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Discussion on the Application Value of Coagulation and Blood Lipid in Endometrial Carcinoma

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Abstract

Objective: To retrospectively analyze the difference of the blood coagulation function, D-dimer, platelet and blood lipid between patients with endometrial carcinoma and patients with endometrial benign lesions, and to explore the correlation with the differentiation and stage of endometrial carcinoma. Methods: The clinical and pathological data of 92 patients with endometrial carcinoma and 92 patients with endometrial hyperplasia without atypia were retrospectively analyzed in our hospital from January 2015 to March 2019. Results: The plasma levels of fibrinogen, D-dimer, cholesterol and platelet in endometrial carcinoma patients were significantly higher than those in endometrial hyperplasia without atypia ($P < 0.05$). Moreover, the plasma levels of fibrinogen and D-dimer were increasing with the increase of the differentiation and stage of endometrial carcinoma ($P < 0.05$). However, the plasma levels of the activated partial thrombopiastin time and the high density lipoprotein in endometrial carcinoma patients were significantly lower than those in endometrial hyperplasia without atypia ($P < 0.05$). Conclusion: The high level of blood lipid can be regarded as the early-warning index in the endometrial carcinoma risk group. And the abnormal blood coagulation function can be regarded as the important index to evaluate the differentiation and stage of endometrial carcinoma. And, it can provide the basis to prevent occurrence, advancing and antithrombotic therapy of endometrial carcinoma.

Keywords

Endometrial Carcinoma, Coagulation Function, D-Dimer, Blood Lipid

凝血及血脂相关指标对子宫内膜癌应用价值的探讨

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摘 要

目的：通过回顾性分析凝血指标、血浆D-二聚体、血小板及血脂指标在子宫内膜良恶性患者中的差异，来探讨这些指标跟子宫内膜癌分期和分化程度之间的相关性。方法：对2015年1月至2019年3月就诊于我院妇科经术前诊刮或术后病理结果证实为子宫内膜癌患者92例和子宫内膜不伴有不典型增生的92例患者的临床病理资料进行回顾性分析。结果：子宫内膜癌组纤维蛋白原(fibrinogen FIB)、D-二聚体(D-dimer D-d)、胆固醇(cholesterol TC)及血小板(platelet PLT)水平明显高于子宫内膜不伴有不典型增生的对照组($P < 0.05$)；且FIB及D-二聚体水平随着分化级别的提高及病理分期的增加而增加($P < 0.05$)，而子宫内膜癌患者的部分凝血活酶时间(activated partial thrombopiastin time APTT)水平及高密度脂蛋白(high density lipoprotein HDL)低于子宫内膜不伴有不典型增生的对照组($P < 0.05$)。结论：高血脂状态可作为子宫内膜癌高危人群的预警指标，而凝血异常可作为评估子宫内膜癌恶性程度或预后的重要参考指标。为预防子宫内膜癌的发生、发展及抗血栓治疗提供依据。

关键词

子宫内膜癌，凝血功能，血浆D-二聚体，血脂

1. 引言

子宫内膜癌是指发生于子宫内膜的一组上皮性恶性肿瘤，为女性生殖道三大恶性肿瘤之一，占女性全身恶性肿瘤的 7%，占女性生殖道恶性肿瘤的 20%~30%。据统计全世界范围内每年约有 38 万人新患子宫内膜癌，每年约 9 万人死于子宫内膜癌，其发病率在世界范围内呈上升趋势，且逐渐年轻化[1] [2] [3] [4]。目前，子宫内膜癌尚无明确的病因，但研究发现血脂与子宫内膜癌的发病存在一定关系，但具体不详[5]。妇科恶性肿瘤通常合并血栓栓塞的发生[6]，而子宫内膜癌患者在治疗之前约有 10%患者存在静脉血栓[7]。子宫内膜癌患者的治疗如手术、化疗、放疗及激素治疗等均能增加静脉血栓发生的危险[8]-[13]。本研究分析凝血指标、血浆 D-二聚体、血小板及血脂水平在子宫内膜良恶性患者中的变化，旨在为子宫内膜良恶性疾病的鉴别诊断、术前子宫内膜癌的分期及子宫内膜癌预防提供参考依据。同时，尽早识别子宫内膜癌的高危人群并采取积极措施，为动态监测子宫内膜癌患者血浆 D-二聚体、血小板及凝血指标必要性提供有力依据，其监测指标可预示血栓栓塞的发生风险，并给予及时的干预措施，提高子宫内膜癌患者预后，降低血栓栓塞的风险。

