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宫颈癌术后复发的危险因素及 SCC-Ag、HR-HPV 对复发的预测价值分析*

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摘要 目的:分析宫颈癌术后复发的危险因素,探讨鳞状细胞癌抗原(SCC-Ag)、高危型人乳头瘤病毒(HR-HPV)对宫颈癌术后复发的预测价值。**方法:**对2010年1月至2017年12月我院收治的宫颈癌患者300例进行回顾性分析,收集其临床资料,所有患者随访2年,定期检测SCC-Ag表达情况及HR-HPV感染情况,根据患者复发情况分为复发组与未复发组,应用单因素和多因素Logistic回归分析宫颈癌术后复发的危险因素,以病理诊断为金标准,分析SCC-Ag、HR-HPV对宫颈癌术后复发的预测价值。**结果:**随访期间出现12例失访,300例患者中完成随访288例,出现复发40例,未复发248例。单因素分析结果显示宫颈癌术后复发与肿瘤直径、分化程度、肿瘤间质浸润情况、临床分期、淋巴结转移、SCC-Ag阳性表达、HR-HPV持续感染有关($P<0.05$),而与发病年龄、体质指数(BMI)、吸烟史、性行为开始年龄、宫颈癌家族史、病理类型、术后放化疗无关($P>0.05$)。多因素Logistic回归分析显示:中低分化、深肌层浸润、临床分期IIA1-IIA2期、有淋巴结转移、SCC-Ag阳性、HR-HPV持续感染是宫颈癌术后复发的危险因素($P<0.05$)。SCC-Ag联合HR-HPV预测宫颈癌术后复发的灵敏度、特异度、阳性预测值、阴性预测值分别为92.50%、87.50%、54.41%、98.64%。**结论:**中低分化、深肌层浸润、临床分期IIA1-IIA2期、有淋巴结转移、SCC-Ag阳性、HR-HPV持续感染是宫颈癌术后复发的危险因素,SCC-Ag联合HR-HPV预测宫颈癌术后复发具有一定价值,值得临床关注。

关键词:宫颈癌;复发;鳞状细胞癌抗原;高危型人乳头瘤病毒

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The Risk Factors of Postoperative Recurrence of Cervical Cancer and the Predictive Value of SCC Ag and HR-HPV*

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ABSTRACT Objective: To analyze the risk factors of postoperative recurrence of cervical cancer, and to investigate the predictive value of serum squamous cell carcinoma antigen (SCC-Ag) level and high-risk human papillomavirus (HR-HPV) infection for postoperative recurrence of cervical cancer. **Methods:** 300 cases of cervical cancer in our hospital from January 2010 to December 2017 were analyzed retrospectively. Clinical data was collected, and all patients were followed up for 2 years. The expression of SCC-Ag and the infection status of HR-HPV were tested regularly, and patients were divided into the recurrence group and the non-recurrence group according to the recurrence situation. Univariate and multivariate Logistic regression analysis was used to analyze the risk factors of postoperative recurrence of cervical cancer, and taking pathological diagnosis as the gold standard, the predictive value of SCC-Ag and HR-HPV for postoperative recurrence of cervical cancer were analyzed. **Results:** During the follow-up period, 12 patients were lost to follow-up and 288 of the 300 patients were followed up, 40 cases recurred, 248 cases did not recur. Univariate analysis showed that postoperative recurrence of cervical cancer was related to tumor diameter, differentiation degree, tumor stromal infiltration, clinical stage, Lymph node metastasis, SCC-Ag positive expression, HR-HPV persistent infection ($P<0.05$). However, it was not associated with age of onset, Body mass index (BMI), smoking history, sexual behavior start age, family history of cervical cancer, pathological type, postoperative radiotherapy and chemotherapy ($P>0.05$). Multivariate logistic regression analysis showed that low differentiation, deep myometrial invasion, clinical stage IIA1-IIA2, lymph node metastasis, SCC-Ag positive, HR-HPV positive were the risk factors of postoperative recurrence of cervical cancer ($P<0.05$). The sensitivity, specificity, positive predictive value and negative predictive value of SCC-Ag combined with HR-HPV were 92.50%, 87.50%, 54.41%, 98.64% respectively. **Conclusion:** Poor differentiation, deep myometrial invasion, clinical stage IIA1-IIA2, lymph node metastasis, SCC-Ag positive and HR-HPV positive are the risk factors of

