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血小板升高与妇科恶性肿瘤的影响 *

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摘要：血小板升高与多种实体肿瘤的发生发展密切相关，研究表明 14% - 38% 的恶性肿瘤患者伴有血小板升高。虽然目前国内外学者对于定义血小板升高的具体标准尚未完全统一，但大致范围在血小板计数大于 220-400× 10^9/L。大量的临床研究证实恶性肿瘤细胞可以分泌多种生长因子及细胞因子促进血小板升高，而升高的血小板又产生促进肿瘤细胞增殖、血管生长及转移的细胞因子。回顾相关文献在许多妇科恶性肿瘤研究中，除外阴癌外，治疗前的血小板升高多与疾病预后不良有关，由于血小板升高可以通过阻断血栓形成细胞因子来预防，因此对其评估在未来可能具有治疗意义。本文将就妇科恶性肿瘤与血小板升高的具体关联性进行探究。

关键词：血小板；卵巢癌；宫颈癌；子宫内膜癌；外阴癌

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Effect of Elevated Platelet Count on Gynecologic Malignancies*

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ABSTRACT: The increase of platelet is closely related to the development of multiple solid tumors, and studies show that between 14% and 38% of malignant tumors are associated with elevated platelets. Although scholars at home and abroad are not yet fully unified in the specific criteria for the definition of platelet elevation, the general range of platelet counts is greater than 220-400× 10^9/ L. A large number of clinical studies have confirmed malignant tumor cells can secrete a variety of cytokines and growth factors to promote thrombocytosis, and increased platelet and promote tumor cell proliferation, cell growth and metastasis of the tumor blood essels and factor. Review of relevant literature in the study of many gynecologic malignant tumors, except vulval cancer treatment before the increased platelet related to prognosis of disease, more because of the increased platelet can prevent thrombosis by blocking cytokines, thus to evaluate the possible therapeutic significance in the future. This paper will explore the specific correlation between gynecological malignant tumor and platelet.

Key words: Platelets; Ovarian Cancer; Cervical Cancer; Endometrial Cancer; Vulvar Cancer

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前言

目前国内外均有文献报导血小板具有多种功能，尤其在恶性肿瘤中扮演着重要角色。现临床研究已经证明血小板升高与许多实体肿瘤[1-4]患者疾病的发生发展有关，也是影响预后的独立因素。血小板在肿瘤微环境中通过与肿瘤细胞形成瘤栓，释放血小板相关细胞因子，这些细胞因子中最常见的是白细胞介素(IL)- 1、IL - 3、IL - 6、IL - 11、白血病抑制因子、粒细胞 - 巨噬细胞群 - 刺激因子等，特别是 IL - 6 作为一个自分泌生长因子，在各种恶性肿瘤中被过度生产。同时血小板还通过促使内皮细胞回缩，诱导新血管形成等不同机制促进肿瘤细胞的生长和转移[5]。临床大量实践证实妇科恶性肿瘤患者多存在凝血功能异常、血栓形成、微循环障碍等体征，对于晚期恶性肿瘤患者血小板计数及凝血功能变化一直是当前学术界关注的热点[6]。本文通过回顾有关妇科恶性肿瘤与血小板升高的国内外文献，总结血小板在卵巢癌、宫颈癌、子宫内膜癌及外阴癌中对疾病发生发展及预后的影响做如下综述。

1 血小板升高与卵巢癌的关系

卵巢癌是严重威胁女性健康的常见的恶性肿瘤之一，其病死率及复发率较高[7]，尽管手术和放化疗的联合治疗使得近年来生存率有所改善[8]，因其易于复发和远处转移，且发现时大部分患者已为晚期，因此给卵巢癌的预防及治疗增加了难度。据文献报导血小板升高是卵巢癌晚期进展和预后不良的标志[9-11]。在超过 30%的上皮性卵巢癌患者中发现血小板增多症(血小板＞450× 10^9/L)，并与肿瘤无进展期和总生存期有关[12-14]。Li 等[15]研究了 180 余名卵巢上皮癌患者的临床资料，发现血小板水平升高与 CA125 值、淋巴结转移、大量腹水及分期有统计学

