

[文章编号] 1671-587X(2024)06-1677-06

DOI:10.13481/j.1671-587X.20240621

卵巢透明细胞癌和卵巢型子宫内膜异位症患者的临床特征分析

袁素珍, 靳焰, 汪雯雯

(华中科技大学同济医学院附属同济医院妇产科, 湖北 武汉 430030)

[摘要] **目的:** 分析卵巢透明细胞癌(OCCC)和卵巢型子宫内膜异位症(OMA)患者的临床特征, 阐明卵巢透明细胞癌的发病特点。**方法:** 回顾性分析2011年3月—2021年5月接受手术治疗且术后病理确诊为OCCC患者80例及术后病理为OMA患者80例的临床资料, 包括一般特征、临床表现特点、实验室指标和影像学检查指标等。比较2组患者的年龄, 体质量指数(BMI), 临床症状如腹痛、阴道出血及其他症状(腹胀、月经紊乱、便秘和阴道分泌物异常等), 术前血清糖类抗原125(CA125)水平, 卵巢囊肿的超声特征, 如卵巢囊肿大小、有无盆腔积液和是否为复杂性囊肿。采用多因素Logistic回归分析OCCC的危险因素, 绘制受试者工作特征曲线(ROC)曲线, 并计算ROC曲线下面积(AUC)。**结果:** 与OMA组比较, OCCC组患者年龄明显升高($P<0.05$), 血清CA125水平明显升高($P<0.05$), 卵巢囊肿直径明显增加($P<0.05$), 有盆腔积液、其他症状和复杂性囊肿患者百分率明显升高($P<0.05$)。多因素Logistic回归分析, 年龄 ≥ 40 岁(OR=56.856, 95%CI: 5.611~576.082, $P=0.001$)、复杂性卵巢囊肿(OR=4.427, 95%CI: 1.025~19.114, $P=0.046$)、合并盆腔积液(OR=8.760, 95%CI: 1.574~48.760, $P=0.013$)和卵巢囊肿大小(OR=1.782, 95%CI: 1.329~2.390, $P<0.01$)是患OCCC的危险因素。卵巢囊肿大小的截断值为7.35 cm时, 其灵敏度(83.75%)和特异度(80.00%)之和最高, AUC为0.883, 对于OCCC的识别具有一定的预测价值。**结论:** 对于年龄 ≥ 40 岁、囊肿直径 ≥ 7.35 cm且为复杂性囊肿, 尤其是伴有盆腔积液的患者, 其恶变为OCCC的风险较高, 建议积极干预。

[关键词] 卵巢透明细胞癌; 卵巢型子宫内膜异位症; 临床特征; 危险因素; 复杂性囊肿

[中图分类号] R737.31 **[文献标志码]** A

Analysis on clinical characteristics of patients with ovarian clear cell carcinoma and ovarian endometriosis

YUAN Suzhen, JIN Yan, WANG Wenwen

(Department of Obstetrics and Gynecology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China)

ABSTRACT **Objective:** To discuss the clinical characteristics of the patients with ovarian clear cell carcinoma (OCCC) and ovarian endometriosis (OMA), and to clarify the features of OCCC onset. **Methods:** A retrospective analysis was conducted on the clinical data of 80 patients with post-operative pathological diagnosis of OCCC and 80 OMA patients diagnosed by post-operative pathology, who received surgical treatment from March 2011 to May 2021. The analysis included general characteristics, clinical manifestations, laboratory indices, and imaging examination indexes. The age, body mass index

[收稿日期] 2023-12-13

[基金项目] 国家自然科学基金青年科学基金项目(81701420)

[作者简介] 袁素珍(1986—), 女, 河南省新乡市人, 主治医师, 医学博士, 主要从事妇科疾病基础和临床方面的研究。

[通信作者] 汪雯雯, 副教授, 副主任医师, 硕士研究生导师(E-mail: wenwenwang@hust.edu.cn)

