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论著

子宫内膜癌血清肿瘤标志物及病理分子标志物与临床病理特征的关系

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摘要 **目的:**探讨子宫内膜癌(EC)血清肿瘤标志物及病理分子标志物与临床病理特征的关系。**方法:**回顾性分析2018年1月—2024年2月天津市人民医院妇科收治的144例原发性EC患者的术前血清肿瘤标志物糖类抗原(CA)125、CA199、CA72-4及术后组织病理分子标志物中雌激素受体(ER)、孕激素受体(PR)、抑癌基因(P53)、Ki-67与其病理类型、分期、分化程度、肌层浸润深度、淋巴脉管间隙浸润、宫颈间质浸润之间的关系。**结果:**国际妇产科联盟(FIGO,2009)EC手术-病理分期Ⅲ~Ⅳ期患者的CA125、CA199、CA72-4水平明显升高,差异有统计学意义(Z=-3.45、-4.10、-2.41,均P<0.05)。肌层浸润深度≥1/2的患者CA125水平明显升高,差异有统计学意义(Z=-2.02,P<0.05),CA125、CA199、CA72-4水平在子宫内膜样腺癌分化程度间比较差异有统计学意义(H=6.07、6.22、10.79,均P<0.05)。CA125、CA199、CA72-4联合用于FIGOⅢ~Ⅳ期、肌层浸润深度≥1/2诊断的曲线下面积(AUC)分别为0.74、0.71。子宫内膜样腺癌ER、PR阳性表达率明显高于非子宫内膜样腺癌(χ^2=26.84、26.47,均P<0.001)。EC Ⅰ~Ⅱ期ER、PR阳性表达率明显高于Ⅲ~Ⅳ期(χ^2=18.81、12.66,均P<0.05)。高分化子宫内膜样腺癌ER、PR阳性表达率明显高于低分化子宫内膜样腺癌(χ^2=18.04、12.62,均P<0.05)。肌层浸润深度<1/2者ER、PR阳性表达率明显高于肌层浸润深度≥1/2者(χ^2=13.17、12.32,均P<0.05)。无淋巴脉管间隙浸润、宫颈间质浸润者ER、PR阳性表达率明显高于有淋巴脉管间隙浸润、宫颈间质浸润者。P53突变型、Ki-67≥65%在组织病理类型间比较差异有统计学意义(χ^2=27.13、8.43,均P<0.05),与子宫内膜样腺癌相比,非子宫内膜样腺癌中P53突变型及Ki-67表达率明显升高。**结论:**CA125、CA199、CA724、ER、PR、P53、Ki-67与EC预后高危因素密切相关。

关键词 子宫内膜癌;肿瘤标志物;病理特征;免疫组化
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The relationship between serum tumor markers and pathological molecular markers of endometrial cancer and clinical pathological features

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Abstract **Objective:** To explore the relationship between serum tumor markers and pathological molecular markers of endometrial cancer (EC) and their clinical pathological characteristics. **Methods:** A retrospective analysis was conducted on 144 cases of primary EC patients admitted in the Department of Gynecology, Tianjin Union Medical Center from January 2018 to February 2024. The relationship between the preoperative serum tumor markers carbohydrate antigen(CA)125, CA199, CA72-4, as well as the postoperative tissue pathological molecular markers including estrogen receptor (ER), progestin receptor (PR), tumor suppressor gene (TP53), Ki-67 and their pathological types, staging, degree of differentiation, depth of myometrial invasion, lymphovascular space invasion, and cervical stromal invasion were evaluated. **Results:** The levels of CA125, CA199, and CA72-4 in patients with stage Ⅲ-Ⅳ EC according to the International Federation of Gynecology and Obstetrics (FIGO, 2009) surgical-pathological staging were significantly elevated, with statistically significant differences(Z=-3.45, -4.10, -2.41, all P<0.05). Patients with myometrial invasion depth of ≥1/2 had significantly elevated levels of CA125, with a statistically significant difference(Z=-2.02, P<0.05). The level of CA125, CA199, and CA72-4 showed statistically significant differences among the differentiation grades of endometrioid adenocarcinoma(H=6.07, 6.22, 10.79, all P<0.05). The area under the curve(AUC) for the combined use of CA125, CA199, and CA72-4 in diagnosing FIGO stages Ⅲ to Ⅳ, with a myometrial invasion depth of ≥1/2, were 0.74 and 0.71, respectively. The positive expression rates of ER and PR in endometrioid adenocarcinoma were significantly higher than those in non-endometrioid adenocarcinoma(χ^2=26.84, 26.47, both P<0.001). The positive expression rates of ER and PR in EC stages Ⅰ-Ⅱ were significantly higher than those in stages Ⅲ-Ⅳ (χ^2=18.81, 12.66, both P<0.05). The positive expression rates of ER and PR in well-differentiated endometrioid adenocarcinoma were significantly higher than those in poorly differentiated endometrioid adenocarcinoma (χ^2=18.04, 12.62, both P<0.05). The positive expression rates of ER and