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postoperative recurrence of cervical cancer. The SCC-Ag combined with HR-HPV has a certain value in predicting postoperative recurrence of cervical cancer, which is worthy of clinical attention.

Key words: Cervical cancer; Recurrence; Squamous cell carcinoma antigen; High risk human papillomavirus

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前言

宫颈癌是女性生殖系统常见的肿瘤,有报道显示,我国每年新发宫颈癌病例约为 98000 例,因宫颈癌死亡的女性超过 30000 例,严重威胁女性健康与生命^[1]。近年来,随着医学技术的不断发展和细胞学检查的普及,大量的宫颈癌患者得以在早期进行手术治疗,使得宫颈癌的预后不断改善。但宫颈癌患者术后复发仍是困扰临床工作者的难题,也是造成患者死亡的重要原因之一^[2,3]。目前对于宫颈癌患者术后复发的机制仍未完全明确,因此,探讨宫颈癌术后复发的危险因素对于疾病防治具有重要的意义。鳞状细胞癌抗原(Squamous cell carcinoma antigen, SCC-Ag)是一种存在于子宫、宫颈和头颈部鳞状上皮癌细胞浆中的糖蛋白,也是宫颈癌筛查的重要指标,其表达情况与患者预后密切相关^[4]。高危型人乳头瘤病毒(High risk human papillomavirus, HR-HPV)是与宫颈癌密切相关的人乳头瘤病毒(Human papillomavirus, HPV)亚型,包括 6、11、16、18 等型,HR-HPV 感染与宫颈癌发病密切相关^[5,6],因此 SCC-Ag 和 HR-HPV 可能对宫颈癌术后复发的预测具有一定价值。本研究分析宫颈癌术后复发的危险因素及 SCC-Ag、HR-HPV 对复发的预测价值,旨在为宫颈癌术后复发的防治提供依据,现报道如下。

1 资料与方法

1.1 一般资料

对 2010 年 1 月至 2017 年 12 月我院收治的宫颈癌患者 300 例进行回顾性分析,纳入标准:(1)所有患者均为宫颈癌初诊患者,经病理诊断确诊^[7];(2)患者接受宫颈癌根治手术;(3)术前病理资料齐全;(4)术后定期接受 SCC-Ag、HR-HPV 检测。排除标准:(1)合并其他恶性肿瘤患者;(2)HPV 疫苗接种史者;(3)临床分期 IIB 期及以上者;(4)妊娠患者。

1.2 研究方法

1.2.1 临床资料的收集 收集患者临床资料,包括:年龄、体质指数(Body mass index, BMI)、吸烟史、性行为开始年龄、宫颈癌家族史、肿瘤直径、病理类型、分化程度、肿瘤间质浸润情况、临床分期、淋巴结转移情况、术后放化疗情况。

1.2.2 随访 所有患者完成 2 年随访,每 3~4 个月通过门诊随访 1 次,检测肿瘤复发情况、SCC-Ag、HR-HPV 表达情况,若发现复发则随访终止,复发判定标准:手术区域或阴道残端重新出现肿块并病理活检确认,远处复发经正电子发射断层显像及病理活检确认。