(BMI), clinical symptoms such as abdominal pain, vaginal bleeding, and other symptoms (bloating, menstrual disorders, constipation, and abnormal vaginal discharge), preoperative serum carbohydrate antigen 125 (CA125) levels, and ultrasound characteristics of ovarian cysts, such as cyst size, presence of pelvic effusion, and complexity, were compared between the patients in two groups. Multivariate Logistic regression analysis was used to identify the risk factors for OCCC, and the receiver operating characteristic (ROC) curve was drawn, and the area under the curve (AUC) was calculated. **Results:** Compared with OMA group, the age of the patients in OCCC group was significantly increased ($P<0.05$), the serum CA125 level was significantly increased ($P<0.05$), the diameter of ovarian cyst was significantly increased ($P<0.05$), and the percentage of the patients with pelvic effusion, other symptoms, and complex cysts was significantly increased ($P<0.05$). The multivariate Logistic regression analysis results showed that age ≥ 40 years (OR=56.856, 95%CI: 5.611–576.082, $P=0.001$), complex ovarian cysts (OR=4.427, 95%CI: 1.025–19.114, $P=0.046$), concomitant pelvic effusion (OR=8.760, 95%CI: 1.574–48.760, $P=0.013$), and size of ovarian cysts (OR=1.782, 95%CI: 1.329–2.390, $P<0.01$) were the risk factors for OCCC. When the cut-off value of the ovarian cyst size was 7.35 cm, the sum of sensitivity (83.75%) and specificity (80.00%) was the highest, and the AUC was 0.883, indicating certain predictive value for identifying OCCC. **Conclusion:** The patients aged ≥ 40 years with cysts ≥ 7.35 cm in diameter, especially those with complex cysts accompanied by pelvic effusion, have a higher risk of malignancy to OCCC, and active intervention is recommended.

KEYWORDS Ovarian clear cell carcinoma; Ovarian endometriosis; Clinical characteristic; Risk factor; Complex cyst

卵巢癌是妇科癌症导致女性死亡的最常见原因,由多种组织学类型组成,其中90%为上皮性卵巢癌^[1]。卵巢透明细胞癌(ovarian clear cell cancer, OCCC)是上皮性卵巢癌的一种,约占上皮性卵巢癌的10%^[2],于1973年被世界卫生组织(World Health Organization, WHO)确认为卵巢癌的一种独特组织学亚型^[3],因其细胞质呈透明的特征,故而被命名为透明细胞癌^[4]。在卵巢癌的各种组织学亚型中,OCCC发病率位居第2位,仅次于卵巢高级别浆液性癌。亚洲是OCCC的高发区,并且有逐年上升和年轻化的趋势^[5-6]。与其他类型上皮性卵巢癌比较,OCCC患者的预后差别较大,主要取决于手术病理分期,早期OCCC患者预后较好。研究^[7-9]显示:国际妇产科学联盟(Federation International of Gynecology and Obstetrics, FIGO) IA和IC1期OCCC患者的5年无病生存期(disease-free survival, DFS)高达84%~100%,IB期OCCC患者的DFS约为56%,而晚期患者的预后因其对化疗不敏感和复发率高,较其他组织学亚型的卵巢癌更差,临床诊治非常困难。研究^[10-12]显示:FIGO III/IV期OCCC患者的中位DFS仅为10.2个月,远低于OCCC总患病人群的4年DFS,且晚期OCCC患者的预后相较于浆液性癌患者更

差。因此,尽早识别OCCC高风险患者至关重要,需要对其及时进行手术治疗和密切随访管理。目前,尚缺乏OCCC针对性的早期识别和临床诊断方案,超声是目前用于识别卵巢恶性肿瘤特征且应用最普遍和可及性最好的一线影像学工具,然而其超声影像特征难以与部分良性卵巢肿瘤[如卵巢型子宫内膜异位症(ovarian endometrioma, OMA)]相鉴别^[13-14]。有研究^[4, 15]从流行病学和基因组学等多角度证实:OCCC与OMA有显著相关性,其相对危险度(relative risk, RR)为12.4。因此,本研究通过分析OCCC和OMA患者的临床特征、血清生物标志物和影像学表现,阐明OCCC的发病特点,辅助临床医生尽早识别OCCC高风险患者并进行及早干预,以提高患者生存率。