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PR in patients with myometrial invasion depth less than 1/2 were significantly higher than in those with invasion depth of ≥1/2(χ^2=13.17, 12.32, both P<0.05). The positive expression rates of ER and PR in patients without lymphovascular space invasion, cervical stromal invasionwere significantly higher than in those with these conditions. The P53 mutation type and Ki-67 expression ≥65% showed statistically significant differences among tissue pathological types (χ^2=27.13, 8.43, both P<0.05), and compared to endometrioid adenocarcinoma, non-endometrioid adenocarcinoma had significantly higher rates of P53 mutation and Ki-67 expression. **Conclusion:** CA125, CA199, CA724, ER, PR, P53, and Ki-67 are closely related to the high-risk prognostic factors of EC.

Key words endometrial cancer; tumor markers; pathological characteristics; immunohistochemistry

子宫内膜癌(endometrial carcinoma, EC)是常见的妇科恶性肿瘤之一。在世界范围内,其发病率呈上升及年轻化趋势。多数早期 EC 患者治疗后的预后良好,有部分患者初诊时已是晚期[1]。早期 EC 患者缺乏特异性的临床表现,有效的诊断及分子标志物有利于 EC 的早诊早治。检验学及分子病理学的发展、分子标志物检测的完善及免疫组化诊断的引入,有助于术前预测 EC 的分期、分级和病理类型。本研究通过回顾性分析 EC 患者术前血清肿瘤标志物及术后病理分子标志物来预测 EC 临床病理特征,以期早期识别 EC,并为不同患者制定个体化的手术方案。

1　对象和方法

1.1　*研究对象*　回顾性分析 2018 年 1 月—2024 年 2 月天津市人民医院妇科收治、病历资料完整的 144 例原发性 EC 患者的临床信息。平均年龄(61.1±9.8)岁,其中绝经后患者 117 例(81.3%),平均年龄(64.2±7.8)岁,绝经前患者 27 例(18.7%),平均年龄(47.7±4.8)岁。纳入标准:原发 EC 行全面分期手术,并经病理检查确诊。排除标准:术前接受过放疗、化疗或激素治疗者。按照国际妇产科联盟(FIGO, 2009)EC 手术-病理分期:Ⅰ~Ⅱ期 119 例(82.6%),Ⅲ~Ⅳ期 25 例(17.4%)。组织病理类型:子宫内膜样腺癌 123 例(85.4%),浆液性癌 6 例(4.2%),混合细胞癌 6 例(4.2%),癌肉瘤 6 例(4.2%),透明细胞腺癌 1 例(0.7%),中肾管腺癌 1 例(0.7%),腺棘皮癌 1 例(0.7%)。子宫内膜样腺癌分化程度:高分化 78 例(63.4%),中分化 33 例(26.8%),低分化 12 例(9.8%)。肌层浸润深度:<1/2 100 例(69.4%),≥1/2 44 例(30.6%)。无淋巴脉管间隙浸润 126 例(87.5%),有淋巴脉管间隙浸润 18 例(12.5%)。无宫颈间质浸润 133 例(92.4%),有宫颈间质浸润 11 例(7.6%)。

1.2　*方法*

1.2.1　主要试剂与仪器　罗氏电化学发光分析仪及配套试剂[罗氏(中国)有限公司];化学发光免疫分析仪 MAGLUMI ® X8 及其配套试剂(深圳新产业生物医学工程股份有限公司);苏木素及伊红(BA-4098, 珠海贝索生物技术有限公司);ER、PR、p53、Ki-67 抗体以及 EnVision 试剂盒(美国 Zymed 公司)。