2. 资料与方法

2.1. 研究对象

一般资料：子宫内膜癌组：2015 年 1 月至 2019 年 3 月就诊于我院妇科经术前诊刮或术后病理结果证实为子宫内膜癌的 92 例患者，年龄 40~78 岁。按国际妇产科联盟[14] (international Federation of Gy-

necology and Obstetric FIGO)标准对患者分组，其中 I 期 36 例，II 期 29 例，III 期~IV 期 27 例。对照组：同期住院并由病理确诊为子宫内膜不伴有不典型增生的患者共 92 例，年龄 40~88 岁。2 组研究对象年龄差异没有显著性($P > 0.05$)。

排除标准：①术前接受过放疗或新辅助化疗的患者；②术前未使用影响凝血及止血的药物；③无其他恶性肿瘤及血液系统疾病病史: 如乳腺癌、甲状腺癌、巨幼红细胞性贫血患者；④近 1 周内无感染性疾病，无血栓及出血性疾病。

2.2. 方法

收集受检者清晨静脉血 2 ml，将其置于枸橼酸钠抗凝液试管中 3000 r/min，常温离心 10 min。应用 Sysme*CA-1500 全自动血凝仪，检测凝血酶原时间(prothrombin time PT)、部分凝血活酶时间(APTT)、纤维蛋白原(FIB)、凝血酶时间(thrombin time TT)、D－二聚体、血小板(PLT)。血脂检测均应用全自动生化仪及同一型号配套试剂，检测胆固醇(TC)、甘油三酯(triglycerides TG)、高密度脂蛋白(HDL)、低密度脂蛋白(low density lipoprotein LDL)。

2.3. 统计学方法

采用 SPSS 24.0 软件进行统计分析。首先对定量资料进行正态性检验，符合正态分布的数据采用均数±标准差($\bar{x} \pm s$)表示组间比较采用 t 检验或方差分析；如不服从正态分布，采用中位数($P25$, $P75$)表示，组间比较采用 Kruskal-wallis 秩和检验。所有分析均采用双侧检验。趋势性检验采用方差分析趋势性检验进行统计分析。以 $P < 0.05$ 作为差别有显著统计学意义的判断标准。

3. 结果

3.1. 凝血指标、血脂指标、血浆 D-二聚体及血小板在子宫内膜癌与子宫内膜不伴有不典型增生的患者间的比较

子宫内膜癌患者的 FIB、D-二聚体、TC 及 PLT 水平明显高于对照组的患者($P < 0.05$)，而子宫内膜癌患者的 APTT 水平及 HDL 低于对照组的患者($P < 0.05$)，差异均具有统计学意义。两组年龄之间差异无统计学意义($P > 0.05$)，其他凝血及血脂相关指标在两者之间差异无统计学意义($P > 0.05$)。见表 1。

Table 1. Comparison of coagulation index, lipid index, plasma d-dimer and platelet analysis in endometrial cancer and control group ($\bar{x} \pm s$)

表 1. 凝血指标、血脂指标、血浆 D-二聚体及血小板分析在子宫内膜癌与对照组的比较($\bar{x} \pm s$)