1 资料与方法

1.1 研究对象和分组 回顾性分析2011年3月—2021年5月于华中科技大学同济医学院附属同济医院妇产科接受手术治疗的160例患者的临床资料,包括一般特征、临床表现特点、实验室指标和影像学检查等。病理诊断均由2名经验丰富的病理医师复核。纳入标准:①术前诊断出卵巢囊肿,术后病理证实为OMA或OCCC;②临床资料完整。排除标准:①病理诊断为任何其他癌症的患者;②既往

接受放疗和化疗或其他全身治疗者; ③其他部位恶性肿瘤转移至卵巢的患者; ④近期有盆腔炎性疾病或其他感染性疾病病史者。根据上述标准纳入OCCC组患者共80例(OCCC组), 按照相应年份匹配, 随机挑选OMA患者80例作为良性对照组(OMA组)。

1.2 数据采集 收集2组患者的临床资料, 包括年龄, 体质量指数(body mass index, BMI), 临床症状如腹痛、阴道出血及其他症状(腹胀、月经紊乱、便秘和阴道分泌物异常等), 术前血清糖类抗原125(carbohydrate antigen 125, CA125)水平, 卵巢囊肿的超声特征, 如卵巢囊肿大小、有无盆腔积液和是否为复杂性囊肿。其中卵巢囊肿大小以囊肿最大直径表示, 盆腔积液以陶氏腔积液 >3 cm记作有盆腔积液, 复杂性囊肿指囊内成分复杂, 除液体外, 还具有分隔或实性组织成分。

1.3 统计学分析 采用SPSS 23.0统计软件进行统计学分析。采用K-S检验对连续性变量进行正态性检验, 2组患者BMI和囊肿大小符合正态分布, 以 $\bar{x}\pm s$ 表示, 2组间样本均数比较采用两独立样本 t 检验; 2组患者血清CA125水平为非正态分布, 以 $M(P25, P75)$ 表示, 组间比较采用Mann-Whitney U 检验; 2组患者年龄、腹痛症状、阴道出血症状、盆腔积液、其他症状和复杂性囊肿以例数(%)表示, 组间比较采用 χ^2 检验。使用病理分组是否为OCCC组作为因变量, 建立Logistic模型, 将单因素分析中有统计学差异的变量纳入多因素Logistic回归分析, 最终结果采用比值比(odds ratio, OR)和95%置信区间(confidence interval, CI)进行描述。Logistic回归分析中有统计学意义的连续型变量进一步绘制受试者工作特征(receiver operating characteristic, ROC)曲线, 评估其对OCCC的预测价值。以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 2组患者一般资料 与OMA组比较, OCCC组患者年龄明显增大($P<0.05$), 血清CA125水平明显升高($P<0.05$), 卵巢囊肿直径明显增加($P<0.05$), 具有盆腔积液、其他症状和复杂性囊肿患者百分率明显升高($P<0.05$), BMI和有腹痛和阴道出血症状患者百分率差异无统计学意义($P>0.05$)。见表1。

2.2 OCCC的危险因素分析 以病理分组是否为

OCCC组作为因变量(0=OMA, 1=OCCC), 以单因素分析中差异有统计学意义的因素(年龄、复杂性囊肿、盆腔积液、其他症状、卵巢囊肿大小和血清CA125水平相较于其正常值的倍数)为自变量(年龄: 1= <30 岁, 2=30~40岁, 3= ≥ 40 岁; 复杂性囊肿: 0=否, 1=是; 盆腔积液: 0=无, 1=有; 其他症状: 0=无, 1=有), 多因素Logistic回归分析结果显示: 年龄 ≥ 40 岁(OR=56.856, 95%CI: 5.611~576.082, $P=0.001$)、复杂性卵巢囊肿(OR=4.427, 95%CI: 1.025~19.114, $P=0.046$)、并发盆腔积液(OR=8.760, 95%CI: 1.574~48.760, $P=0.013$)和卵巢囊肿大小(OR=1.782, 95%CI: 1.329~2.390, $P<0.01$)是患OCCC的危险因素。见表2。