1.2.3 SCC-Ag 检测 于门诊复查时采集患者空腹静脉血 2 mL,经 3500 r/min 离心分离血清,离心半径 12 cm,置于 -20℃ 冰箱中保存备用,应用微粒子酶免疫分析法测定血清 SCC-Ag 水平,

试剂盒购自美国雅培公司,当血清 SCC-Ag $\geq 1.5 \mu\text{g/L}$ 为阳性。

1.2.4 HR-HPV 检测 于门诊复查时采集患者阴道残端分泌物,应用专用特制毛刷在阴道残端旋转 3~5 圈,应用 HR-HPV 杂交捕获试剂盒检测表达情况,试剂盒购自美国 Digene 公司,当样本相对对光值/阳性定标阈值 ≥ 1.0 判定为阳性。

1.3 统计学方法

应用 SPSS26.0 软件进行统计学分析,计量资料以(均数 $\pm$ 标准差)的形式表示,行 t 检验,计数资料以百分率表示,行卡方检验,应用单因素分析及多因素 Logistic 回归分析宫颈癌术后复发危险因素,四格表法计算 SCC-Ag、HR-HPV 预测宫颈癌术后复发的灵敏度、特异度、阳性预测值、阴性预测值,灵敏度 = 真阳性人数 / (真阳性人数 + 假阴性人数) $\times 100\%$, 特异度 = 真阴性人数 / (真阴性人数 + 假阳性人数) $\times 100\%$, 阳性预测值 = 真阳性人数 / (真阳性人数 + 假阳性人数) $\times 100\%$, 阴性预测值 = 真阴性人数 / (真阴性人数 + 假阴性人数) $\times 100\%$ 。 $P < 0.05$ 表明数据具有统计学意义。

2 结果

2.1 宫颈癌患者术后复发的单因素分析

300 例患者中完成随访 288 例,失访 12 例,随访时间 24 个月,出现复发 40 例,记为复发组,未复发 248 例,记为未复发组。结果显示,复发组肿瘤直径 $\geq 4 \text{ cm}$ 、中低分化、深肌层浸润、IIA1-IIA2 期、淋巴结转移、SCC-Ag 阳性、HR-HPV 阳性比例显著高于未复发组($P < 0.05$),两组发病年龄、BMI、吸烟史、性行为开始年龄、宫颈癌家族史、病理类型、术后放化疗比较差异无统计学意义($P > 0.05$),见表 1。

2.2 宫颈癌术后复发的多因素 Logistic 回归分析

以宫颈癌术后是否复发为因变量(赋值:是 = 1,否 = 0),以表 1 中差异有统计学意义的指标作为自变量并进行赋值:肿瘤直径($\geq 4 \text{ cm} = 1, < 4 \text{ cm} = 0$)、分化程度(中低分化 = 1,高分化 = 0)、肿瘤间质浸润(深肌层 = 1,浅肌层 = 0)、临床分期(IIA1-IIA2 期 = 1, IA2-IB2 期 = 0)、淋巴结转移(有 = 1,无 = 0)、SCC-Ag 表达情况(阳性 = 1,阴性 = 0)、HR-HPV 表达情况(阳性 = 1,阴性 = 0),纳入多因素 Logistic 回归分析模型。结果显示,中低分化、深肌层浸润、临床分期 IIA1-IIA2 期、有淋巴结转移、SCC-Ag 阳性、HR-HPV 阳性是宫颈癌术后复发的危险因素($P < 0.05$),见表 2。

2.3 SCC-Ag、HR-HPV 对宫颈癌术后复发的预测价值

以病理诊断为金标准,SCC-Ag 预测宫颈癌术后复发的灵敏度、特异度、阳性预测值、阴性预测值分别为 72.50%(29/40)、76.61%(190/248)、33.33%(29/87)、94.53%(190/201),HR-HPV 预测宫颈癌术后复发的灵敏度、特异度、阳性预测值、阴性预测值分别为 85.00%(34/40)、78.63%(195/248)、39.08%(34/87)、

表 1 宫颈癌患者术后复发的单因素分析[n(%)]

Table 1 Univariate analysis of postoperative recurrence of cervical cancer [n (%)]

