

# Villoglandular adenocarcinoma of cervix: pathologic features, clinical management, and outcome

Peng Guo<sup>1,2,\*</sup>

Pengfei Liu<sup>1,\*</sup>

Junjun Yang<sup>1</sup>

Tong Ren<sup>1</sup>

Yang Xiang<sup>1</sup>

<sup>1</sup>Department of Obstetrics and Gynecology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100730, People's Republic of China;

<sup>2</sup>Department of Obstetrics and Gynecology, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou 510080, People's Republic of China

\*These authors contributed equally to this work

**Background:** The objective of the study was to investigate the management and prognosis of patients with villoglandular adenocarcinoma (VGA) of the uterine cervix.

**Materials and methods:** The clinical presentation, pathology, management, and prognosis of 41 patients with VGA or other types of cervical adenocarcinoma (ADC) were retrospectively reviewed.

**Results:** During the patient follow-up period, the proportion of VGA was 8.1% in the cervical ADC cohort (41/507). The median age of the patients with VGA was 41.0 years. The most common presenting symptom was cervical contactive bleeding. There were 38 patients classified as FIGO stage IA1–IB. The median follow-up period was 38.5 months. There were no patient deaths, and only one patient showed recurrence. One of the patients delivered a healthy baby at 34 weeks of gestation prior to treatment with radical hysterectomy. The HPV HC2 test results showed that most patients were positive for HPV infection. HPV 16, 18, and 56 were positive in the 8 patients with HPV type test results. There were significant differences in the grade, depth of stromal invasion, lymph node metastasis, and recurrence between the VGA cases of FIGO stage I and the other types of cervical ADC of FIGO stage I ( $p < 0.05$ ).

**Conclusion:** This study confirmed that VGA is a type of well-differentiated cervical cancer characterized by shallow stromal invasion, less lymph node metastasis. VGA is associated with less recurrence than other types of cervical ADC.

**Keywords:** villoglandular adenocarcinoma, uterine cervix, management, prognosis

## Introduction

The incidence of cervical adenocarcinoma (ADC) has increased over the past several decades in young women, and there has been a marked decrease in cervical squamous cell carcinoma (SCC).<sup>1,2</sup> The proportion of ADC steadily increased from 5% to more than 20%.<sup>3</sup> ADC is more difficult to detect and has a worse outcome than SCC. Additionally, ADC has a higher incidence of lymph node metastasis, distant metastases, recurrences, and worse survival outcome.<sup>3–5</sup>

Villoglandular adenocarcinoma (VGA) of the cervix was first reported by Young and Scully in 1989.<sup>6</sup> VGA is a rare well-differentiated subtype of ADC that usually occurs in young women and is associated with a better prognosis than ADC.<sup>7,8</sup> Histologically, VGA is a superficially infiltrative tumor with an exophytic growth with long and slender papillary form, limited mitosis, minimal cytologic atypia, and minimal vascular space invasion.<sup>9,10</sup> VGA is characterized as superficially infiltrative and shows infrequent lymph node invasion and lymphovascular space invasion.<sup>11,12</sup> Therefore,

Correspondence: Yang Xiang  
Department of Obstetrics and Gynecology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, No. 1 Shuaifuyuan Wangfujing Dongcheng District, Beijing 100730, People's Republic of China  
Email xiangy@pumch.cn

conservative surgery such as cone biopsy is conducted.<sup>13,14</sup> However, the present recognition and evaluation of this rare tumor type is limited. In this study, we reviewed the clinical and pathological features of 41 patients with VGA and investigated the risk factors for clinical treatment and prognosis.

## Materials and methods

The data of patients with ADC from January 1995 to January 2017 (Peking Union Medical College Hospital [PUMCH], People's Republic of China) were retrospectively reviewed, and written informed consent was obtained from each patient. The procedures were approved by the Ethics Committee of Human Experimentation of PUMCH and are in accordance with the Helsinki Declaration of 1964.