1.2.2　血清肿瘤标志物检查　取患者术前空腹静脉血检测血清肿瘤标志物糖类抗原(CA)125、CA199、CA72-4 水平。应用罗氏电化学发光分析仪及配套试剂检测 CA125、CA199 表达水平;应用化学发光免疫分析仪 MAGLUMI ® X8 及其配套试剂检测 CA72-4 表达水平,检测过程均严格按照试剂盒使用说明书进行。异常标准分为:CA125≥35 U/mL, CA199≥ 27.2 U/mL, CA72-4≥ 7.0 U/mL。

1.2.3　免疫组化染色　子宫标本均用中性缓冲甲醛液固定、脱水、石蜡包埋、切片。将石蜡切片烤片 65℃ 1 h;二甲苯脱蜡,梯度乙醇水化,自来水冲洗;苏木素染色 1~2 min,伊红染色 30~60 s;梯度乙醇脱水,中性树胶封片。并用石蜡切片分别做雌激素受体(ER)、孕激素受体(PR)、抑癌基因(P53)、Ki-67 的免疫组织化学染色。免疫组织化学采用 EnVision 法:组织石蜡切片脱蜡至水,3%过氧化氢室温孵育 10 min,蒸馏水冲洗,抗原修复;PBS 液冲洗后滴加一抗(1∶100),4℃过夜;PBS 液冲洗后滴加二抗(1∶200),37℃孵育 30 min;PBS 液冲洗,显色,蒸馏水冲洗,苏木素复染、脱水,透明中性树胶封片。由两名有经验的病理医师观察其组织学形态,并进行免疫组化分析。ER、PR、p53、Ki-67 阳性表达均位于细胞核,呈棕黄色。组织切片于高倍镜下计数阳性细胞占同类细胞数的百分比,随机选取 10 个高倍视野取平均值,阳性细胞数>10%为阳性。比较不同病理特征 EC 患者血清 CA125、CA199、CA72-4 水平及 ER、PR、PTEN、p53、Ki-67 表达情况。计算以上肿瘤标志物单独与联合诊断的敏感性及特异性并绘制受试者工作特征(receiver operating characteristic, ROC)曲线,比较诊断效能。

1.3　*统计学处理*　采用 SPSS26.0 软件进行统计学分析,非正态分布的计量资料以[M(P25, P75)]表示,组间比较采用秩和检验;计数资料以 n(%)表示,组

间比较采用χ^2检验。使用二分类 *Logistic* 回归模型的概率值 *P* 绘制 CA125、CA199、CA72-4、(CA125+CA199+CA72-4)检测的 ROC 曲线。*P*<0.05 为差异有统计学意义。

2 结果

2.1 EC 患者血清肿瘤标志物与临床病理特征关系

CA125 中位数为 15.2(10.1,28.9)U/mL,CA199 中位数为 14.5(6.9,42.1)U/mL,CA72-4 中位数为 2.3(1.2,4.4)U/mL。按照 FIGO2009,EC 手术-病理分期Ⅲ~Ⅳ期患者的 CA125、CA199、CA72-4 明显升高(*Z*=-3.45、-4.10、-2.41,均 *P*<0.05)。肌层浸润深度≥1/2 的患者 CA125 明显升高(*Z*=-2.02,*P*<0.05)。CA125、CA199、CA72-4 在子宫内膜样腺癌分化程度间比较存在统计学意义(*P*<0.05),见表 1。

表 1 血清肿瘤标志物与临床病理特征的关系[*M*(*P25*,*P75*)]

Tab.1 Relationship between serum tumor markers and clinical pathological characteristics [*M*(*P25*,*P75*)]