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意义，并且发现血小板升高的患者更不易施行理想减瘤术。Cohen 等[16]报道称，血小板计数升高与不满意的肿瘤细胞减灭术相关，明显缩短了复发性疾病的总生存期。这与大多数学者研究相符。Gerestein 等[17]将 118 名卵巢癌患者的血小板计数进行单变量和多变量分析，发现血小板计数可作为 PFS 和 OS 的预测指标。与无复发的患者相比，有进行性疾病的患者和死于疾病的患者的血清血小板计数均较高。此外，BakkumGamez 等人[18]发现术前血小板增多症与术后肠梗阻在上皮性卵巢癌、输卵管癌和原发性腹膜癌有独立的联系。目前几项研究评估了预防血小板增多症在卵巢癌患者中的作用意义重大。Egan 等[19]研究表明血小板附着于卵巢癌细胞，而卵巢癌细胞诱导血小板活化，二者相互作用，形成了恶性循环。Coward 等[20]研究结果表明，肿瘤细胞和宿主组织中细胞因子的增加导致了卵巢癌患者的血小板计数升高，而在患肿瘤的小鼠中应用抗血小板抗体显著降低了肿瘤细胞的生长和血管生成。因此，现在越来越多的证据表明，除了肿瘤相关的因素外，血小板计数升高与卵巢癌患者的生存率有关，并试图研究确定其在卵巢癌中成为独立的预后因素，靶向干预这些细胞因子，抑制血小板升高可能具有治疗卵巢癌的潜力，可为卵巢癌的治疗提供新方向，从而更好地指导个体化治疗策略，并预测患者的预后和生存。

2 血小板升高与宫颈癌的关系

宫颈癌是妇科常见恶性肿瘤之一，其发病率高居全球女性恶性肿瘤第二位，死亡率排名第四[21]。目前多数研究已经评估了血小板升高对宫颈癌的影响，偶尔会产相互矛盾的结果。血小板升高在早期宫颈癌患者中发生率为 25.5%，与肿瘤的分期、肿物的大小及复发相关[22]。申太峰等[23]研究提示宫颈癌患者血小板升高与疾病晚期、脉管瘤栓转移、非鳞状细胞癌及深肌层浸润相关。Hernandez 等[24-26]人对 113 名接受放射治疗的宫颈癌患者进行的第一次研究(1992 年)中发现血小板升高是预后不良的独立指标。另一妇科肿瘤学小组在 2000 年对 291 例没有腹主动脉淋巴结转移的宫颈癌患者研究中，其中有 86 例(29.6%)血小板升高。研究还发现，与血小板计数正常的患者相比，血小板升高患者的死亡率高达 55%。Rodriguez 等[27]对宫颈癌 IB 期患者的研究指出血小板升高与血小板计数正常的(82 比 83.5%)患者的 5 年生存率间差异有统计学意义(P= 0.4)，两项研究结果相符。与此形成对照的是，Lopes 等[28]提出血小板升高并不是在宫颈癌患者中独立的预后因素，他们回顾了 643 名宫颈癌患者的血小板计数，并将其与患者的年龄、疾病分期、组织学类型、淋巴结是否转移进行研究。在单变量分析中，血小板升高的患者 5 年生存率明显低于血小板计数正常的患者(57.1 比 76.5%)。当对疾病分期进行调整后，血小板升高并没有对病人的生存率产生明显的影响。多变量生存分析表明，血小板升高并不是宫颈癌患者生存状况不佳的独立预后因素。这项结果与 De Jong 等[29]的研究相似。虽然血小板计数在不同病理类型及不同疾病分期的宫颈癌患者中存在非常大的差异，但血小板计数对其预后有一定的预测作用[30]。抑制影响血小板增多的相关细胞因子是否可以改善病人的复发及预后，延长生存期，提高生存质量，需要更多的前瞻性研究及临床实践进一步证实。