In this study, 41 patients with VGA were identified in the cohort of 507 ADC patients. The standards of pathological VGA diagnosis were the following: 1) a diagnosis made based on complete excision of the primary tumor, rather than on biopsy; 2) the tumor presented as a villoglandular structure or papillary structure with vascular axis, and the invasion is limited to the tumor edge without deep infiltration; and 3) the cellular morphology is relatively mild, nuclei show mild or moderate atypia, and karyokinesis is infrequent. In PUMCH, every pathological diagnosis was made by two pathologists and reviewed by a senior pathologist. Every intractable case would be discussed in department to make sure that the histopathological diagnoses were reliable.

The  $\chi^2$  test was used for comparisons of qualitative data and for the clinicopathological parameters between VGA and other types of ADC. Fisher's exact test was used when the 2 cells (50%) had an expected count less than 5. A *t*-test was used for the quantitative data. Statistical significance was assumed as  $p < 0.05$ . The statistical analyses were performed using the SPSS 13.0 statistical software.

## Results

There were 41 patients diagnosed with VGA (8.1%) during the study period. The median patient age was 41.0 years (range, 27–66 years). The most common presenting symptom was cervical contactive bleeding (28/41). The FIGO stage was IA in 4 patients, IB in 34 patients, IIA in 1 patient, and IIB in 2 patients. There were 32 patients who received imaging examinations including color Doppler ultrasonography, magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography–computed tomography (PET-CT). The imaging examinations of 28 patients showed cervical placeholder and malignant lesions.

In the cohort of 37 patients who were treated with radical hysterectomy with or without pelvic lymphadenectomy

(6/37), 30 patients received bilateral salpingo-oophorectomy (BSO) and 7 received bilateral salpingectomy for ovary conservation. Two patients who desired to preserve fertility received pelvic lymphadenectomy to confirm that there was no lymph node metastasis before receiving further radical vaginal trachelectomy. There were 15 patients who received adjuvant treatments. The detailed treatment descriptions and decisions for treatment are shown in Table 1.

The median follow-up period was 38.5 months (range 19–121 months), and there were no patient deaths during this time. One patient showed recurrent disease. The presenting symptom of the recurrent patient was cervical contactive bleeding, and the cytological test was negative. Additionally, the CA125 level was elevated (69.1 U/mL). The patient was FIGO stage IB1 and underwent nerve-sparing laparoscopic radical hysterectomy, BSO, and pelvic lymphadenectomy. The pathology showed well-differentiated VGA, and the infiltration depth was 5 mm. There were no adjuvant treatments conducted. The tumor recurred in the pelvic 8 months after initial surgery. The PET-CT indicated there was a highly metabolic lesion on the left side of the pelvic floor, and the serum CA125 level was increased to 71.2 U/mL. Exploratory laparotomy was conducted to remove the pelvic mass. The pathology results indicated metastatic ADC. The immunohistochemistry indicated AE1/AE3 (+), CEA (+), p16 (+), and p53 (+). The patient received 6 courses of postoperative chemotherapy. However, at 20 months after the initial surgery, an ultrasound test showed a mass with low density in the vaginal stump. The biopsy results showed well-differentiated VGA. The patient received concurrent chemoradiation therapy.

One patient was diagnosed with VGA at 13 weeks of gestation with FIGO stage IB1. MRI indicated no signs of lymph node metastasis. The patient received conization and cervical cerclage at 16 weeks of gestation. The pathology showed moderately differentiated VGA and there was a negative margin. The patient received 4 courses of chemotherapy with regimens of paclitaxel (240 mg) plus carboplatin (400 mg) at 20 weeks of gestation. At 34 weeks of gestation, the patient underwent cesarean section, radical abdominal hysterectomy, bilateral salpingectomy, and pelvic lymph node dissection. The postoperative pathology was negative. There was no recurrence during the follow-up period of 37 months, and the baby was healthy.

