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ORIGINAL ARTICLE

Clinical significance of the pattern-based classification in endocervical adenocarcinoma, usual and variants

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Abstract

Background The Silva system is a pattern-based classification system that stratifies endocervical adenocarcinomas (AC) into 3 categories to assess the risk of lymph node (LN) metastasis. This study aimed to evaluate whether this novel risk stratification system is applicable to all endocervical AC, including usual and variant, and to suggest a suitable management plan for cervical AC.

Methods We retrospectively retrieved consecutive pathology cases with a final diagnosis of endocervical AC treated via radical hysterectomy and pelvic lymphadenectomy. Specimens were classified by consensus according to the Silva system based on "pattern of invasion" as A, B, or C, further clinical/pathologic features were assessed according to pattern-based classification.

Results A total of 76 cases of invasive cervical AC were evaluated. Of these, 63 (82.9%) were categorized as usual-type endocervical AC and 13 (17.1%) as special types. Among those with usual and variants, all patients with pattern A tumor had no LN metastasis and did not develop recurrence. Likewise, multivariate analysis revealed that LN metastasis and pattern C or B tumors are significant independent predictors of disease-free survival (DFS). Although pattern A tumors had no LN metastasis, they also developed complications after surgery, similar to pattern B or C tumors.

Conclusion Regardless of histologic subtypes, pattern A tumors had no LN metastasis and no recurrence. Thus, the Silva classification system can influence the clinical management of all types of endocervical AC. Conservative management is reasonable in all patients with endocervical AC with pattern A tumors.

Keywords Endocervical adenocarcinoma · Pattern-based classification · Management

Introduction

Cervical adenocarcinoma (AC) is the second most frequent cervical carcinoma following squamous cell carcinoma (SCC), and its incidence has been increasing in recent decades, accounting for 20–25% of all cervical cancers [1]. Both SCC and AC are almost always associated with high-risk human papillomavirus (HPV) infection, but a few subtypes such as gastric-type, clear cell, serous, and mesonephric AC seem to be unrelated to HPV infection [2]. Moreover, compared with SCC, AC is more closely associated with risk factors such as obesity, nulliparity, and prolonged oral contraceptives use [3]. However, although SCC and AC have different histologies, sites of origin, epidemiology, prognostic factors, patterns of spread, and rates of failure after treatment, they are staged and treated similarly [1]. In the National Comprehensive Cancer Network guidelines

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[4], there is no difference in the treatment strategy between SCC and AC. The current treatment modality for cervical AC is based on stage and histopathologic factors, including tumor size, lymphovascular invasion (LVI), lymph node (LN) metastasis, resection margin status, depth of invasion, and microscopic parametrial involvement [5].

Although the mean age at presentation of cervical cancer (i.e., between 45 and 50 years old) is similar across histologic types [6], the incidence of AC is increasing in young women [7]. This profoundly affects the choice of treatment given that the recommended treatment modalities for AC, including radical hysterectomy, affect fertility and childbearing capability [4] and yield a high rate of complications, such as urinary dysfunction, lymphedema, and nerve-site injury [8]. Therefore, individualized treatment plans should be considered for AC to optimize treatment and patients outcomes. High stage, angiolymphatic invasion, high grade, and destructive pattern of stromal invasion are known as poor prognostic factors of AC [9, 10]. In 2013, a novel method of stratifying patients into risk categories based on the pattern of stromal invasion has been proposed for usual-type endocervical AC [10]. This new system, the Silva system, has the potential to considerably reduce the number of unnecessary radical procedures in patients with early-stage disease [10]. However, studies assessing the accuracy of the Silva system for AC were only limited to usual-type HPV-related endocervical AC and did not include any of the other variants (e.g., gastric-type, clear cell, serous, mesonephric AC) [10, 11]. Given the rarity and poorer prognosis of other types of AC [12, 13], the applicability of the Silva system for variant type AC has not been investigated. Although these subtypes of AC are less frequent than the usual type, they have poor clinical outcomes and can be overtreated [12]. Moreover, although their prognosis is different than that of the usual type, the treatment modalities and the prognostic factors are the same. Therefore, it is necessary to establish a criterion for appropriate treatment for all types of AC based on objective evaluation.

This study aimed to evaluate whether the Silva system is applicable to all endocervical AC, including usual and variants, and to suggest a suitable management plan for endocervical AC.