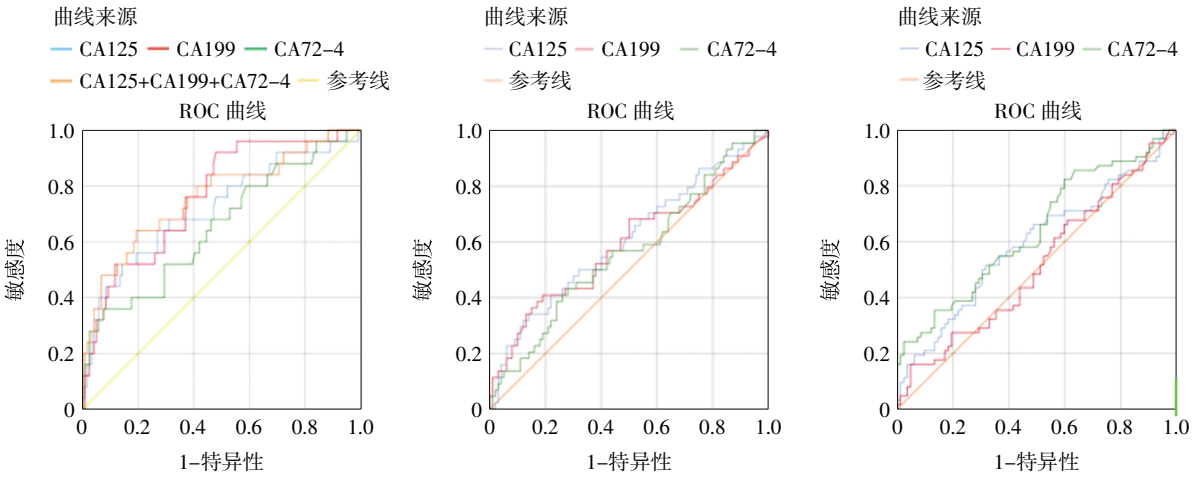
指标	*n*	CA125	*Z*/*H*	*P*	CA199	*Z*/*H*	*P*	CA72-4	*Z*/*H*	*P*
组织病理类型			-0.51	>0.05		-0.38	>0.05		-0.95	>0.05
子宫内膜样腺癌	123	15.35(10.50,28.95)			14.80(6.95,38.40)			2.38(1.22,4.33)		
非子宫内膜样腺癌	21	13.62(9.80,21.80)			12.80(7.60,109.82)			1.66(0.93,2.79)		
FIGO 分期			-3.45	<0.05		-4.10	<0.001		-2.41	<0.05
Ⅰ~Ⅱ期	119	14.15(9.55,25.95)			12.29(6.14,30.91)			2.28(1.14,3.68)		
Ⅲ~Ⅳ期	25	35.60(14.80,83.70)			69.26(17.68,210.40)			3.08(1.70,17.58)		
子宫内膜样腺癌分化程度			6.07	<0.05		6.22	<0.05		10.79	<0.05
高分化	78	13.05(9.30,26.00)			14.80(6.90,35.60)			2.28(1.08,3.45)		
中分化	33	20.70(13.69,32.20)			19.82(8.10,69.26)			2.98(1.66,10.46)		
低分化	12	25.70(11.79,96.45)			8.36(3.60,16.80)			3.38(2.25,5.86)		
肌层浸润深度			-2.02	<0.05		-1.70	>0.05		-1.17	>0.05
<1/2	100	14.40(9.50,26.05)			12.72(6.94,30.91)			2.29(1.16,3.54)		
≥1/2	44	18.75(11.19,46.00)			18.02(7.05,107.91)			2.62(1.25,5.38)		
淋巴脉管间隙浸润			-1.59	>0.05		-0.01	>0.05		-1.40	>0.05
无	126	14.65(9.80,28.00)			15.05(7.00,40.20)			2.30(1.13,3.99)		
有	18	23.74(10.87,51.83)			13.39(6.70,71.70)			2.56(1.53~5.89)		
宫颈间质浸润			-1.53	>0.05		-1.65	>0.05		-1.86	>0.05
无	133	14.81(10.10,28.00)			14.08(6.90,35.60)			2.28(1.16,3.99)		
有	11	28.81(12.45,92.58)			18.10(10.90,333.05)			3.09(2.62,7.06)		

注:CA125:糖类抗原 125;CA199:糖类抗原 199;CA72-4:糖类抗原 72-4

进一步分析 CA125、CA199、CA72-4 在 EC FIGO 分期中的诊断价值,曲线下面积(AUC)分别为 0.72、0.76、0.65,三者联合诊断 AUC 为 0.76。FIGO Ⅲ~Ⅳ期 CA125 的诊断界值是 33.90,敏感性 52.0%,特异性 85.7%;CA199 的诊断界值是 12.67,敏感性 92.0%,特异性 52.1%;CA72-4 的诊断界值是 8.88,敏感性 64.0%,特异性 92.4%。分析 CA125 在 EC 肌层浸润深度中的诊断价值,AUC 为 0.61,肌层浸润深度≥1/2 的 CA125 诊断界值是 36.31,敏感性 65.9%,特异性 86.0%。CA72-4 在子宫内膜样腺癌高分化及中低分化程度中的诊断价值,AUC 为 0.64。中低分化子宫内膜样腺癌的 CA72-4 的诊断界值是 4.85,敏感性 60.0%,特异性 87.2%,见图 1。