Factors	Recurrent group(n=40)	Non-recurrent group(n=248)	χ^2	P
Age of onset(years)				
≥ 50	31(77.50)	198(79.84)	0.116	0.734
<50	9(22.50)	50(20.16)		
BMI(kg/m ²)				
<24	26(65.00)	136(54.84)	1.445	0.229
≥ 24	14(35.00)	112(45.16)		
Smoking history				
Yes	8(20.00)	56(22.58)	0.133	0.716
No	32(80.00)	192(77.42)		
Sexual behavior start age(years)				
<18	9(16.13)	43(14.60)	0.620	0.431
≥ 18	31(93.87)	205(85.40)		
Family history of cervical cancer				
Yes	28(70.00)	188(75.81)	0.619	0.431
No	12(30.00)	60(24.19)		
Tumor diameter(cm)				
<4	18(45.00)	155(62.50)	4.398	0.036
≥ 4	22(55.00)	93(37.50)		
Pathological type				
Squamous cell carcinoma	33(82.50)	212(85.48)	0.241	0.623
Non squamous cell carcinoma	7(17.50)	36(14.52)		
Degree of differentiation				
Highly differentiated	11(27.50)	169(68.15)	24.279	0.000
Moderately or lowly differentiated	29(72.50)	79(31.85)		
Infiltration of tumor stroma				
Superficial muscularis	15(37.10)	170(68.58)	14.514	0.000
Deep muscularis	25(62.90)	78(31.42)		
Clinical stages				
Phase IA2 to IB2	9(22.50)	151(60.89)	20.556	0.000
Phase IIA1 to IIA2	31(77.50)	97(39.11)		
Lymph node metastasis				
Yes	34(85.00)	81(32.66)	39.337	0.000
No	6(15.00)	167(67.34)		
Postoperative radiotherapy and chemotherapy				
Yes	21(52.50)	134(54.03)	0.037	0.857
No	19(47.50)	114(45.97)		
Detection result of SCC-Ag				
Positive	29(72.50)	58(15.32)	44.214	0.000
Negative	11(27.50)	190(84.68)		
Detection result of HR-HPV				
Positive	34(85.00)	53(21.37)	66.145	0.000
Negative	6(15.00)	195(78.63)		

97.01%(195/201), SCC-Ag 联合 HR-HPV 预测宫颈癌术后复发的灵敏度、特异度、阳性预测值、阴性预测值分别为 92.50% (37/40)、87.50%(217/248)、54.41%(37/68)、98.64%(217/220), 见表 3。

表 2 宫颈癌术后复发危险因素的多因素 Logistic 回归分析

Table 2 Multivariate logistic regression analysis of risk factors for postoperative recurrence of cervical cancer

Factors	β	SE	Wald χ^2	P	OR (95%CI)
Tumor diameter ≥ 4 cm	0.263	0.046	3.587	0.087	1.031(0.726~1.208)
Moderately or lowly differentiation	0.351	0.171	7.851	0.017	2.316(1.877~2.879)
Deep muscularis infiltration	0.343	0.034	7.163	0.022	2.137(1.742~2.663)
clinical stages Phase IIA1 to IIA2	0.459	0.197	7.174	0.026	2.174(1.729~2.382)
Lymph node metastasis	0.734	0.206	9.325	0.002	2.192(1.793~2.446)
SCC-Ag positive	0.607	0.147	11.441	0.001	3.026(2.651~3.118)
HR-HPV positive	0.582	0.401	12.302	0.000	3.361(2.713~4.034)

表 3 SCC-Ag、HR-HPV 检测结果及复发情况的比较

Table 3 Comparison of SCC-Ag and HR-HPV detection results and recurrence

Results	SCC-Ag detection		HR-HPV detection		SCC-Ag+HR-HPV detection	
	Positive	Negative	Positive	Negative	Positive	Negative
Recurrence	29	11	34	6	37	3
Non-recurrence	58	190	53	195	31	217