2.3 卵巢囊肿大小预测OCCC的ROC曲线 卵巢囊肿大小的截断值为7.35 cm时, 其灵敏度(83.75%)和特异度(80.00%)之和最高, ROC曲线下面积(area under curve, AUC)为0.883, 其95%CI为0.829~0.936, 对于OCCC的识别具有一定的预测价值。见图1。

3 讨论

OCCC是上皮性卵巢癌中的一种少见且特殊的组织学亚型, 通常与子宫内膜异位症有关。研究^[16]显示: OCCC的发生有显著的人种和地域差异, 在亚洲地区更为常见。在我国有关OCCC患病率少有报道, 仅中国医学科学院北京协和医院的资料显示OCCC患病率为9.7%^[17]。OCCC患者少有家族史, 乳腺癌易感基因(breast cancer susceptibility gene, BRCA)1和BRCA2的突变也较少见。研究^[18]发现: 少数OCCC的发生来源于有DNA错配修复蛋白突变的Lynch综合征。大部分OCCC具有前驱病变, 研究^[4, 19]显示: 约三分之一的OCCC病灶直接起源于子宫内膜异位病灶, 以OMA最常见, 因此在OMA患者的诊治和随访过程中应警惕其发生OCCC的可能。本研究结果显示: 与OMA组比较, OCCC组患者 ≥ 40 岁、复杂性囊肿和盆腔积液患者百分率明显升高, 卵巢囊肿直径明显增大, 除腹痛和阴道出血以外的压迫症状(如便秘)、腹胀、痛经、月经紊乱和阴道分泌物异常等其他症状更明显。

与其他上皮性卵巢癌患者比较, OCCC患者发病年龄较小, 但其相对于良性囊肿患者年龄明显升高。在本研究中OCCC组 ≥ 40 岁的患者占93.75%, 与

表1 2组患者一般资料
Tab. 1 Clinical data of patients in two groups (n=80)

Variable	OCCC	OMA	$\chi^2/t/Z$	P
Age(year) (n/%)			86.040	<0.01
<30	2(2.50)	27(33.75)		
30-40	3(3.75)	36(45.00)		
≥40	75(93.75)	17(21.25)		
BMI(kg·m ⁻²)($\bar{x}\pm s$)	22.19±2.55	21.39±2.86	-1.251	0.215
CA125(U·mL ⁻¹)[M(P25,P75)]	165.95(55.65,513.15)	34.85(15.72,77.28)	-6.044	<0.01
Abdominal pain(n/%)				
Yes	30(37.50)	20(25.00)	2.909	0.088
No	50(62.50)	60(75.00)		
Vaginal bleeding(n/%)			0.427	0.514
Yes	6(7.50)	4(5.00)		
No	74(92.50)	76(95.00)		
Pelvic effusion(n/%)			16.410	<0.01
Yes	38(47.50)	14(17.50)		
No	42(52.50)	66(82.50)		
Other symptoms(n/%)			10.417	<0.01
Yes	58(72.50)	38(47.50)		
No	22(27.50)	42(52.50)		
Complex ovarian cyst(n/%)			27.435	<0.01
Yes	53(66.25)	20(25.00)		
No	27(33.75)	60(75.00)		
Ovarian cyst size(cm)($\bar{x}\pm s$)	12.27±5.36	6.04±2.59	-9.366	<0.01