指标	对照组(n = 92)	子宫内膜癌患者(n = 92)	*t* 值	*P*
Age	55.41±4.973	55.22±9.935	−0.16	0.8660
PT (s)	11.12 ± 0.67	11.27 ± 0.77	−1.46	0.1456
APTT (s)	32.65 ± 3.11	30.27 ± 3.13	5.18	<0.0001
TT (s)	19.69 ± 1.61	19.96 ± 2.31	−0.92	0.3588
FIB (g/L)	3.30 ± 0.47	3.57 ± 0.83	−2.69	0.0078
PLT (10^9/L)	294.12 ± 63.72	272.22 ± 81.98	2.02	0.0445
D-d (ug/L)	128.92 ± 67.72	380.92 ± 706.63	−3.41	0.0008
TC (mmol/L)	4.34 ± 0.88	4.61 ± 0.87	−2.08	0.0388
TG (mmol/L)	1.62 ± 0.98	1.89 ± 1.08	−1.80	0.0743
LDL (mmol/L)	2.83 ± 0.83	2.90 ± 0.82	−0.53	0.5955
HDL (mmol/L)	1.39 ± 0.40	1.25 ± 0.32	2.55	0.0115

3.2. 凝血指标、血脂指标、血浆 D-二聚体及血小板在子宫内膜中的比较

将子宫内膜癌患者按照不同分期进行分析，并进行趋势性检验。结果发现，FIB 及 D-二聚体水平随着分期的增加而增加($P < 0.05$)，差异均具统计学意义。不同分化程度的子宫内膜癌患者的年龄、其他凝血指标及血脂对比，差异无统计学意义($P > 0.05$)。见表 2。

Table 2. Comparison of coagulation index, lipid index, plasma d-dimer and platelet analysis in different stages of endometrial cancer($\bar{x} \pm s$)
表 2. 凝血指标、血脂指标、血浆 D-二聚体及血小板分析在子宫内膜癌各分期中的比较($\bar{x} \pm s$)

指标	I 期(n = 36)	II 期(n = 29)	III~IV 期(n = 27)	*P*
Age	56.25 ± 8.49	54.21 ± 11.66	54.93 ± 9.97	0.6045
PT (s)	11.17 ± 0.81	11.29 ± 0.62	11.40 ± 0.86	0.2435
APTT (s)	30.41 ± 3.22	31.02 ± 3.00	29.27 ± 2.99	0.1534
TT (s)	19.64 ± 2.02	19.85 ± 2.27	20.51 ± 2.67	0.1428
FIB (g/L)	3.36 ± 0.37	3.46 ± 0.88	3.97 ± 1.06 *	0.0035
PLT (10^9/L)	280.08 ± 84.75	282.83± 77.55	250.33 ± 81.67	0.1558
D-d (ug/L)	184.97± 113.42	175.00± 61.34	863.37± 1176.48	0.0001
TC (mmol/L)	4.58 ± 0.98	4.68 ± 0.73	4.57 ± 0.90	0.9623
TG (mmol/L)	2.04 ± 1.12	1.92 ± 1.34	1.66 ± 0.65	0.1794
LDL (mmol/L)	3.01 ± 0.93	2.95 ± 0.65	2.69 ± 0.8	0.9719
HDL (mmol/L)	1.2 ± 0.31	1.33 ± 0.30	1.25 ± 0.35	0.5075

3.3. 凝血指标、血脂指标、血浆 D-二聚体及血小板在子宫内膜癌各分化程度中的比较

将子宫内膜癌患者按照不同分化程度进行分析，并进行趋势性检验。结果发现，FIB 及 D-二聚体水平随着分化级别的提高而增加($P < 0.05$)，差异均具有统计学意义。不同分化程度的子宫内膜癌患者的年龄、其他凝血指标及血脂对比，差异无统计学意义($P > 0.05$)。见表 3。

Table 3. Comparison of coagulation index, lipid index, plasma d-dimer and platelet analysis in the differentiation of endometrial cancer($\bar{x} \pm s$)
表 3. 凝血指标、血脂指标、血浆 D-二聚体及血小板分析在子宫内膜癌各分化程度中的比较($\bar{x} \pm s$)