3 血小板升高与子宫内膜癌的关系

近年来，随着老龄化趋势，子宫内膜癌发病率呈逐年递增[31]。在子宫内膜癌中，血小板升高的差异很大，在 1.5～33.9%之间[32-34]。大多数研究认为血小板升高是子宫内膜癌预后不良的重要指标[33,35]，这在单变量和多变量分析中都是成立的。Gucer 等[33]对 135 例患者研究中发现子宫内膜异位、G2 和 G3 期的肿瘤患者，以及子宫内膜浸润癌和淋巴结浸润的患者，血小板升高的发生率及复发率明显增高。在多因素分析中，血小板升高是子宫内膜癌预后差的预测因子。Gorelic 等[34]报道，在子宫内膜癌患者中 III、IV 期比 II 期患者血小板计数高。血小板正常的子宫内膜癌患者的 PFS 和 OS 明显优于血小板升高的患者。血小板计数正常(n=21)的患者 OS 中位数是 24.0± 4.5 个月，血小板升高(n = 8)的患者 OS 中位数为 7.0± 3.8 个月，P = 0.015 有统计学意义。Scholz 等人[36]在 59 例 III 或 IV 期子宫内膜癌中多变量分析研究指出血小板升高对患者 5 年 DFS 和 OS 有统计学意义。Kologlu 等[37]对 190 例子宫内膜癌患者研究中，发现血小板升高与肿瘤的分期和分级两个因素无关。回顾上述文献，血小板和子宫内膜病变似乎相互作用，促进子宫内膜癌的疾病进展。通过控制血小板升高可减缓子宫内膜癌的预后及复发，为子宫内膜癌的病理生理学提供了新的线索，为临床提供了生物标志物的新途径[38]。

4 血小板升高与外阴癌的关系

外阴癌在女性生殖系统恶性肿瘤中以鳞癌多见，绝经后妇女发病率较高，但其发病率相对较低，近年来由于环境的变化、饮食习惯的改变、人类乳头瘤病毒(HPV)感染率的增加，外阴癌患者的发病率逐年递增，并趋于年轻化[39,40]。Lavie 等[41]研究了 201 例外阴癌患者的血小板计数，并将其与患者的年龄、病程、淋巴结转移、组织学类型及结果相关联。发现血小板升高与肿瘤大小、淋巴结转移发生率、疾病分期无相关性。血小板升高的患者的 5 年生存率与正常血小板计数（分别为 89.29 和 76.47%)无显著差异[42]。结合近些年研究表明外阴鳞癌患者的疾病发展及预后与血小板升高无统计学意义。

5 小结与展望

综上所述，血小板升高是晚期疾病的标志之一，也是卵巢癌患者生存率低的主要因素。在单变量和多变量分析中发现血小板升高与卵巢癌患者的组织学分级、FIGO 分期、术后残余灶以及 CA125 水平密切相关，有统计学意义。研究表明血小板计数升高可能成为卵巢癌细胞侵袭、浸润及转移的不良预后指标，并且可能协助 CA125 在疾病早期提高诊断、评估手术的难易程度、监测术后复发及判断预后等方面发挥作用。而且血小板采集方便，是临床常用的检验指标，便于临床推广，更利于临床应用。目前血小板升高与宫颈癌研究存在很大差异，但大多数研究显示，在单因素分析中血小板升高是影响预后的指标，并与多因素分析中的高肿瘤负担有关。在子宫内膜癌中，血小板计数升高与已知的预后因素有关，如高等级、深层浸润、淋巴结转移、晚期和不良反应。只有在外阴癌中，血小板升高似乎并不是一个提示预后指标。因此通过大量数据反复论证，推断出