表2 Logistic回归分析OCCC的危险因素
Tab. 2 Risk factors of OCCC analyzed by Logistic regression analysis

Variable	B	SE	OR(95%CI)	P
Age(year)				
<30			1.000	
30-40	-2.588	1.942	0.075(0.002-3.381)	0.183
≥40	4.041	1.182	56.856(5.611-576.082)	0.001
Complex ovarian cyst				
Yes	1.488	0.746	4.427(1.025-19.114)	0.046
No			1.000	
Pelvic effusion				
Yes	2.170	0.876	8.760(1.574-48.760)	0.013
No				
Other symptoms				
Yes	1.311	0.740	3.709(0.871-15.806)	0.076
No			1.000	
Ovarian cyst size(cm)	0.578	0.150	1.782(1.329-2.390)	<0.01
CA125 fold	-0.008	0.018	0.992(0.958-1.027)	0.639

Note: Normal value range of serum CA125 level is 0-35 U·L⁻¹; Divide actual value of CA125 by 35 to get multiple of CA125.

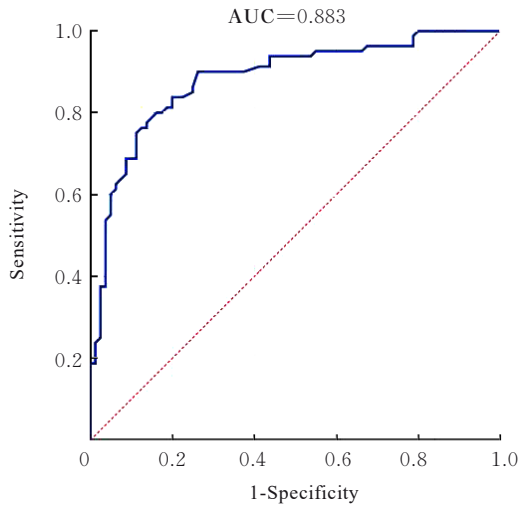


图1 卵巢囊肿大小预测OCCC的ROC曲线

Fig. 1 ROC curves of OCCC predicted by ovarian cyst size

KADAN等^[20]和HUANG等^[21]的研究结果一致。

CA125是目前使用最广泛的妇科恶性肿瘤标志物之一。研究^[12, 22]显示: CA125对OCCC患者诊断和预后的预测价值并不确切, 且OCCC尚无特异性生物标志物, OCCC患者通常仅有血清CA125水平轻度升高。本研究结果显示: 与OMA组比较, OCCC组患者血清CA125水平明显升高, 但多因素Logistic回归结果提示CA125水平升高并非OCCC的危险因素。因此, 血清CA125水平对于预测OCCC的价值较低, 仍需开发新的诊断标志物来预测发现早期的OCCC。

OCCC和OMA的首发症状常为腹痛、盆腔包块和阴道出血。与其他类型卵巢癌比较, OCCC较少形成腹水。本研究结果显示: 2组患者腹痛和阴道出血症状无明显差异, 与OMA组比较, OCCC组患者盆腔积液和其他症状患者所占百分率明显升高, 且盆腔积液是患OCCC的危险因素。

子宫内膜异位症患者发生卵巢癌的风险增加1.2~1.8倍, 且组织学类型多为透明细胞癌和子宫内膜样癌, 子宫内膜异位囊肿的影像学检查通常提示其为非单纯性囊肿, 且常伴有血清CA125水平升高, 因此, 此2项阳性表现通常会增加妇科医生分辨良恶性囊肿的困难^[23-25]。本研究结果显示: 与OMA组比较, OCCC组患者复杂性囊肿百分率明显升高, 卵巢囊肿大小明显增加, 且复杂性囊肿是患OCCC的危险因素, 与KADAN等^[20]和HUANG等^[21]的研究结果一致, 与OCCC的超声表达特点相符^[26]。

