSI	1.15 (0.62–2.14)	0.663

CI, confidence interval; HPV, human papillomavirus; LVSI, lympho-vascular space invasion; OR, odds ratio.

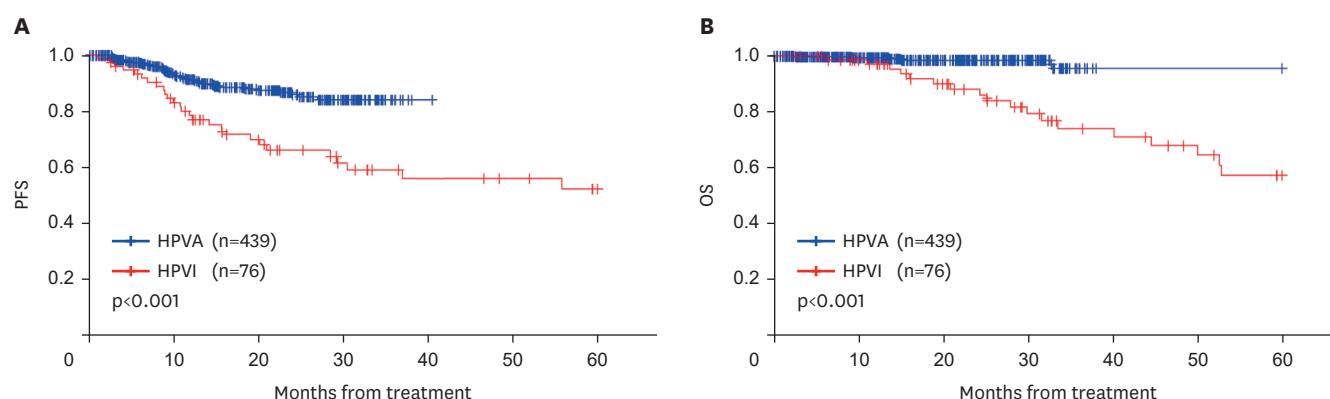


Fig. 2. Kaplan–Meier curve for (A) PFS and (B) OS in HPVA and HPVI cervical cancer. HPVA, human papillomavirus-associated; HPVI, human papillomavirus-independent; OS, overall survival; PFS, progression-free survival.

HPVA adenocarcinomas, respectively (**Fig. S1**). Additionally, survival outcomes were similar between the SCC and AC/ASC groups within the HPVA group (**Fig. S2**).

DISCUSSION

In this study, we observed that false-negative cytology results were significantly more frequent in HPVI cervical cancer cases than in HPVA cases. Furthermore, high-grade cytological abnormalities were observed less frequently in HPVI tumors. In the adenocarcinoma subgroup, similar trends were noted, though not statistically significant. Among patients with HPVA cancers, false-negative results of cervical cytology tests were more common in AC/ASC than in SCC. In terms of clinical outcomes, HPVI cervical cancers were associated with more aggressive features—including larger tumor size, higher rates of LVSI and nodal metastasis—and significantly worse PFS and OS [18–21]. To address potential differences in baseline clinicopathologic characteristics between HPVA and HPVI groups, we performed multivariable analyses adjusting for age, stage, tumor size, LVSI, and parametrial invasion. Because all HPVI tumors in this cohort were adenocarcinomas, histologic subtype was not included in the multivariable model to avoid collinearity. Instead, we performed additional subgroup analyses restricted to adenocarcinoma cases and within the HPVA cohort to separately evaluate the effects of HPV status and histology. In this adjusted model, HPVI status remained significantly associated with negative cytology.

In this study, approximately 40% of the HPVI cases yielded false-negative cytological results. Although cytological screening has historically played a critical role in cervical cancer prevention, its sensitivity for detecting glandular and HPV-negative lesions remains suboptimal [15,22]. Even among HPVA tumors, Pap tests were numerically less sensitive for adenocarcinoma than for SCC. This suggests an intrinsic limitation of cytology in detecting non-squamous histology, irrespective of the HPV status [23]. In the HPVA cohort, larger tumor size was independently associated with negative cytology. One possible explanation is that some tumors, particularly those with endophytic growth patterns, may expand within the cervical stroma without extensive surface exfoliation, thereby reducing the likelihood of abnormal cells being captured during cytologic sampling. Alternatively, delayed diagnosis due to initially negative cytology may allow tumors to grow larger before detection.

Beyond HPV status, anatomical factors may also contribute to the high false-negative rate observed in HPVI tumors. Many HPVI adenocarcinomas, particularly gastric-type lesions, tend to exhibit endophytic growth, arise deep within the endocervical glands, and show minimal surface exfoliation, which substantially reduces the likelihood that malignant cells are captured during routine cytologic sampling [11,16,20]. These morphologic features could partly explain the frequent cytologic underdetection observed in HPVI cervical cancers.

We applied a 3-tier classification system—normal, low-grade, and high-grade abnormalities—based on the ASCCP guidelines to improve clinical interpretability [10]. Interestingly, false-negative cytology was more common in patients with FIGO stage III–IV disease, which contrasts with the general assumption that advanced-stage cancers are more readily detected. Moreover, these patients exhibited higher recurrence and mortality rates, although the differences were not statistically significant. This suggests that reliance on cytology may delay diagnosis in clinically important cases and reinforces the covert clinical characteristics of HPVI cervical cancer [24].