There were 28 patients who received cytological testing within 3 months prior to surgery. There was 1 patient with atypical squamous cells of undetermined significance, and 3 patients showed cervical ADC. Additionally, there were 5 patients with high-grade squamous intraepithelial lesion

Table 1 The clinical characteristics, treatment, and follow-up of patients with VGA

No	Age (years)	Chief complaint	FIGO stage	Treatment	Adjuvant treatment	Follow-up (months)	Recurrence	Outcome
1	36	Diagnosed during regular clinical examination	IA1	Conization; LRH + BS + ovarian suspension	—	11	—	NED
2	47	Diagnosed during regular clinical examination	IA1	Conization; LRH + BSO	—	23	—	NED
3	56	Cervical contactive bleeding	IB1	RAH + BSO + PLND	—	47	—	NED
4	52	Abnormal vaginal bleeding	IIB	RAH + BSO + high ligation of ovarian vein	NAC + RT + PC	88	—	NED
5	58	Postmenopausal bleeding	IA1	LRH + BSO + PLND	—	31	—	NED
6	33	Cervical contactive bleeding	IB1	LRH + BSO + PLND	Po-CCRT	18	—	NED
7	35	Diagnosed during regular clinical examination	IB1	PLND + RVT	—	19	—	NED
8	46	Abnormal vaginal bleeding	IB1	RAH + BSO + PLND	—	LOST	—	Lost
9	42	Abnormal vaginal discharge	IB2	RAH + BSO + PLND	NAC + RT + PC	32	—	NED
10	50	Diagnosed during regular clinical examination	IB1	RAH + BSO + PLND	—	32	—	NED
11	35	Cervical contactive bleeding	IB1	LRH + BS + PLND	—	25	—	NED
12	41	Cervical contactive bleeding	IB1	NSLRH + BSO + PLND	—	37	+	AWD
13	35	Cervical contactive bleeding	IB1	LRH + BS + PLND	—	26	—	NED
14	46	Cervical contactive bleeding	IB1	RAH + BSO + PLND	—	29	—	NED
15	66	Postmenopausal bleeding	IB1	RAH + BSO + PLND	—	104	—	NED
16	43	Diagnosed during regular clinical examination	IB1	Conization; RAH + BSO + PLND	—	37	—	NED
17	51	Cervical contactive bleeding	IB1	NSLRH + BSO + PLND	—	18	—	NED
18	47	Diagnosed during regular clinical examination	IB1	Conization; RAH + BSO	Pre-CCRT	37	—	NED
19	34	Cervical contactive bleeding	IB1	RAH + BSO + PLND	PC	35	—	NED
20	32	Cervical contactive bleeding	IB2	NSLRH + BSO + PLND	NAC+Po-CCRT+PC	32	—	NED
21	32	Abnormal vaginal discharge	IB1	LRH + BSO + PLND	—	12	—	NED
22	36	Abnormal vaginal discharge	IB1	Conization + UCC; CS + RAH + BS + PLND	NAC	20	—	NED
23	32	Cervical contactive bleeding	IB1	LRH + BS + PLND	—	12	—	NED
24	55	Cervical contactive bleeding	IB1	NSLRH + BSO + PLND + PALND	Po-CCRT	6	—	NED
25	38	Cervical contactive bleeding	IB1	NSLRH + BSO + PLND + PALND	Po-CCRT	23	—	NED
26	27	Abnormal vaginal discharge	IB1	PLND + RVT	PC	4	—	NED
27	44	Cervical contactive bleeding	IB1	LRH + BSO + PLND	—	12	—	NED
28	40	Abnormal vaginal discharge	IB1	LRH + BS + PLND	—	14	—	NED
29	49	Abnormal vaginal discharge	IIA1	RAH + BSO + high ligation of ovarian vein + PLND	Po-CCRT	20	—	NED
30	41	Cervical contactive bleeding	IB1	LRH + BSO + PLND	—	6	—	NED
31	40	Cervical contactive bleeding	IIB	LRH + BSO	NAC + Pre-CCRT	2	—	NED
32	41	Diagnosed during regular clinical examination	IB1	RAH + BSO + PLND	—	35	—	NED
33	30	Cervical contactive bleeding	IB1	Conization; NSARH + BS + PLND + PALND + ovarian suspension	Po-CCRT	49	—	NED
34	34	Cervical contactive bleeding	IA2	Conization; RAH + BSO + PLND	NAC+Po-CCRT	49	—	NED
35	45	Cervical contactive bleeding	IB1	RAH + BSO + PLND	—	16	—	NED
36	45	Cervical contactive bleeding	IB1	RAH + BSO + PLND	—	10	—	NED
37	60	Cervical contactive bleeding	IB1	LRH + BSO + PLND + PALND	—	11	—	NED
38	64	Cervical contactive bleeding	IB2	LRH + BSO	Pre-CCRT	11	—	NED
39	28	Cervical contactive bleeding	IB1	Conization	—	5	—	NED
40	32	Diagnosed during regular clinical examination	IB1	Conization	—	10	—	NED
41	46	Cervical contactive bleeding	IB1	RAH + BSO + PLND	—	59	—	NED