Materials and methods

Case selection and histopathologic review

This retrospective study has been approved by the Institutional Review Board of Busan Paik Hospital, Korea (IRB No. 17–0136). Written informed consent was obtained from all patients. We retrieved data on consecutive pathology cases with a final diagnosis of cervical AC treated surgically with radical hysterectomy with pelvic lymphadenectomy. A total of 76 cases of hysterectomy samples and corresponding conization specimens collected in Busan Paik Hospital from January 2005 to December 2016 were reviewed by two experienced pathologists (HJC and HYP).

All tumor sections were histologically reviewed. The tumor contour and presence of stromal inflammation and desmoplasia were evaluated using low-power magnification. Meanwhile, stromal destruction and single or small clusters of cell detachment were evaluated using high-power magnification. Gland growth pattern (including cribriform, papillary, canalicular, or solid) and gland morphology (including round, angulated, or opened) were also observed. To determine LVI, intratumoral and peritumoral stroma were closely inspected. Specimens were classified by consensus according to the Silva system based on "pattern of invasion" as A, B, or C (Fig. 1). Silva pattern A tumors are characterized by well-demarcated glands frequently forming groups with relatively well-preserved lobular architecture. These should not be diagnosed in the presence of any desmoplastic reaction, isolated invasive cells, LVI, high-grade cytologic features, solid architecture, or confluent papillary pattern. However, complex intraglandular proliferations (cribriform or papillae) are acceptable if they are <5 mm in greatest dimension. Pattern B carcinomas feature localized (limited/early) destructive invasion in a background of pattern A. Individual or small clusters of tumor cells are seen in desmoplastic or inflamed stroma, and these foci are single, multiple, or lineal at the base of the tumor but should not exceed 5 mm in diameter. LVI is acceptable in pattern B tumors but not solid growth. Pattern C tumors show diffuse destructive stromal invasion by infiltrating glands associated with desmoplastic stromal response. The glands are often angulated or fragmented/incomplete and open to the stroma. LVI, solid, poorly differentiated, architecturally high-grade components or confluent growth (glands, papillae, or mucin lakes) filling a $4\times$ field (>5 mm) is included in pattern C tumors [10].

Data analyzed included patient age at diagnosis, tumor histotype, depth of invasion (mm), tumor size, histologic grade, LVI, LN metastasis, pathologic staging as per the International Federation of Gynecology and Obstetrics guideline, HPV infection, recurrence, survival, and postoperative complications according to the Silva classification system.

HPV detection method

We used the GoodGene HPV DNA Genotyping Chip kit (GoodGene Inc., Seoul, Korea), a polymerase chain reaction (PCR)-based DNA microarray system, following the manufacturer's recommendations. The HPV DNA chip identifies 22 HPV genotypes; 15 high-risk (16, 18, 31, 33, 35, 39, 45,