HPV testing has also shown limited utility in detecting HPVI tumors. Although nearly all HPVA tumors tested positive for HPV, the majority of HPVI tumors tested negative in HPV assays, consistent with their etiologic classification [14,25]. The limited detectability of HPVI tumors by both cytology and HPV testing indicates a diagnostic blind spot within the current screening paradigms.

In Korea, the national HPV vaccination program was introduced in 2016 and has achieved high uptake in the adolescent population. Given that vaccination reduces the incidence of HPVA cancer, the relative burden of HPVI tumors may increase. These tumors, which cannot be prevented by vaccination, may constitute a growing proportion of cervical cancer cases in the post-vaccine era. Given their tendency to present at more advanced stages and the current lack of effective early detection methods, improved strategies for their recognition and diagnosis are becoming increasingly important [25,26].

Emerging molecular evidence highlights the distinct pathogenesis of HPVI tumors. These cancers frequently harbor mutations in TP53, KRAS, and PTEN, exhibit low p16 expression, lack HPV DNA, and are often accompanied by a non-inflamed tumor microenvironment and unique immunohistochemical profiles [5,12,19]. These molecular characteristics may explain their resistance to conventional therapies and support the need for alternative diagnostic and therapeutic approaches. Although no targeted treatments or screening modalities are currently tailored for HPVI tumors, several promising approaches have been proposed, including artificial intelligence-assisted cytology, advanced HPV genotyping, and biomarker panels such as miR-21 and miR-155 [22,27].

Given these emerging alternative diagnostic considerations, the potential implications of the distinctive molecular and immunophenotypic features of HPVI cervical cancers for cytologic evaluation have also been addressed. HPVI cervical cancers have been reported to show aberrant p53 expression, loss of diffuse p16 staining, and frequent TP53 mutations, findings that have been primarily demonstrated in tissue-based studies [28–30]. Although these features are not incorporated into routine cytology-based screening, limited reports describing recognizable cytomorphologic patterns in selected HPVI precursor lesions suggest that cytology may occasionally capture characteristic architectural features [30]. However, current evidence remains insufficient to support the routine application of immunocytochemical or

molecular assays on cytologic specimens, as standardized protocols and prevalence data are lacking [30,31]. These observations suggest that integration of cytomorphologic assessment with an understanding of the underlying molecular pathology may inform future adjunctive diagnostic approaches in selected, diagnostically challenging cases.

A major strength of this study is its large single-institution cohort with long-term follow-up, which allowed for a comprehensive comparison of cytological, pathological, and survival outcomes. The use of a unified histological classification system and a clinically relevant cytology classification improves the applicability and consistency of the findings. Moreover, this is one of the few studies that directly compares cytological performance between HPVA and HPVI cancers with matched histology and outcome data.

However, this study had some limitations. First, HPV test results were not available for all patients, potentially limiting the ability to correlate molecular findings across the entire cohort. Second, cytological interpretations spanned over 2 decades, during which diagnostic practices and laboratory standards may have evolved. Lastly, the retrospective nature and single-institution design may limit the generalizability of the findings.

The results of this study suggest that current cervical cancer screening strategies may have limitations in detecting HPVI tumors, which tend to present with more subtle cytological features. As the incidence of HPVA cervical cancers potentially declines with widespread HPV vaccination, HPVI tumors may comprise a relatively larger proportion of cervical cancer cases in the future. These findings indicate potential need for greater clinical attention to this subgroup and support further research into alternative or adjunctive screening tools, such as molecular biomarkers or enhanced cytological techniques, that could aid in earlier detection and improved patient outcomes.

In conclusion, HPVI cervical cancers, particularly adenocarcinomas, remain difficult to detect using current cytology- and HPV-based screening methods. Their distinct biology, subtle cytological presentation, and aggressive clinical course underscore the need for greater attention to this subgroup, particularly as HPV vaccination continues to shift the overall landscape of cervical cancer. As HPV vaccination continues to reduce the burden of HPVA cervical cancers, the relative clinical importance of HPVI tumors may become more prominent. Recognizing the diagnostic limitations of current cytology- and HPV-based screening strategies for these tumors will therefore be increasingly important in the evolving landscape of cervical cancer prevention. Further refinement of cytological interpretation and the development of novel diagnostic biomarkers may help improving early detection and ultimately enhancing patient outcomes.

SUPPLEMENTARY MATERIALS

Table S1

Baseline characteristics of the patients (adenocarcinoma only)

Table S2

Cervical cytology test results for adenocarcinoma according to HPV status

Table S3

Cervical cytology test results for HPV-associated cervical cancer according to histological type

Table S4

Multivariable logistic regression analysis of factors associated with negative cytology in adenocarcinoma group

Table S5

Multivariable logistic regression analysis of factors associated with negative cytology in HPV-associated cervical cancer group

Fig. S1

Kaplan–Meier curve for (A) progression-free survival and (B) overall survival in HPV-associated and HPV-independent adenocarcinoma.

Fig. S2

Kaplan–Meier curve for (A) progression-free survival and (B) overall survival in HPV-associated according to histological type.

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