3 讨论

目前,临床上对于宫颈癌仍主张早期诊断手术治疗,但术后复发是宫颈癌手术治疗面临的重要难题。有报道显示宫颈癌术后 2 年复发率约为 15%~40%,不同患者术后复发率存在一定差异^[8,9]。宫颈癌复发不仅给治疗带来了困难,还严重影响患者预后^[10-12]。如能通过严密的随访,并针对复发的危险因素给予干预或早期识别,早期发现复发肿瘤并给予有效干预措施,将有助于延长患者的生存期,改善患者预后。

臧建新报道表明肿瘤深肌层浸润、肿瘤低分化程度及区域淋巴结转移是宫颈癌复发的危险因素^[13]。孙桂霞等报道,体质指数较低、肿瘤大小超过 4 cm、临床分期 III 期、淋巴结转移是老年宫颈癌患者术后复发的危险因素^[14]。本研究除将患者临床病理特征纳入分析外还综合分析了患者的性生活情况、家族史等,通过分析发现,复发组肿瘤直径 ≥ 4 cm、中低分化、深肌层浸润、IIA1-IIA2 期、淋巴结转移、SCC-Ag 阳性表达、HR-HPV 阳性表达比例显著高于未复发组,进一步多因素 Logistic 分析发现,中低分化、深肌层浸润、临床分期 IIA1-IIA2 期、有淋巴结转移、SCC-Ag 阳性、HR-HPV 阳性是宫颈癌术后复发的危险因素。肿瘤的分化程度是指肿瘤组织在形态和功能上与正常组织的相似之处,与正常组织相似程度越小,表明肿瘤分化程度越低^[15,16]。研究表明,肿瘤分化程度是决定肿瘤恶性程度的重要指标^[17,18]。中低分化肿瘤的组织结构和细胞形态与正常组织差别更大,恶性程度更高,因此治疗后更易复发。Xu F 等报道,随着宫颈癌浸润深度的增加,患者外周血中循环癌细胞数量增加^[19]。Fu S 等研究报道,骨髓内散在的宫颈癌细胞数量与宫颈癌浸润深度呈正相关^[20]。本研究显示发生深肌层浸润宫颈癌术后复发风险是未发生深肌层浸润宫颈癌的 2.137 倍,这是因为发生深

肌层浸润的宫颈癌患者术前可能更易发生肿瘤外周血和骨髓的扩散,因此术后发生复发的风险更高^[21]。临床分期是指导肿瘤治疗和评估预后的重要指标。已有报道显示,恶性肿瘤患者术后生存率与肿瘤分期有密切关系^[22,23],临床分期 IIA1-IIA2 期肿瘤系局部晚期宫颈癌,术后发生复发的风险更高。淋巴结转移是肿瘤常见的转移方式,恶性肿瘤细胞可以穿过淋巴管壁,随淋巴液进入淋巴结^[24,25],这部分患者经过手术、放疗后虽然将原本病灶中的肿瘤细胞杀灭,但随淋巴转移的肿瘤细胞可能再次出现并增殖,导致肿瘤复发。既往研究已表明 SCC-Ag 与 HR-HPV 阳性与宫颈癌不良预后相关,且是宫颈癌复发的危险因素^[26,27]。

目前临床上对于宫颈癌术后随访主要采取妇科检查、阴道残端脱落细胞学检测和影像学检查等^[28]。由于宫颈癌术后导致解剖结构改变,妇科检查以及脱落细胞学检测受取样部位的制约,影响了诊断效果^[29],而正电子发射断层显像/CT 虽然具有较高的灵敏度和特异度,但费用较为昂贵,不适宜反复检测^[30]。本研究结果显示 SCC-Ag 联合 HR-HPV 预测宫颈癌术后复发的灵敏度、特异度、阳性预测值、阴性预测值分别为 92.50%、87.50%、54.41%、98.64%,提示对宫颈癌患者术后进行随访,定期检测 SCC-Ag、HR-HPV,可以为宫颈癌术后复发诊断提供帮助。