**Abbreviations:** VGA, villoglandular adenocarcinoma; AWD, alive with disease; BS, bilateral salpingectomy; BSO, bilateral salpingo-oophorectomy; Po-CCRT, postoperative concurrent chemoradiation therapy; Pre-CCRT, preoperative concurrent chemoradiation therapy; CS, cesarean section; LRH, laparoscopic radical hysterectomy; NAC, neoadjuvant chemotherapy; NED, no evidence of disease; NSARH, nerve-sparing abdominal radical hysterectomy; NSLRH, nerve-sparing laparoscopic radical hysterectomy; PC, postoperative chemotherapy; PALND, paraortic lymph node dissection; PLND, pelvic lymph node dissection; RAH, radical abdominal hysterectomy; RT, radiation therapy; RVT, radical vaginal trachelectomy; UCC, uterine cervical cerclage.

and 6 patients with atypical glandular cell. The remaining 13 patients had negative results. We found that 9 of 12 patients with HPV HC2 test results were positive for HPV infection. HPV 16, 18, and 56 were positive in the 8 patients with HPV type test results. The cytology and HPV testing results are shown in Table 2. The immunohistochemistry results indicated positive p16 and Ki-67 expression but negative PR and ER expression in most patients.

There were 41 patients with VGA and 326 patients with ADC who received radical hysterectomy in the cohort of 507 ADC patients. The clinicopathological parameters of the 41 patients with VGA and 326 patients with ADC were compared. The data in Table 3 show that there were significant differences in the grade, depth of stromal invasion, lymph node metastasis, and recurrence between the VGA cases of FIGO stage I and the other types of cervical ADC of FIGO stage I ( $p < 0.05$ ). VGA is a type of well-differentiated cervical cancer characterized by shallow stromal invasion, less

lymph node metastasis, and less recurrence than other types of cervical ADC.

## Discussion

VGA of the cervix has a younger patient prevalence and better prognosis than other variants of cervical ADC. As shown in Table 4, we reviewed the VGA literature for the cervix and found there were a total of 203 patients with VGA reported. The patients' ages ranged from 33 to 52 years, and the majority of patients were FIGO stage I. There were 13 patients presenting with LVSI, 7 patients with LN metastasis, 12 patients with recurrence, and 8 patients who died of this disease.<sup>6,7,12,13,15–24</sup>

In this study, 1 patient had disease recurrence and was alive with disease. There were no obvious risk factors in this patient except for the consistent elevated serum CA125 level during the preoperative and follow-up period.

The favorable prognosis for VGA patients permits a more conservative surgical approach in selected patients including

**Table 2** Cytological test and HPV test with VGA of the cervix

Patient	Cytological test	HPV type test	HC2 HPV DNA	Clinical symptoms	Outcome
1	AGC	HPV 18+, HPV 56+	0.7	Diagnosed during regular clinical examination	NED
3	N			Cervical contactive bleeding	NED
5	ADC			Postmenopausal bleeding	NED
6	N			Cervical contactive bleeding	NED
7	HSIL			Diagnosed during regular clinical examination	NED
8	AGC			Abnormal vaginal bleeding	NED
10	N			Diagnosed during regular clinical examination	NED
11	ASCUS			Cervical contactive bleeding	NED
12	N			Cervical contactive bleeding	AWD
13	N			Cervical contactive bleeding	NED
15	AGC	HPV 18+	287.1	Postmenopausal bleeding	NED
16	AGC			Diagnosed during regular clinical examination	NED
18	HSIL			Diagnosed during regular clinical examination	NED
19	HSIL			Cervical contactive bleeding	NED
21	ADC			Abnormal vaginal discharge	NED
22	N			Abnormal vaginal discharge	NED
23	N			Cervical contactive bleeding	NED
26	AGC			Abnormal vaginal discharge	NED
27	HSIL			Cervical contactive bleeding	NED
28	N			Abnormal vaginal discharge	NED
29	N	HPV 16+	5.64	Abnormal vaginal discharge	NED
30				Cervical contactive bleeding	NED
32	HSIL			Diagnosed during regular clinical examination	NED
33	N			Cervical contactive bleeding	NED
35	AGC			Cervical contactive bleeding	NED
36				Cervical contactive bleeding	NED
37	ADC			Cervical contactive bleeding	NED
38	N			Cervical contactive bleeding	NED
39	N			Cervical contactive bleeding	NED
40				Diagnosed during regular clinical examination	NED
41	N	HPV 16+, HPV 18+	6.87	Cervical contactive bleeding	NED