指标	低分化(n = 30)	中分化(n = 28)	高分化(n = 34)	*P*
Age	57.63 ± 10.88	52.89 ± 9.75	55.00 ± 8.97	0.2892
PT (s)	11.29 ± 0.88	11.16 ± 0.66	11.35 ± 0.76	0.7459
APTT (s)	29.59 ± 2.77	30.87 ± 2.64	30.37 ± 3.72	0.3171
TT (s)	20.00 ± 2.04	19.46 ± 2.53	20.34 ± 2.32	0.5561
FIB (g/L)	3.94 ± 0.98	3.56 ± 0.84	3.26 ± 0.50	0.0008
PLT (10^9/L)	266.20 ± 71.11	295.11 ± 104.4	258.68 ± 67.13	0.7130
D-d (ug/L)	719.33 ± 1157.25	229.07± 172.01	207.38± 145.35	0.0031
TC (mmol/L)	4.71 ± 0.82	4.58 ± 1.00	4.55 ± 0.83	0.4814
TG (mmol/L)	1.78 ± 1.02	1.78 ± 1.00	2.08 ± 1.21	0.2653
LDL (mmol/L)	2.96 ± 0.77	2.92 ± 0.79	2.82 ± 0.90	0.9876
HDL (mmol/L)	1.19 ± 0.27	1.30 ± 0.37	1.27 ± 0.32	0.3531

4. 讨论

自 20 世纪中期以来，随着人们生活水平及饮食结构的改变，妇科恶性肿瘤发病率与死亡率也增加，恶性肿瘤患者体内存在异常的凝血状态，恶性肿瘤患者最常见的并发症及死亡原因之一就是血栓形成与出血[15] [16] [17] [18]。因此，妇科恶性肿瘤病因及与凝血功能的问题日益受到重视。

多数研究显示血脂、血糖、血压等代谢异常与子宫内膜癌发病风险密切相关。本研究进一步探索血脂异常与子宫内膜癌之间的关系，结果显示子宫内膜癌患者中 TC 水平呈正相关关系；与 HDL 水平呈负相关关系，而与子宫内膜癌的分期及分化程度无相关。

D-二聚体是纤维蛋白原经凝血酶水解、XIIIa 活化形成的交联纤维蛋白[19]，肿瘤细胞可刺激子宫内膜细胞的凝血途径，导致促凝血物质分泌、纤维蛋白原水解增加及纤维蛋白水平降低，从而产生 D-二聚体[20] [21]，D-二聚体可促进肿瘤细胞的再生、粘附及血管的再生[22]，有研究表明，在乳腺癌[23]、胃癌[24]、结肠癌[25]、肺癌[26]及鼻咽癌[27]中 D-二聚体水平有明显增高。APTT 主要反应内源性凝血是否正常。FIB 可有效反应体内血栓前状态。血小板是止血反应的一种细胞成分。

本研究发现子宫内膜癌患者的 FIB 及 D-二聚体水平明显高于子宫内膜不伴有不典型的增生患者($P < 0.05$)，且随着分期增加及分化程度越差而增加($P < 0.05$)，差异均具有统计学意义，而子宫内膜癌患者的 APTT 及 PLT 水平低于子宫内膜不伴有不典型的增生患者($P < 0.05$)差异均具有统计学意义，提示 FIB、D-二聚体、APTT 及 PLT 水平在术前判断子宫内膜良恶性肿瘤可能有一定的参考价值，而 FIB、D-二聚体对初步判断子宫内膜癌的分期及分化程度有相关性。

综上所述，TC 及 HDL 与子宫内膜癌发生风险有关，通过检测 TC 及 HDL 等血脂生化指标尽早识别具有发生子宫内膜癌可能的高风险人群并积极采取预防措施。FIB、D-二聚体、PLT 及 APTT 对于子宫内膜良、恶性病变的鉴别有意义，而 FIB 及 D-二聚体为子宫内膜癌患者术前分期及分化程度的初步判断提供依据，动态检测子宫内膜癌患者血浆中 D-二聚体浓度及凝血功能指标，筛查子宫内膜癌高风险人群，对其早预防、早诊断、早治疗，改善患者的预后，提高患者生存期，从而降低死亡率。凝血指标和 D-二聚体对子宫内膜癌的临床诊断、治疗和预后有着重要的临床价值。

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