综上所述,中低分化、深肌层浸润、临床分期 IIA1-IIA2 期、有淋巴结转移、SCC-Ag 阳性、HR-HPV 阳性是宫颈癌术后复发的危险因素,SCC-Ag 联合 HR-HPV 预测宫颈癌术后复发具有一定的预测价值,值得临床重点关注。

参考文献(References)

- [1] 刘萍. 中国大陆 13 年宫颈癌临床流行病学大数据评价[J]. 中国实用妇科与产科杂志, 2018, 34(1): 41-45

- [2] Lyu Y, Ding L, Gao T, et al. Influencing Factors of High-Risk Human Papillomavirus Infection and DNA Load According to the Severity of Cervical Lesions in Female Coal Mine Workers of China[J]. J Cancer, 2019, 10(23): 5764-5769
- [3] Burki TK. Outcomes after minimally invasive surgery in cervical cancer[J]. Lancet Oncol, 2018, 19(12): e674
- [4] Kubik S, Moszynska-Zielinska M, Fijuth J, et al. Assessment of the relationship between serum squamous cell carcinoma antigen (SCC-Ag) concentration in patients with locally advanced squamous cell carcinoma of the uterine cervix and the risk of relapse [J]. Prz Menopauzalny, 2019, 18(1): 23-26
- [5] 赵培玉, 陈敦峰, 秦锦龙, 等. Cervista HR-HPV DNA 检测联合 TCT 在宫颈癌筛查中的临床价值[J]. 检验医学, 2017, 32(4): 322-325
- [6] Rebolj M, Brentnall AR, Mathews C, et al. 16/18 genotyping in triage of persistent human papillomavirus infections with negative cytology in the English cervical screening pilot [J]. Br J Cancer, 2019, 121(6): 455-463
- [7] 张晓磊, 彭娟, 郑建华. 宫颈癌 FIGO 分期的修订及治疗[J]. 国际生殖健康 / 计划生育杂志, 2011, 30(2): 153-154
- [8] Tsuchida K, Murakami N, Kato T, et al. Postoperative pelvic intensity-modulated radiation therapy reduced the incidence of late gastrointestinal complications for uterine cervical cancer patients[J]. J Radiat Res, 2019, 60(5): 650-657
- [9] Tian S, Yang X, Zhang L, et al. Polymorphic variants conferring genetic risk to cervical lesions support GSTs as important associated loci[J]. Medicine (Baltimore), 2019, 98(41): 17487
- [10] 朱晓南, 美丽帕, 沈谷群, 等. 局部晚期宫颈癌新辅助化疗后病理明显缓解的 25 例临床分析 [J]. 现代生物医学进展, 2018, 18(21): 4107-4109, 4086
- [11] Wang H, Ma Y, Li R, et al. Associations of Cervicovaginal Lactobacilli With High-Risk Human Papillomavirus Infection, Cervical Intraepithelial Neoplasia, and Cancer: A Systematic Review and Meta-Analysis[J]. J Infect Dis, 2019, 220(8): 1243-1254
- [12] Guleria C, Suri V, Kapoor R, et al. Human papillomavirus 16 infection alters the Toll-like receptors and downstream signaling cascade: A plausible early event in cervical squamous cell carcinoma development[J]. Gynecol Oncol, 2019, 155(1): 151-160
- [13] 臧建新. 老年 I b~II a 期宫颈癌术后放疗后复发的危险因素[J]. 中国老年学杂志, 2019, 39(10): 2372-2374
- [14] 孙桂霞, 张冬丽, 田君. 老年宫颈癌患者术后复发的高危因素及其病理特征[J]. 中国老年学杂志, 2019, 39(18): 4445-4447
- [15] 李晓颖, 胡彩妮, 段红艳. ≥ 60 岁宫颈癌患者治疗结局、生存期及影响预后的危险因素分析 [J]. 临床医学研究与实践, 2019, 4(29): 16-17
- [16] Xu D, Wang D, Wang S, et al. Correlation Between Squamous Cell Carcinoma Antigen Level and the Clinicopathological Features of Early-Stage Cervical Squamous Cell Carcinoma and the Predictive Value of Squamous Cell Carcinoma Antigen Combined With Computed Tomography Scan for Lymph Node Metastasis [J]. Int J Gynecol Cancer, 2017, 27(9): 1935-1942