此外, CHIANG等^[27]发现: 年龄增大、居住于高度城市化地区、收入低或高、抑郁、盆腔炎及子宫内膜异位症后未生育均会使子宫内膜异位症患者处于患卵巢癌的高风险中。本研究结果显示: 年龄 ≥ 40 岁是患OCCC的危险因素。

本研究存在以下局限性: ①本研究是单中心的回顾性研究, 且病例数量较少; ②本研究纳入的影像学数据仅限于囊肿大小和囊肿的复杂性, 囊肿结构特征例如血流信号、壁厚、结节和乳头状突起等未进行描述。

综上所述, 对于年龄 ≥ 40 岁、直径 ≥ 7.35 cm且为复杂性囊肿, 尤其是伴有盆腔积液的患者, 临床医师需警惕, 建议其手术治疗; 对于不符合上述高风险标准的患者可以结合临床症状、血清CA125水平和影像学检查进行连续监测, 如出现囊肿变化、症状出现或血清CA125水平升高则建议及时进行手术治疗。本研究结果为临床医师处理OMA提供了参考, 但还需进一步开展大样本、多中心的临床研究进行验证。

利益冲突声明:

所有作者声明不存在利益冲突。

作者贡献声明:

袁素珍参与研究设计、数据收集、统计学分析和论文撰写, 靳焰参与数据收集和整理分析, 汪雯雯参与研究设计和论文审校。

[参考文献]

- [1] TORRE L A, TRABERT B, DESANTIS C E, et al. Ovarian cancer statistics, 2018[J]. CA Cancer J Clin, 2018, 68(4): 284-296.
- [2] TAN D S, KAYE S. Ovarian clear cell adenocarcinoma: a continuing enigma[J]. J Clin Pathol, 2007, 60(4): 355-360.
- [3] SILVERBERG S G. Ultrastructure and histogenesis of clear cell carcinoma of the ovary [J]. Am J Obstet Gynecol, 1973, 115(3): 394-400.
- [4] 中国医师协会妇产科医师分会妇科肿瘤学组. 卵巢透明细胞癌临床诊治中国专家共识(2022年版)[J]. 中国实用妇科与产科杂志, 2022, 38(5): 515-523.
- [5] MACHIDA H, MATSUO K, YAMAGAMI W, et al. Trends and characteristics of epithelial ovarian cancer in Japan between 2002 and 2015: a JSGO-JSOG joint study[J]. Gynecol Oncol, 2019, 153(3): 589-596.
- [6] GAN M F, TAI Z X, YU Y J, et al. Next-generation sequencing shows the genomic features of ovarian clear