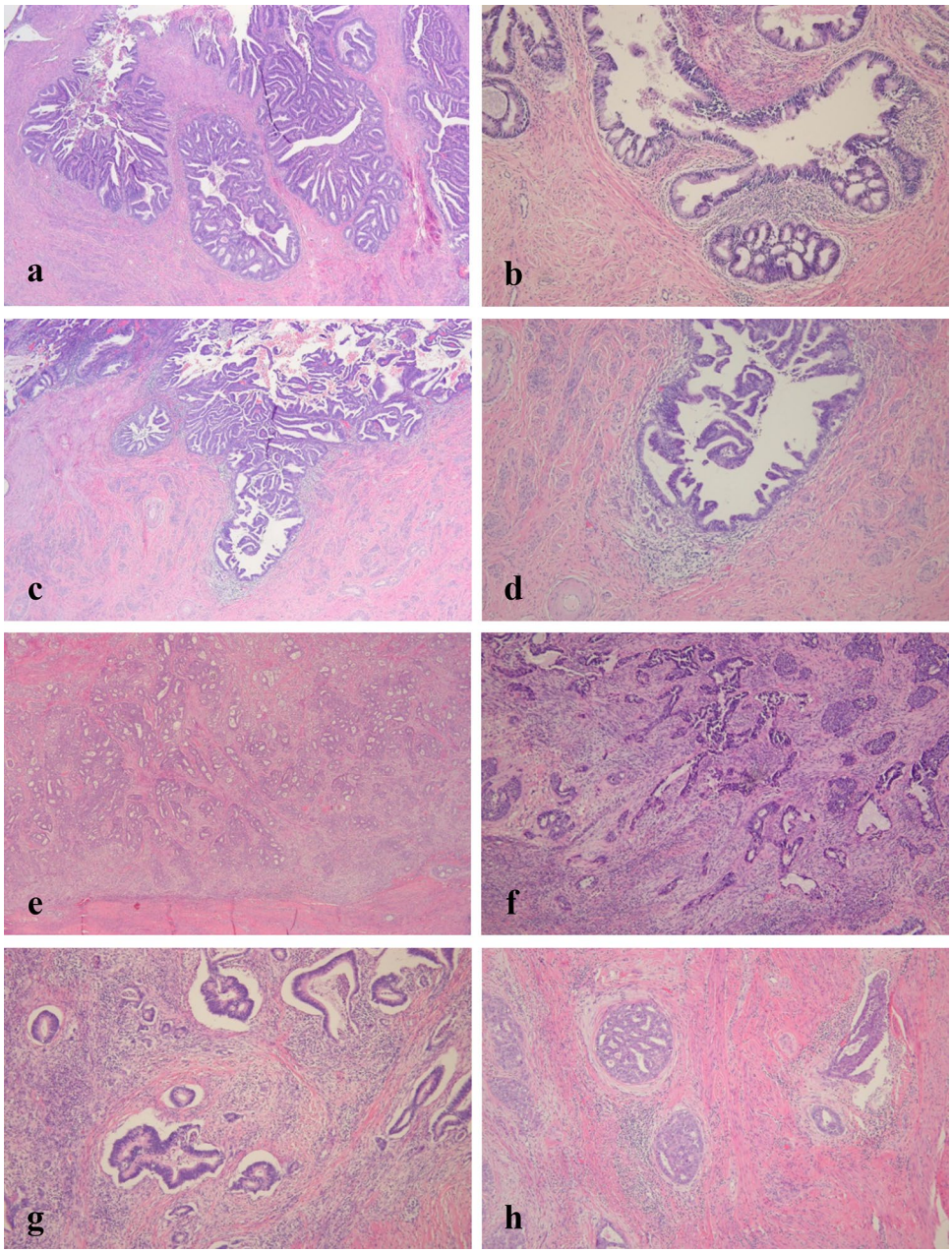

Fig. 1 **a**, **b** Non-destructive invasive endocervical adenocarcinoma corresponding to pattern A. **a** Glandular density is increased, and the tumor shows papillary and focal cribriform structures without solid growth. **b** The glands show round and pushing contours. No single cells or cell detachment is observed. **c**, **d** Localized destructive endocervical adenocarcinoma corresponding to pattern B. **c** Most of the tumor is composed of well-demarcated glands. **d** High-power magnification of the focally inflamed stroma shows small groups of infiltrative tumor cells separated from the round glands. **e**–**h** Diffuse destructive endocervical adenocarcinoma corresponding to pattern C. **e** Markedly complex and irregular glands are associated with extensive desmoplastic response. **f** Canalicular patterned glands and some solid, poorly differentiated components are observed. **g** Variable sizes and shapes of glands of incomplete, opened glands are forming infiltrative borders. Angulated glands are interspersed in desmoplastic stroma. **h** Lymphovascular space invasion. (**a**–**h**: H&E; **a**, **c**, **e**: ×40 magnification; **b**, **d**, **f**, **g**, **h**: ×100 magnification)

51, 52, 53, 56, 58, 59, 66, and 68) and 7 low-risk genotypes (6, 11, 34, 40, 42, 43 and 44). Briefly, DNA was isolated from a swab sample using a DNA isolation kit (GoodGene Inc., Seoul, Korea). The target L1 region of HPV DNA was then amplified and labeled by a single dye (indocarbocyanine-dUTP; NEN Life Science Products, Inc., Boston, MA, USA). The PCR products of all samples were detected using electrophoresis with 2.0% agarose gel. The samples were mixed with a hybridization solution (GoodGene Inc. Seoul, Korea). Hybridization was performed at 48℃ for 30 min. The hybridized HPV DNA was visualized using a DNA chip scanner (GoodGene scanner, Nano storage Inc, Seoul, Korea).