**Abbreviations:** VGA, villoglandular adenocarcinoma; ADC, adenocarcinoma; AGC, atypical glandular cell; AWD, alive with disease; ASCUS, atypical squamous cells of undetermined significance; HSIL, high-grade squamous intraepithelial lesion; N, negative; NED, no evidence of disease.

**Table 3** Comparison of VGA with other ADCs of FIGO I on clinicopathological parameters

Characteristics	VGA (n=38)	ADC (n=226)	p
Age (median, range), years	41 (26–66)	42 (20–72)	0.42
FIGO stage			0.44
IA	4	31	
IB1	31	151	
IB2	3	44	
Grade			0.000
Well	33	109	
Moderate	5	70	
Poor	0	45	
Tumor size			0.158
≤4 cm	35	189	
>4 cm	3	35	
Depth of stromal invasion			0.000
≤1/2	36	145	
>1/2	2	81	
LVS1			0.060
Negative	37	194	
Positive	1	32	
Vaginal resection margin			0.433
Negative	35	215	
Positive	3	11	
Parametrial invasion			0.324
Negative	36	220	
Positive	2	6	
LN metastasis			0.001
Negative	37	194	
Positive	1	32	
Ovary preservation			0.239
No	29	191	
Yes	9	35	
Recurrence			0.038
No	37	193	
Yes	1	33	

**Abbreviations:** VGA, villoglandular adenocarcinoma; ADCs, adenocarcinomas; LN, lymph node; LVS1, lymph vascular space invasion.

young women with localized disease and those who wish to maintain fertility.<sup>25</sup> There were 16 patients reported in the literature who underwent fertility-preserving surgery such as cervical conization and radical trachelectomy.<sup>6,7,12,13,15–24</sup> In this study, 2 patients who desired to preserve fertility received pelvic lymphadenectomy to rule out lymph node metastasis. Radical vaginal trachelectomy was then conducted, and there was no recurrence during the follow-up period. Currently, surgical resection range and treatment options for ADC patients are considered to be uses in VGA patients. But, our clinical data and previous studies indicate that VGA is less invasive than ADCs. As VGA has more positive prognosis, the surgery extent could be narrowed for stage I VGA patients. This is what should be further studied in future.

The treatment for cervical cancer associated with pregnancy is complicated, and there is currently no specific

treatment scheme. Previous studies reported less radical fertility-sparing surgery for patients in FIGO stage IA2–IB1. The treatment included laparoscopic pelvic lymphadenectomy and cervical conization, which was then followed by neoadjuvant chemotherapy.<sup>26–28</sup> In the VGA patients of this study, we compared the recurrence between with and without adjuvant treatment; the patients with adjuvant treatment showed less recurrence rate ( $p < 0.001$ ). Several studies compared primary surgery or concurrent chemoradiation therapy in pregnant women with FIGO stage IB cervical cancer with delivery delay. Neoadjuvant chemotherapy of paclitaxel plus cisplatin followed by radical surgery and postoperative chemotherapy could be considered a feasible alternative to preserve fertility.<sup>29,30</sup> One patient in this study maintained pregnancy until 34 weeks of gestation before radical hysterectomy and delivered a healthy baby. MRI for this patient indicated no lymph node metastasis, and cervical conization confirmed the pathological type, grade, depth of stromal invasion, and lymph vascular space invasion. The patient was treated using neoadjuvant chemotherapy with paclitaxel plus cisplatin during the second trimester.