2.2 EC 病理分子标志物表达与临床病理特征关系

ER、PR 阳性表达在组织病理类型、FIGO 分期、子宫内膜样腺癌分化程度、肌层浸润深度、有无淋巴脉管间隙浸润、有无宫颈间质浸润间比较差异有统计学意义(均 *P*<0.05)。子宫内膜样腺癌 ER、PR 阳性表达率明显高于非子宫内膜样腺癌(χ^2=26.84、26.47,均 *P*<0.001)。EC Ⅰ~Ⅱ期 ER、PR 阳性表达率明显高于Ⅲ~Ⅳ期(χ^2=18.81、12.66,均 *P*<0.05)。高分化子宫内膜样腺癌 ER、PR 阳性表达率明显高于低分化子宫内膜样腺癌(χ^2=18.04、12.62,均 *P*<0.05)。肌层浸润深度<1/2 者 ER、PR 阳性表达率明显高于肌层浸润深度≥1/2 者(χ^2=13.17、12.32,均 *P*<0.05)。无淋巴脉管间隙浸润、宫颈间质浸润 ER、PR 阳性表达率明显高于有淋巴脉管间隙浸润、宫颈间质浸润。P53 突变型、Ki-67≥65%在组织病理类型间比较差异有统计学意义(χ^2=27.13、8.43,均 *P*<0.05),与子宫内膜样腺癌相比,非子宫内膜样腺癌中 P53 突变型及 Ki-67 表达率明显升高,见表 2。



注：CA125：糖类抗原 125；CA199：糖类抗原 199；CA72–4：糖类抗原 72–4；ROC：受试者工作特征；EC：子宫内膜癌

图 1　ROC 曲线评价 CA125、CA199、CA72–4 在EC 病理特征中的诊断价值

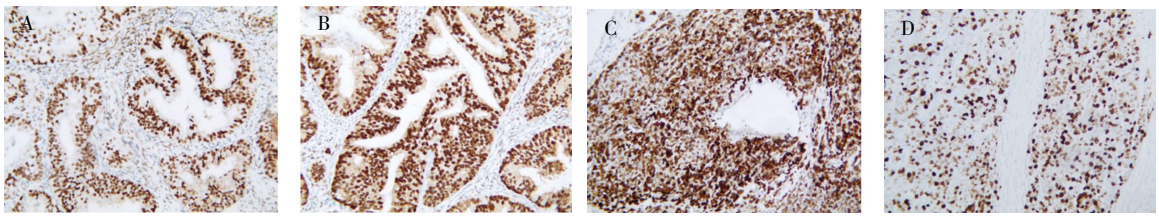
Fig.1　Analysis of ROC curve in the diagnostic value of CA125，CA199，CA72–4 in pathological characteristics of endometrial cancer

表 2　病理分子标志物与临床病理特征的关系[*n*（%）]

Tab.2　Relationship between pathological molecular markers and clinical pathological characteristics [*n*（%）]

指标	ER⁺	χ^2	*P*	PR⁺	χ^2	*P*	P53⁺	χ^2	*P*	Ki–67≥65%	χ^2	*P*
组织病理类型	113(84.3)	26.84	<0.001	87(64.9)	26.47	<0.001	44(32.1)	27.13	<0.001	33(34.0)	8.43	<0.05
子宫内膜样腺癌	103(89.6)			82(71.3)			27(23.3)			23(28.0)		
非子宫内膜样腺癌	10(52.6)			5(26.3)			17(81.0)			10(68.7)		
FIGO 分期	113(84.3)	18.81	<0.05	87(64.9)	12.66	<0.05	44(32.1)	2.51	>0.05	33(34.0)	1.01	>0.05
Ⅰ~Ⅱ期	96(88.1)			71(65.1)			33(29.2)			29(36.3)		
Ⅲ~Ⅳ期	17(68.0)			16(64.0)			11(45.8)			4(23.5)		
子宫内膜样腺癌分化程度	103(89.6)	18.04	<0.001	82(71.3)	12.62	<0.05	27(23.3)	4.82	>0.05	23(28.0)	1.94	>0.05
高分化	69(97.2)			58(81.7)			14(19.7)			13(26.0)		
中分化	28(87.5)			20(62.5)			7(21.9)			5(23.8)		
低分化	6(50.0)			4(33.3)			6(50.0)			5(45.5)		
肌层浸润深度	113(84.3)	13.17	<0.05	87(64.9)	12.32	<0.05	44(32.1)	0.10	>0.05	33(34.0)	0.64	>0.05
<1/2	77(85.6)			59(65.6)			31(33.0)			20(31.3)		
≥1/2	36(81.8)			28(63.6)			13(30.2)			13(39.4)		
淋巴脉管间隙浸润	113(84.3)	27.99	<0.001	87(64.9)	18.78	<0.001	44(32.1)	3.04	>0.05	33(34.0)	0.03	>0.05
无	104(89.7)			80(69.0)			35(29.4)			29(33.7)		
有	9(50.0)			7(38.9)			9(50.0)			4(36.4)		
宫颈间质浸润	113(84.3)	15.33	<0.05	87(64.9)	17.41	<0.05	44(32.1)	1.58	>0.05	33(34.0)	0.99	>0.05
无	105(85.4)			83(67.5)			39(30.7)			29(32.6)		
有	8(72.7)			4(36.4)			5(50.0)			4(50.0)		