Statistical analysis

Statistical analyses were performed using MedCalc version 14.8.1 (Frank Schoonjans, Ghent University, Belgium). Categorical variables were compared using chi-square tests and Fisher's exact tests. The mean, median, and standard deviation were calculated for continuous variables, which were compared using Mann–Whitney *U* test for two groups and Kruskal–Wallis test for three or more unmatched groups. Kaplan–Meier plots and the log-rank test were used to compare the independent variables and survival. Univariate and multivariate Cox proportional hazard models were used to assess the relationship

between the independent and dependent variables. A p value of less than 0.05 was considered statistically significant.

Results

Of 76 cases of invasive cervical AC, 63 (82.9%) were categorized as usual-type endocervical AC and 13 cases (17.1%) as variants (8 gastric, 3 endometrioid, 1 villoglandular, and 1 serous type).

Twenty-three cases (30.3%) had morphologic features that corresponded to pattern A, 22 patients (28.9%) had tumors with morphologic features that corresponded to pattern B, and the remaining 31 patients (40.8%) had tumors with morphologic features of pattern C.

Two pathologists disagreed in the 3 cases (3.9%) at first (C versus B and B versus A), but finally accord in all the pattern after reviewing second reviewing and discussion.

Analysis of general characteristics of patients according to pattern classification

The characteristics of the patients were not significantly different among those with patterns A, B, and C tumors. Patients with pattern A tumors were younger than those with pattern B or C tumors, but there was no statistically significant difference.

All pattern A tumors were stage I and none of the cases had LVI and LN metastasis. In 16 (69.6%) of these cases, the depth of invasion was less than 1/3, and 8 (34.8%) of cases had tumor size less than 2 cm. Thirteen cases (56.5%) were grade 1 tumors, 8 cases (34.8%) were grade 2 tumors, and 2 cases (8.7%) were grade 3 tumors.

Although usual-type endocervical AC was more common than variants (82.9% vs. 17.1%), there was no difference in the proportion according to patterns ($P=0.820$).

Pattern B or C tumors were larger ($P=0.026$), had deeper invasion ($P<0.001$), higher stage ($P=0.007$), and demonstrated a higher frequency of LVI and LN metastasis ($P<0.001$) than pattern A tumors. Fifteen (48.4%) patients with pattern C tumors showed LN metastasis, and LVI was present in 22 cases (71.0%) (Table 1).

Seventy-two patients underwent an HPV test, and the rate of HPV infection was not significantly different according to patterns. Regarding the HPV types according to the patterns, pattern A tumors were more strongly associated with HPV 16 infection (72.2%), while pattern B and C tumors were significantly related to HPV 18 infection (75.0% and 56.5%, respectively) ($P<0.001$) (Table 1).

Table 1 General characteristics of patients according to pattern classification

Characteristics	Pattern classification, *n* (%)			
	A ($n=23$)	B ($n=22$)	C ($n=31$)	*P* value
Age (mean ± SD, years)	46.6 ± 9.8	47.2 ± 9.1	50.8 ± 9.1	0.085
Menopause				0.686
No	15 (65.2)	16 (72.7)	19 (61.3)	
Yes	8 (34.8)	6 (27.3)	12 (38.7)	
LN metastasis				< 0.001*
No	23 (100)	18 (81.8)	16 (51.6)	
Yes	0 (0)	4 (18.2)	15 (48.4)	
LVI				< 0.001*
No	23 (100)	17 (77.3)	9 (29.0)	
Yes	0	5(22.7)	22 (71.0)	
Stage				0.007*
I	23 (100)	17 (77.3)	20 (64.5)	
II	0 (0)	5 (22.7)	11 (35.5)	
Invasion depth				< 0.001*
< 1/3	16 (69.6)	5 (22.7)	1 (3.2)	
≥ 1/3	7 (30.4)	17 (77.3)	30 (96.8)	
Tumor size				0.026*
< 2 cm	8 (34.8)	2 (9.1)	3 (9.7)	
≥ 2 cm	15 (65.2)	20 (90.9)	28 (90.3)	
Grade				0.012*
1	13 (56.5)	12 (54.5)	6 (19.4)	
2	8 (34.8)	6 (27.3)	12 (38.7)	
3	2 (8.7)	4 (18.2)	13 (41.9)	
Histologic type				0.820
Usual	20 (31.7)	18 (28.6)	25 (39.7)	
Variant	3 (23.1)	4 (30.8)	6 (46.2)	
HPV infection	A ($n=20$)	B ($n=22$)	C ($n=30$)	0.275
Positive	18 (90.0)	20 (90.9)	23 (76.7)	
Negative	2 (10.0)	2 (9.1)	3 (23.3)	
HPV typing	A ($n=18$)	B ($n=20$)	C ($n=23$)	< 0.001*
HPV 16	13 (72.2)	5 (25.0)	5 (21.7)	
HPV 18	5 (27.8)	15 (75.0)	13 (56.5)	
[a]Others	0 (0.0)	0 (0.0)	5 (21.7)	