VGA is a rare tumor type that accounts for approximately 5% in cervical ADCs.<sup>15</sup> This tumor is histologically characterized by tall and thin papillae with minimal cellular atypia. The characteristic histological features of various epithelia have been reported, and it is known that the papillae are lined by 1 or more layers of cells with endocervical, endometrioid, or intestinal differentiation.<sup>31</sup> In this study, preoperative cytological tests were negative in 11 patients (28.9%). The results from the study by Choi et al indicate the abnormal architectural patterns such as three-dimensional papillary structures, nuclear overlapping, and nuclear hyperchromasia are important clues to suspect the possibility of a VGA. However, liquid-based cytology shows better preserved nuclear details such as prominent nucleoli and irregular nuclear membranes and can facilitate the diagnosis of VGA.<sup>23</sup>

The etiology of VGA remains unclear. Several studies have suggested that HPV infection was involved in the pathogenesis of VGA. The first report of positive HPV 18 in VGA was published in 2000.<sup>32</sup> HPV 18 and 16 were significantly associated with VGA in the study of Jones et al.<sup>20</sup> It has been shown that HPV infection might be more prevalent in VGA than in other types of ADC.<sup>33</sup> Our results demonstrated that HPV testing might be important in the screening and diagnosis of VGA.

This study is a retrospective review and has several limitations. First, the HPV testing was not prevalent in all patients. Therefore, the pathologic role of HPV in VGA should be



**Table 4** Literature review of VGA

Reference	Cases	Age	Stage	SI	LVSI	LN metastasis	Fertility preserving	Recurrence	DOD
Young and Scully <sup>6</sup>	13	33	I13	≤1/2, 6	0	0	1	0	0
Kaku et al <sup>15</sup>	7	45	II0	>1/2, 2	2	2	0	1	1
			II2	>1/2, 3					
Utsugi et al <sup>16</sup>	13	45	II0	≤1/2, 11	4	1	ND	0	0
			II3	>1/2, 1					
Khunamornpong et al <sup>17</sup>	15	39	II4	≤1/2, 12	3	2	0	0	0
			III1	>1/2, 3					
Jones et al <sup>17</sup>	24	37	ND	≤1/2, 23	0	0	5	0	0
				>1/2, 1					
Costa et al <sup>12</sup>	4	52	ND	ND	ND	ND	ND	0	0
Lataifeh et al <sup>18</sup>	28	38	I19	ND	ND	ND	2	3	5
			II7						
			III2						
Kim et al <sup>19</sup>	15	40	ND	≤1/2, 10	2	1	4	3	0
				>1/2, 5					
Jones et al <sup>20</sup>	12	38	ND	≤1/2, 11	ND	ND	0	2	1
				>1/2, 1					
Hopson et al <sup>13</sup>	3	35	I3	≤1/2, 2	0	0	0	0	0
				>1/2, 1					
Reed et al <sup>21</sup>	5	34.2	ND	ND	0	0	0	0	0
Korach et al <sup>22</sup>	9	38.8	I8	ND	ND	ND	2	1	1
			III1						
Choi et al <sup>23</sup>	3	47	ND	ND	1	1	0	0	0
Hagiwara et al <sup>24</sup>	8	36	I7	≤1/2, 7	0	0	0	0	0
			III1	>1/2, 0					
Stanley-Christian et al <sup>8</sup>	3	33	I3	≤1/2, 3	0	0	1	1	0
			II0	>1/2, 1					
Present study	41	42	I38	≤1/2, 37	1	0	5	1	0
			II3	>1/2, 4					

**Abbreviations:** VGA, villoglandular adenocarcinoma; DOD, died of disease; LN, lymph node; LVSI, lymph vascular space invasion; ND, not described; SI, stromal invasion.

further investigated. Second, the sample population is limited for this rare tumor, and it is difficult to distinguish VGA from other types of ADC. Thus, it is critical to perform a meta-analysis or more multicenter prospective studies to investigate the most accurate diagnosis and proper treatment for VGA.