注：ER：雌激素受体；PR：孕激素受体；P53：抑癌基因 P53 蛋白；Ki–67：细胞增殖标志物 Ki–67 蛋白；共 134 例内膜癌行 ER 免疫组化（内膜样癌 115 例，非内膜样癌 19 例），其中 113 例 ER⁺（内膜样癌 103 例，非内膜样癌 10 例）



注：A：ER 在子宫内膜样腺癌（G1）阳性表达；B：PR 在子宫内膜样腺癌（G1）中阳性表达；C：p53 在子宫内膜样腺癌（G3）呈弥漫性表达；D：Ki–67 在子宫内膜样腺癌（G3）80%阳性表达

图 2　ER、PR、p53、Ki–67 在子宫内膜样腺癌中的表达情况（×200）

Fig.2　Expression of ER，PR，p53，and Ki–67 in endometrioid adenocarcinoma（×200）

3 讨论

研究发现CA125水平与EC FIGO分期、分化程度、肌层浸润深度等相关，与本研究结果一致[2-4]。文献报道11%~43%EC患者的血清CA125水平>35 U/mL，本研究为20.8%。CA125>35 U/mL与ECⅢ/Ⅳ期、中低分化、肌层浸润深度>50%、淋巴脉管间隙浸润、宫颈间质浸润、淋巴结转移、腹水细胞学阳性显著相关[5]。血清CA125≥14.30 U/mL和CA199≥14.06 U/mL是EC发生的重要预测因子[2,6]。本研究中EC患者CA125中位数为15.2(10.1,28.9)U/mL。研究发现PET-CT的CA125最大标准化摄取阀SUVmax为16.42 U/mL[7]。CA125 SUVmax与FIGO分期、组织病理类型、肌层浸润深度显著相关[7-8]。文献报道血清CA125>43.645 U/mL是预测子宫内膜样腺癌深肌层浸润的最佳临界值[9]，本研究为36.31 U/mL。CA125≥222 U/mL临床病理分期风险增加[10]，而在本研究中FIGOⅢ~Ⅳ期CA125的诊断界值是33.90 U/mL。

CA199在胃肠道肿瘤的诊断和预后中具有广泛的应用价值。在EC中的临床应用价值具有一定的研究前景。CA199在几乎所有EC组织中均有检测到，且分布最均匀、升高时间较早[11-12]。本研究中CA199阳性率为31.9%。术前血清CA199水平可作为EC患者术前危险分层及术后预后评估的指标[13-14]。本研究中CA199中位数为14.5（6.9,42.1）U/mL。研究发现血清CA199≥14.06 U/mL和CA125≥14.30 U/mL是EC发生的重要预测因子[2,6]。本研究中不同FIGO分期、子宫内膜样腺癌分化程度间CA199水平差异有统计学意义(均P<0.05)。