LN lymph node, *LVI* lymphovascular invasion

*$P<0.05$

[a]HPV 45, low-risk types

Comparison of characteristics according to patterns between usual and variants of AC

Regardless of histologic types, the rate of recurrence was significantly different according to the patterns. Among patients with usual type of tumors and variants, those with pattern A showed no recurrences ($P=0.002$ and $P=0.049$, respectively). Meanwhile, among those with usual type, patients with pattern A and B tumors survived longer than

those with pattern C tumors ($P=0.001$), but there was no significant difference in survival among those with variants according to patterns. All pattern A tumors had no LN metastasis and no LVI regardless of histologic type (usual and variant), and the incidence of LN metastasis and LVI was significantly different between those with pattern A and those with pattern B or C tumors ($P=0.004$, $P<0.001$ and $P=0.014$, $P=0.025$, respectively). By contrast, the stage, depth of invasion, tumor size and grade were not significantly different according to patterns in the variants (Table 2).

Prognosis according to pattern classification

Postoperative complications including lymph edema and bladder dysfunction occurred in 23 patients (30.3%), but there was no significant difference according to patterns (Table 3). Although none of the patients with pattern A had LN metastasis and LVI, they underwent radical hysterectomy with LN dissection. One patient (4.3%) had lymph edema, and 7 patients (30.4%) had bladder dysfunction (Table 3).

Patients with pattern A tumor had no recurrence, but 2 patients (9.1%) with pattern B tumor and 14 patients (45.2%) with pattern C tumor recurred. Pattern C tumors had high recurrence rate ($P<0.001$). During the follow-up period, all patients with pattern A and B tumors were alive, but only 71% of patients with pattern C tumors survived ($P<0.001$) (Table 3).

The 5-year survival rate of pattern A and B tumors was 100%, while that of pattern C tumors was 66.8%. Those who had pattern C tumors had the worst survival ($P<0.001$). The rate of DFS was also 100% in pattern A tumors, 90.4% for pattern B tumors, and 48.4% for pattern C tumors. Pattern

Table 2 Comparison of characteristics according to patterns between usual and variant types of AC

Characteristics	Usual type ($n=63$)				Variant type ($n=13$)			
	Pattern A ($n=20$)	Pattern B ($n=18$)	Pattern C ($n=25$)	*P* value	Pattern A ($n=3$)	Pattern B ($n=4$)	Pattern C ($n=6$)	*P* value
Recur				0.002*				**0.049***
No	20 (100)	17 (94.4)	15 (60.0)		3 (100)	3 (75.0)	2 (33.3)	
Yes	0	1 (5.6)	10 (40.0)		0 (0)	1 (25.0)	4 (66.7)	
Survival				0.001*				0.314
Yes	20 (100)	18 (100)	17 (68.0)		3 (100)	4 (100)	5 (83.3)	
No	0 (0)	0	8 (32.0)		0 (0)	0 (0)	1 (16.7)	
LN metastasis				0.004*				0.014*
No	20 (100)	15 (83.3)	15 (60.0)		3 (100)	3 (75.0)	1 (16.7)	
Yes	0 (0)	3 (16.7)	10 (40.0)		0 (0)	1 (25.0)	5 (83.3)	
LVSI				< 0.001*				0.025*
No	20 (100)	15 (83.3)	8 (32.0)		3 (100)	2 (50)	1 (16.7)	
Yes	0 (0)	3 (16.7)	17 (68.0)		0 (0)	2 (50)	5 (83.3)	
Stage				0.019*				0.237
I	20 (100)	15 (83.3)	17 (68.0)		3 (100)	2 (50)	3 (50)	
II	0 (0)	3 (16.7)	8 (32.0)		0 (0)	2 (50)	3 (50)	
Invasion depth				< 0.001*				0.150
< 1/3	15 (75.0)	5 (27.8)	1 (4.0)		1 (33.3)	0 (0)	0	
≥ 1/3	5 (25.0)	13 (72.2)	24 (96.0)		2 (66.7)	4 (100)	6 (100)	
Tumor size				0.042*				0.750
< 2 cm	7 (35.0)	2 (11.1)	2 (8.0)		1 (33.3)	0	1 (16.7)	
≥ 2 cm	13 (65.0)	16 (88.9)	23 (92.0)		2 (66.7)	4 (100)	5 (83.3)	
Grade				0.008*				0.135
1	10 (50.0)	9 (50.0)	3 (12.0)		3 (100)	3 (75.0)	3 (50.0)	
2	8 (40.0)	5 (27.8)	9 (36.0)		0 (0)	1 (25.0)	3 (50.0)	
3	2 (10.0)	4 (22.2)	13 (52.0)		0 (0)	0 (0)	0 (0)	
HPV infection (+)	52/60 (86.7)			0.379	9/12 (75.0)			0.449