## Acknowledgment

This research was supported by National Natural Science Foundation of China (81472446) and China Postdoctoral Science Foundation (2012M510354).

## Disclosure

The authors report no conflicts of interest in this work.

## References

- Mathew A, George PS. Trends in incidence and mortality rates of squamous cell carcinoma and adenocarcinoma of cervix-worldwide. *Asian Pac J Cancer Prev*. 2009;10(4):645–650.
- Seoud M, Tjalma WA, Ronsse V. Cervical adenocarcinoma: moving towards better prevention. *Vaccine*. 2011;29(49):9148–9158.
- Galic V, Herzog TJ, Lewin SN, et al. Prognostic significance of adenocarcinoma histology in women with cervical cancer. *Gynecol Oncol*. 2012;125(2):287–291.
- Lee YY, Choi CH, Kim TJ, et al. A comparison of pure adenocarcinoma and squamous cell carcinoma of the cervix after radical hysterectomy in stage IB-IIA. *Gynecol Oncol*. 2011;120(3):439–443.
- Park JY, Kim DY, Kim JH, Kim YM, Kim YT, Nam JH. Outcomes after radical hysterectomy in patients with early-stage adenocarcinoma of uterine cervix. *Br J Cancer*. 2010;102(12):1692–1698.
- Young RH, Scully RE. Villoglandular papillary adenocarcinoma of the uterine cervix. A clinicopathologic analysis of 13 cases. *Cancer*. 1989;63(9):1773–1779.
- Jones MW, Silverberg SG, Kurman RJ. Well-differentiated villoglandular adenocarcinoma of the uterine cervix: a clinicopathological study of 24 cases. *Int J Gynecol Pathol*. 1993;12(1):1–7.
- Stanley-Christian H, Heim BK, Hines JF, Hall KL, Willett GD, Barnes WA. Villoglandular adenocarcinoma of the cervix: a report of three cases and review of literature. *Gynecol Oncol*. 1997;66(2):327–330.
- Khunamornpong S, Siriaunkgul S, Suprasert P. Well-differentiated villoglandular adenocarcinoma of the uterine cervix: cytomorphologic observation of five cases. *Diagn Cytopathol*. 2002;26(1):10–14.
- Novotny DB, Ferlisi P. Villoglandular adenocarcinoma of the cervix: cytologic presentation. *Diagn Cytopathol*. 1997;17(5):383–387.
- Macdonald RD, Kirwan J, Hayat K, Herrington CS, Shawki H. Villoglandular adenocarcinoma of the cervix: clarity is needed on the histological definition for this difficult diagnosis. *Gynecol Oncol*. 2006;100(1):192–194.