- cell cancer and compares the genetic architectures of high-grade serous ovarian cancer and clear cell carcinoma in ovarian and endometrial tissues[J]. *Peer J*, 2023, 11: e14653.
- [7] IIDA Y, OKAMOTO A, HOLLIS R L, et al. Clear cell carcinoma of the ovary: a clinical and molecular perspective[J]. *Int J Gynecol Cancer*, 2021, 31(4): 605-616.
- [8] CHAN J K, TEOH D, HU J M, et al. Do clear cell ovarian carcinomas have poorer prognosis compared to other epithelial cell types? A study of 1411 clear cell ovarian cancers[J]. *Gynecol Oncol*, 2008, 109(3): 370-376.
- [9] XIE Y K, KONG W M, LUO D, et al. Ovarian clear cell carcinoma: genomic characterization, pathogenesis and targeted therapy[J]. *Anticancer Res*, 2023, 43(8): 3401-3410.
- [10] IRODI A, RYE T, HERBERT K, et al. Patterns of clinicopathological features and outcome in epithelial ovarian cancer patients: 35 years of prospectively collected data[J]. *BJOG*, 2020, 127(11): 1409-1420.
- [11] OLIVER K E, BRADY W E, BIRRER M, et al. An evaluation of progression free survival and overall survival of ovarian cancer patients with clear cell carcinoma versus serous carcinoma treated with platinum therapy: an NRG Oncology/Gynecologic Oncology Group experience[J]. *Gynecol Oncol*, 2017, 147(2): 243-249.
- [12] LIU H, XU Y B, JI J L, et al. Prognosis of ovarian clear cell cancer compared with other epithelial cancer types: a population-based analysis [J]. *Oncol Lett*, 2020, 19(3): 1947-1957.
- [13] 丁璐璟, 龚亚红, 李顺珍, 等. 彩色多普勒超声检测在卵巢良恶性肿瘤鉴别诊断中的价值[J]. *中国超声医学杂志*, 2022, 38(4): 418-421.
- [14] KOBAYASHI H. Clinicopathological characteristics, molecular features and novel diagnostic strategies for the detection of malignant transformation of endometriosis (Review)[J]. *Exp Ther Med*, 2023, 25(6): 279.
- [15] FUJIWARA K, SHINTANI D, NISHIKAWA T. Clear-cell carcinoma of the ovary[J]. *Ann Oncol*, 2016, 27(Suppl 1): i50-i52.
- [16] ZHU C C, ZHU J, QIAN L L, et al. Clinical characteristics and prognosis of ovarian clear cell carcinoma: a 10-year retrospective study [J]. *BMC Cancer*, 2021, 21(1): 322.
- [17] WANG S, QIU L, LANG J H, et al. Clinical analysis of ovarian epithelial carcinoma with coexisting pelvic endometriosis[J]. *Am J Obstet Gynecol*, 2013, 208(5): 413.e1-413.e5.
- [18] BENNETT J A, MORALES-OYARVIDE V, CAMPBELL S, et al. Mismatch repair protein expression in clear cell carcinoma of the ovary: incidence and morphologic associations in 109 cases[J]. *Am J Surg Pathol*, 2016, 40(5): 656-663.
- [19] HÖHN A K, BRAMBS C E, HILLER G G R, et al. 2020 WHO classification of female genital tumors [J]. *Geburtshilfe Frauenheilkd*, 2021, 81(10): 1145-1153.
- [20] KADAN Y, FIASCONE S, MCCOURT C, et al. Predictive factors for the presence of malignant transformation of pelvic endometriosis[J]. *Eur J Obstet Gynecol Reprod Biol*, 2015, 185: 23-27.
- [21] HUANG K J, LI Y X, WU C J, et al. Sonographic features differentiating early-stage ovarian clear cell carcinoma from endometrioma with atypical features [J]. *J Ovarian Res*, 2022, 15(1): 84.
- [22] KOBAYASHI H, SUGIMOTO H, ONISHI S, et al. Novel biomarker candidates for the diagnosis of ovarian clear cell carcinoma[J]. *Oncol Lett*, 2015, 10(2): 612-618.
- [23] MURAKAMI K, KOTANI Y, SHIRO R, et al. Endometriosis-associated ovarian cancer occurs early during follow-up of endometrial cysts [J]. *Int J Clin Oncol*, 2020, 25(1): 51-58.
- [24] KRÁLÍČKOVÁ M, LAGANÀ A S, GHEZZI F, et al. Endometriosis and risk of ovarian cancer: what do we know?[J]. *Arch Gynecol Obstet*, 2020, 301(1): 1-10.
- [25] LEENEN S, HERMENS M, DE VOS VAN STEENWIJK P J, et al. Immunologic factors involved in the malignant transformation of endometriosis to endometriosis-associated ovarian carcinoma [J]. *Cancer Immunol Immunother*, 2021, 70(7): 1821-1829.
- [26] ROBINSON K A, MENIAS C O, CHEN L W, et al. Understanding malignant transformation of endometriosis: imaging features with pathologic correlation[J]. *Abdom Radiol*, 2020, 45(6): 1762-1775.
- [27] CHIANG A J, CHANG C, HUANG C H, et al. Risk factors in progression from endometriosis to ovarian cancer: a cohort study based on medical insurance data[J]. *J Gynecol Oncol*, 2018, 29(3): e28.