LN lymph node, *LVI* lymphovascular invasion

*$P<0.05$

Table 3 Prognosis according to pattern classification

	Pattern classification, n (%)			*P* value
	A (*n* = 23)	*B* (*n* = 22)	*C* (*n* = 31)	
Complications				0.295
No	15 (65.2)	18 (81.8)	20 (64.5)	
Yes	8 (34.8)	4 (18.2)	11 (35.5)	
Lymph edema				0.902
No	22 (95.7)	21 (95.5)	28 (90.3)	
Yes	1 (4.3)	1 (4.5)	3 (9.7)	
Bladder dysfunction				0.389
No	16 (69.6)	19 (86.4)	23 (74.2)	
Yes	7 (30.4)	3 (13.6)	8 (25.8)	
Recurrence				< 0.001*
No	23 (100)	20 (90.9)	17 (54.8)	
Yes	0	2 (9.1)	14 (45.2)	
Survival (mean OS)	142.3 months	136.2 months	99.5 ± 5.3 months	< 0.001*
Yes	23 (100)	22 (100)	22 (71.0)	
No	0	0	9 (29.0)	

OS overall survival

*$P < 0.05$

A tumors had better prognosis than pattern B or C tumors ($P < 0.001$) (Fig. 2 a, b).

Analysis of prognostic factors of survival and DFS

Figure 3 shows the univariate hazard ratios of 5-year survival (a) and DFS (b) according to each of the independent factors. LN metastasis was significantly associated with shorter 5-year survival. Although patients with pattern C tumor had shorter 5-year survival, there was no significant association. Moreover, univariate analysis of DFS revealed that LN metastasis, pattern C tumor, tumor invasion depth ≥ 1/3, and stage II tumors were all significantly associated with short DFS. Multivariate analysis of DFS revealed that LN metastasis (hazard ratio [HR], 11.17; 95% confidence interval [CI], 3.08–40.48) and Silva pattern C or B (HR, 4.81; 95% CI 1.12–20.60) remained as significant independent predictors of DFS, while invasion depth and stage were not significant (Table 4).

Discussion

The incidence of cervical AC has been increasing, and it is becoming a prevalent gynecologic cancer [7, 14]. In addition, the age of patients with cervical AC has become younger than that of patients with cervical squamous cell carcinoma (SCC). Specifically, an increasing number of AC patients are in their reproductive age. Clinical stage remains the most important prognostic factor and the