12. Costa MJ, McIlroy KR, Trelford J. Cervical carcinoma with glandular differentiation: histological evaluation predicts disease recurrence in clinical stage I or II patients. *Hum Pathol.* 1995;26(8):829–837.
13. Hopson L, Jones MA, Boyce CR, Tarraza HM Jr. Papillary villoglandular carcinoma of the cervix. *Gynecol Oncol.* 1990;39(2):221–224.
14. Ballo MS, Silverberg SG, Sidaway MK. Cytologic features of well-differentiated villoglandular adenocarcinoma of the cervix. *Acta Cytol.* 1996;40(3):536–540.
15. Kaku T, Kamura T, Shigematsu T, et al. Adenocarcinoma of the uterine cervix with predominantly villoglandular papillary growth pattern. *Gynecol Oncol.* 1997;64(1):147–152.
16. Utsugi K, Shimizu Y, Akiyama F, Umezawa S, Hasumi K. Clinicopathologic features of villoglandular papillary adenocarcinoma of the uterine cervix. *Gynecol Oncol.* 2004;92(1):64–70.
17. Khunamornpong S, Maleemonkol S, Siriaunkgul S, Pantusart A. Well-differentiated villoglandular adenocarcinoma of the uterine cervix: a report of 15 cases including two with lymph node metastasis. *J Med Assoc Thai.* 2001;84(6):882–888.
18. Lataifeh IM, Al-Hussaini M, Uzan C, Jaradat I, Duvillard P, Morice P. Villoglandular papillary adenocarcinoma of the cervix: a series of 28 cases including two with lymph node metastasis. *Int J Gynecol Cancer.* 2013;23(5):900–905.
19. Kim J, Sung JH, Lee E, et al. Prognostic factors influencing decisions about surgical treatment of villoglandular adenocarcinoma of the uterine cervix. *Int J Gynecol Cancer.* 2014;24(7):1299–1305.
20. Jones MW, Kounelis S, Papadaki H, et al. Well-differentiated villoglandular adenocarcinoma of the uterine cervix: oncogene/tumor suppressor gene alterations and human papillomavirus genotyping. *Int J Gynecol Pathol.* 2000;19(2):110–107.
21. Reed W, Abeler VM, Tropé CG. Villous glandular adenocarcinoma of the uterine cervix. A subtype with favourable prognosis? *Tidsskr Nor Laegeforen.* 1993;113(20):2569–2571.
22. Korach J, Machtinger R, Perri T, et al. Villoglandular papillary adenocarcinoma of the uterine cervix: a diagnostic challenge. *Acta Obstet Gynecol Scand.* 2009;88(3):355–358.
23. Choi Y, Kim H, Choi H, et al. Liquid-based cytology of villoglandular adenocarcinoma of the cervix: a report of 3 cases. *Korean J Pathol.* 2012;46(2):215–220.
24. Hagiwara T, Kaku T, Kobayashi H, Wake N, Saito T. Well-differentiated villoglandular adenocarcinoma of the uterine cervix: assessment of cytological features by histological subtypes. *Acta Cytol.* 2013;57(1):61–68.
25. Lakhtakia R, Singh MK, Taneja P, Kapila K, Kumar S. Villoglandular papillary adenocarcinoma of the cervix: case report. *J Surg Oncol.* 2000;74(4):297–299.
26. Maneo A, Chiari S, Bonazzi C, Mangioni C. Neoadjuvant chemotherapy and conservative surgery for stage IB1 cervical cancer. *Gynecol Oncol.* 2008;111(3):438–443.
27. Landoni F, Parma G, Peiretti M, et al. Chemo-conization in early cervical cancer. *Gynecol Oncol.* 2007;107(1 Suppl 1):S125–S126.
28. Kong TW, Lee EJ, Lee Y, Chang SJ, Son JH, Ryu HS. Neoadjuvant and postoperative chemotherapy with paclitaxel plus cisplatin for the treatment of FIGO stage IB cervical cancer in pregnancy. *Obstet Gynecol Sci.* 2014;57(6):539–543.
29. Li J, Wang LJ, Zhang BZ, Peng YP, Lin ZQ. Neoadjuvant chemotherapy with paclitaxel plus platinum for invasive cervical cancer in pregnancy: two case report and literature review. *Arch Gynecol Obstet.* 2011;284(3):779–783.
30. Fruscio R, Villa A, Chiari S, et al. Delivery delay with neoadjuvant chemotherapy for cervical cancer patients during pregnancy: a series of nine cases and literature review. *Gynecol Oncol.* 2012;126(2):192–197.
31. Kurman RJ, Ronnett BM, Sherman ME, Wilkinson EJ. *Atlas of Tumor Pathology: Tumours of the Cervix, Vagina and Vulva.* 4th Series. Washington, DC: American Registry of Pathology; 2010:179–185.
32. Yamazawa K, Matsui H, Seki K, et al. Human papillomavirus-positive well-differentiated villoglandular adenocarcinoma of the uterine cervix: a case report and review of the literature. *Gynecol Oncol.* 2000;77(3):473–477.
33. Duggan MA, McGregor SE, Benoit JL, Inoue M, Nation JG, Stuart GC. The human papillomavirus status of invasive cervical adenocarcinoma: a clinicopathological and outcome analysis. *Hum Pathol.* 1995;26(3):319–325.

## Cancer Management and Research

### Publish your work in this journal

Cancer Management and Research is an international, peer-reviewed open access journal focusing on cancer research and the optimal use of preventative and integrated treatment interventions to achieve improved outcomes, enhanced survival and quality of life for the cancer patient. The manuscript management system is completely online and includes

Submit your manuscript here: <https://www.dovepress.com/cancer-management-and-research-journal>

a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Dovepress