目前，关于血清CA72-4与EC关系的研究较少。关于EC患者血清CA72-4阳性率报道不一。Hareyama等[15]报道31.9%的EC患者血清CA72-4高于临界值。Soper等[16]发现EC中CA72-4的阳性率为23.9%，病变局限于子宫体时阳性率为4%，子宫外转移时阳性率为30%[16]。本研究中CA72-4阳性率为16.0%，CA72-4中位数为2.3(1.2,4.4)U/mL。血清CA72-4阳性与肌层浸润深度、附件转移、淋巴脉管间隙浸润、盆腔和主动脉旁淋巴结转移相关，多因素分析显示血清CA72-4阳性与附件转移显著相关[15]。CA72-4与子宫内膜癌的TNM分期、组织分化程度密切相关，敏感性和特异性分别为58.33%和76.47%[17]。本研究中不同FIGO分期、子宫内膜样腺癌分化程度间CA72-4水平差异有统计学意义(均P<0.05)，FIGOⅢ~Ⅳ期、中低分化子宫内膜样腺癌的CA72-4的敏感性分别为64.0%、60.0%，特异性分别为92.4%、87.2%。

ER、PR、P53和Ki-67的表达呈一定相关性，可独立或联合应用于EC临床病理特征的评价[18-19]。

ER、PR表达在组织病理类型、FIGO分期、子宫内膜样腺癌分化程度、肌层浸润深度、有无淋巴脉管间隙浸润、有无宫颈间质浸润差异有统计学意义(均P<0.05)，与既往文献报道一致[20-22]。关于ECER和PR的阳性表达率文献报道不一，与FIGO分期、子宫内膜样腺癌分化程度相关[23-25]。本研究中子宫内膜样腺癌ER、PR阳性表达率为84.3%、64.9%。在低危型EC中，ER和PR的阳性表达率为60%~90%，在高危型EC中，ER和PR的阳性表达率为10%~55%[22]。雌孕激素受体阳性细胞百分比是EC复发和生存的重要预后因素，其浓度越高，总生存预后较好。ER阳性细胞>30%的患者总体预后明显更好，PR阳性细胞>40%的低分化EC患者生存率明显提高[24]。PR表达缺失是Ⅰ~Ⅱ期子宫内膜样腺癌患者术后复发的一个重要的独立危险因素[26]。

P53是一种肿瘤抑制基因，其阳性表达通常提示肿瘤组织的分化差、恶性程度高、预后不良。本研究中不同组织病理类型间P53表达差异有统计学意义(P<0.05)，未发现P53表达与组织分化程度、FIGO分期相关。P53的总阳性率为32.1%，其中在子宫内膜样腺癌中表达阳性率为22.0%，在非子宫内膜样腺癌中表达阳性率为81.0%。既往研究发现，P53的总阳性率为32%~49%，P53的总阳性率在早期EC为10%~15%，晚期EC为40%~52%[27-30]，在特殊病理类型及低分化EC组织中P53阳性率高于子宫内膜样腺癌及高分化EC组织[31]，与本研究结果一致。P53在70%~90%的浆液性EC和10%~35%的子宫内膜样腺癌中过表达，其中在子宫内膜样腺癌患者中P53过表达与组织学3级相关[32]。以往研究中，乳头状浆液性中P53的阳性率明显高于子宫内膜样腺癌[33]。80%的浆液性EC具有P53免疫反应性，而子宫内膜样腺癌仅为20%，非典型子宫内膜增生均无p53免疫反应性[34]。

Ki-67是一种广泛用于评估细胞增殖状态的生物标志物，可以反映肿瘤细胞的增殖活性，与肿瘤的侵袭性和预后密切相关。本研究中Ki-67≥65%表达在组织病理类型间比较差异有统计学意义(P<0.05)。目前EC中Ki-67的界值缺乏统一标准，不同研究Ki-67的中位数分布在10%~65%[35-38]。Ki-67表达与组织病理类型、FIGO分期、肌层浸润深度和分化程度相关[39-40]。本研究以Ki-67≥65%为临界值，发现Ki-67≥65%表达在组织病理类型间比较差异

有统计学意义($P<0.05$)。Ki-67>35%是预测子宫内膜样腺癌深肌层浸润的最佳临界值[40]。Ki-67 水平在低分化和 ER、PR 阴性的 EC 中较高[41],ER 阴性的子宫内膜癌 Ki-67 阳性百分比显著高于 ER 阳性的 EC[42]。

ER、PR、P53 和 Ki-67 的表达状态有助于了解 EC 临床病理特征,预测其恶性程度及预后[43],为选择治疗方案提供依据。

综合分析 EC 患者术前血清肿瘤标志物及术后病理分子标志物,有助于术前全面了解其临床病理特征、选择合适的手术范围、制定规范的综合治疗方案及评估预后。

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(下转第 92 页)

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(2024-09-11 收稿)

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