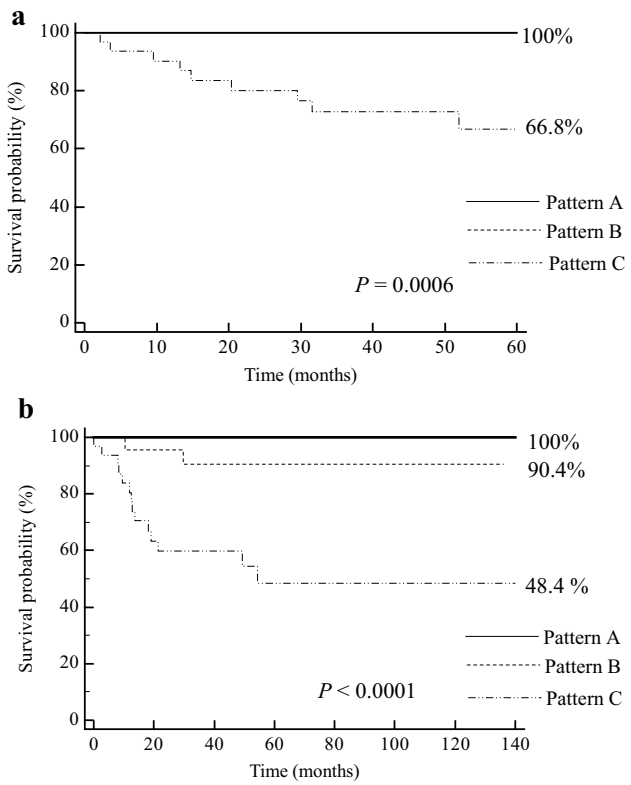

Fig. 2 The 5-year survival (**a**) and DFS (**b**) of patients according to pattern of invasion. **a** The 5-year survival rate of pattern A and B tumors were better than that of pattern C tumors (100% vs. 66.8%, $P = 0.0006$). **b** The DFS of pattern A tumor was better than that of pattern B or C tumors (100% vs. 90.4% or 48.4%, $P < 0.0001$). DFS, disease-free survival

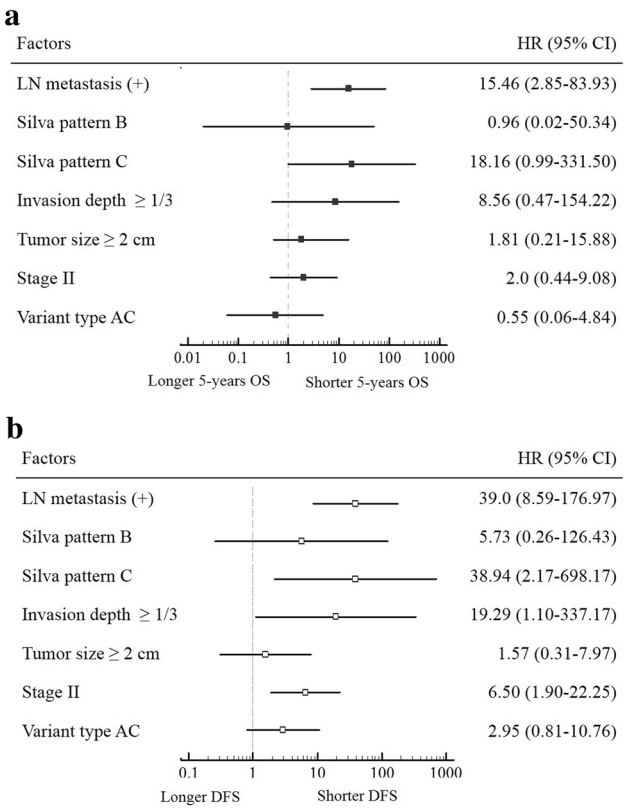

Fig. 3 Forest plot of hazard ratios for 5-year OS and DFS according to baseline prognostic factors and Silva classification with cervical adenocarcinoma ($n=76$). **a** HR for OS. **b** HR for DFS. *OS* overall survival, *HR* hazard ratio, *DFS* disease-free survival

Table 4 Cox's proportional hazard model analysis of prognostic factors for DFS in patients with cervical adenocarcinoma

Variables	Unfavorable/favorable	HR (95% CI)	*P* value
LN metastasis	Positive/negative	11.17 (3.08–40.48)	< 0.001*
Silva system	Pattern C or B/pattern A	4.81 (1.12–20.60)	0.035*
Invasion depth	≥ 1/3/ < 1/3	–	0.953
Stage	≥ II/I	1.97 (0.73–5.36)	0.185

Multivariate Cox's analysis method

DFS disease-free survival, confidence interval, *HR* hazard ratio, *LN* lymph node

*$P < 0.05$; exact significance (two sided)

standard factor for determining the appropriate treatment modality for all cervical cancer subtypes, including AC. Similar to SCC, most patients with AC are treated with radical hysterectomy and LN dissection as standard treatment. These treatment modalities affect fertility and can cause surgery-related complications. Therefore, differential treatment criteria appear to be needed for AC, and objective standards need to be established as a basis for conservative treatment of young patients with AC.