- [17] Ali MAM, Bedair RN, Abd El Atti RM. Cervical high-risk human papillomavirus infection among women residing in the Gulf Cooperation Council countries: Prevalence, type-specific distribution, and correlation with cervical cytology [J]. Cancer Cytopathol, 2019, 127(9): 567-577
- [18] Ciavattini A, Serri M, Di Giuseppe J, et al. Long-term observational approach in women with histological diagnosis of cervical low-grade squamous intraepithelial lesion: an Italian multicentric retrospective cohort study[J]. BMJ Open, 2019, 9(7): e024920
- [19] Xu F, Li Y, Fan L, et al. Preoperative SCC-Ag and thrombocytosis as predictive markers for pelvic lymphatic metastasis of squamous cervical cancer in early FIGO stage [J]. J Cancer, 2018, 9 (9): 1660-1666
- [20] Fu S, Niu Y, Zhang X, et al. Squamous cell carcinoma antigen, platelet distribution width, and prealbumin collectively as a marker of squamous cell cervical carcinoma [J]. Cancer Biomark, 2018, 21(2): 317-321
- [21] Wen YF, Cheng TT, Chen XL, et al. Elevated circulating tumor cells and squamous cell carcinoma antigen levels predict poor survival for patients with locally advanced cervical cancer treated with radiotherapy[J]. PLoS One, 2018, 13(10): e0204334
- [22] 刘梦君, 李玉芝, 王丽华, 等. 鳞状细胞癌抗原检测联合磁共振成像对判断早期宫颈癌盆腔淋巴结转移的临床意义[J]. 中国癌症杂志, 2019, 29(2): 136-141
- [23] Oh J, Bae JY. Optimal cutoff level of serum squamous cell carcinoma antigen to detect recurrent cervical squamous cell carcinoma during post-treatment surveillance[J]. Obstet Gynecol Sci, 2018, 61(3): 337-343
- [24] 贾克娟. 宫颈癌患者发生盆腔淋巴结转移独立危险因素分析[J]. 实用癌症杂志, 2019, 34(1): 151-154
- [25] 余慧, 张涛红, 曾宪玲, 等. 1011 例子宫颈癌临床病理特征及盆腔淋巴结转移危险因素分析 [J]. 实用妇产科杂志, 2018, 34(10): 759-762
- [26] Mao Q, Liu X, Chen C, et al. A dual-label time-resolved fluorescence immunoassay for the simultaneous determination of carcinoembryonic antigen and squamous cell carcinoma antigen [J]. Biotechnol Appl Biochem, 2018, 65(6): 816-821
- [27] Kares S, Veijalainen O, Kholová I, et al. HIGH-RISK HPV testing as the primary screening method in an organized regional screening program for cervical cancer: the value of HPV16 and HPV18 genotyping[J]. APMIS, 2019, 127(11): 710-716
- [28] Park SH, Lee JY, Nam EJ, et al. Prediction of perioperative complications after robotic-assisted radical hysterectomy for cervical cancer using the modified surgical Apgar score [J]. BMC Cancer, 2018, 18(1): 908
- [29] Alvarez RM, Biliatis I, Rockall A, et al. MRI measurement of residual cervical length after radical trachelectomy for cervical cancer and the risk of adverse pregnancy outcomes: a blinded imaging analysis[J]. BJOG, 2018, 125(13): 1726-1733
- [30] Wu P, Xiong H, Yang M, et al. Co-infections of HPV16/18 with other high-risk HPV types and the risk of cervical carcinogenesis: A large population-based study[J]. Gynecol Oncol, 2019, 155(3): 436-443