The Silva classification system, which is a new pattern-based classification, is a promising tool to achieve this goal [15]. The Silva classification system categorizes endocervical AC into 3 patterns based on invasion pattern. Compared with clinical stage, these patterns allow clinicians to predict the risk of LN metastasis more accurately [10, 11, 16]. Similar to findings in other studies [10, 11, 15], all cases with pattern A had no LN metastasis and no recurrence, and all these patients survived.

Although the number of usual type cases was higher than that of variants (63 cases vs. 13 cases), there was no difference in the histologic types according to patterns. Other studies [12, 13] reported that variant tumors have poor prognosis, and most of them were classified as pattern C; however, not all of the variant tumors were classified as pattern C in our study.

Among the variants of AC, the gastric type is known to show aggressive prognosis [13]. Gastric-type AC is usually unrelated to HPV infection, and patients tend to present at higher stage. Even those with stage I disease show metastasis to the omentum, liver, brain, and bone [12]. Therefore, gastric-type AC has significantly worse prognosis compared with usual type [12].

Despite the small number of variant cases in the current study, the subtypes were varied considerably. A total of 3 of the 8 cases of gastric types were classified as pattern A; 3, pattern B; and 2, pattern C. All 3 cases of endometrioid types and 1 case of serous type were classified as pattern C, and the 1 case of villoglandular type was classified as pattern B. Because of the small number of patients, it is difficult to determine any statistical significance, but all patients with gastric type did not show poor prognosis. Patients with gastric type tumor with pattern A had no LN metastasis and no recurrence. Therefore, although variant tumors are known to have poor prognosis, they should still be analyzed according to their patterns.

Among those with usual type AC, all patients with pattern A tumors had stage I disease and had no LN metastasis and no LVI. Moreover, patients with pattern A tumors had no recurrence, and all of them survived. These results were similar to those in other studies [17, 10, 15]. Similar to patients with usual type, all patients of variant types with pattern A tumors had stage I disease, no LN metastasis, and no LVI. Although the small number of variant tumors included may affect data analysis, patients with pattern A tumors had good prognosis as evidenced by the absence of recurrence and the survival of all these patients. By contrast, four patients with pattern C tumors (66.7%) recurred, and one patient (16.7%) died due to cancer-related cause.

HPV-16 is the predominant causative infection in SCC, while it is HPV-18 in AC [18]. In our study, HPV-16

infection was predominant among pattern A tumors, while HPV-18 infection was more common in pattern B or C tumors. Recent studies [15, 19, 20] revealed that HPV infection-related endocervical AC could be classified by invasion pattern, and the Silva classification system is a valuable tool to predict the prognosis of invasive endocervical AC.

In our study, patients developed postoperative complications such as bladder dysfunction or lymphedema, and these complications occurred regardless of the severity of cancer and tumor patterns. Patients with pattern A tumors without LN metastasis had complications, and there was no significant difference in the incidence of complications in patients with pattern B or C tumors who had LN metastasis. Therefore, determining the necessity of lymphadenectomy according to patterns may be suitable to minimize postoperative morbidities in patients without LN metastasis.

In this study, LN metastasis was associated with pattern classification in all types of endocervical AC, and the results showed that the Silva classification system can be used to determine the appropriate treatment modalities in all types of cervical AC. Therefore, we suggest conservative management would be the recommended treatment approach when pattern A tumor is seen in the conization. If the cervical conization reveals pattern C tumor, a radical hysterectomy with lymphadenectomy would be appropriate treatment. If the biopsy specimen reveals pattern B, then hysterectomy with sentinel lymph node biopsy would be appropriate management.

The main limitation of the study is its retrospective design and the small number of cases included. Cervical AC is relatively rare, but all available and eligible cases were included. Future studies should include more cases and validate the system in variants of AC. We can consider external review with a multicenter study in further studies on larger numbers of tumors. In conclusion, conservative treatment of cervical AC has become common practice in gynecologic oncology in an effort to preserve fertility and decrease morbidity after treatment [21–23]. The Silva classification system is applicable to all cervical AC and could improve the accuracy of determining appropriate treatment modalities.

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Compliance with ethical standards

Conflict of interest The authors have declared no conflicts of interest.

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