血小板升高的临界值与化疗效果的关系,将有利于临床工作的开展,这也是我们下一步准备做的工作。通过卵巢癌细胞和小鼠模型的研究发现,阻断血小板的细胞因子可能会阻止血小板活化和血小板增多。这些细胞因子可能是治疗干预妇科实体肿瘤的新的潜在靶点。虽然其他妇科恶性肿瘤没有报道过类似的研究,但是抑制血小板升高在妇科肿瘤未来治疗中仍具有重要意义[43]。

参 考 文 献(References)

[1] V outsadakis I A. Thrombocytosis as a prognostic marker in gastrointestinal cancers [J]. World Journal of Gastrointestinal Oncology, 2014, 6(2): 34-40

[2] Brown K M, Domin C, Aranha G V, et al. Increased preoperative platelet count is associated with decreased survival after resection for adenocarcinoma of the pancreas [J]. American Journal of Surgery, 2005, 189(3): 278-282

[3] Feng J F, Huang Y, Lu W S, et al. Preoperative platelet count in esophageal squamous cell carcinoma: is it a prognostic factor [J]. Langenbecks Archives of Surgery, 2013, 398(8): 1115-1122

[4] Liu H B, Gu X L, Ma X Q, et al. Preoperative platelet count in predicting lymph node metastasis and prognosis in patients with non-small cell lung cancer[J]. Neoplasma, 2013, 60(2): 203-208

[5] Davis A, Afsharkharghan V, Sood A K. Platelet effects on ovarian cancer[J]. Seminars in Oncology, 2014, 41(3): 378-384

[6] 杨曦,廖秦平,吴成,等;子宫内膜细胞学检查在子宫内膜癌筛查中的应用[J].中华妇产科杂志, 2013, 48(12): 884-890

[7] Mourits M J, de Bock G H. European/U.S. Comparison and Contrasts in Ovarian Cancer Screening and Prevention in a High-Risk Population[J]. Am Soc Clin Oncol Educ Book, 2017, (37): 124-127

[8] Lim H J, Ledger W. Targeted therapy in ovarian cancer [J]. Womens Health, 2016, 12(3): 363-378

[9] Cozzi G D, Samuel J M, Fromal J T, et al. Thresholds and timing of pre-operative thrombocytosis and ovarian cancer survival: analysis of laboratory measures from electronic medical records[J]. Bmc Cancer, 2016, 16(1): 612-617

[10] Antonia D, Voutsadakis I A. Thrombocytosis as a prognostic marker in stage III and IV serous ovarian cancer [J]. Obstetrics and Gynecology Science, 2014, 57(6): 457-463

[11] Stone R L, Nick A M, Mcneish I A, et al. Paraneoplastic thrombocytosis in ovarian cancer [J]. N Engl J Med, 2012, 366(7): 610-618

[12] Bottsfordmiller J, Choi H J, Dalton H J, et al. Differential platelet levels affect response to taxane-based therapy in ovarian cancer [J]. Clinical Cancer Research An Official Journal of the American Association for Cancer Research, 2015, 21(3): 602-610

[13] Cozzi G D, Samuel J M, Fromal J T, et al. Thresholds and timing of pre-operative thrombocytosis and ovarian cancer survival: analysis of laboratory measures from electronic medical records[J]. Bmc Cancer, 2016, 16(1): 612-623

[14] Stone R L, Nick A M, Mcneish I A, et al. Paraneoplastic thrombocytosis in ovarian cancer [J]. N Engl J Med, 2012, 366(7): 610-618

[15] Cass I, Karlan B Y, Li A J, et al. The prognostic significance of hrombocytosis in epithelial ovarian carcinoma [J]. Gynecologic Oncology, 2004, 92(1): 211-214

[16] Cohen J G, Tran A Q, Rimel B J, et al. Thrombocytosis at secondary cytoreduction for recurrent ovarian cancer predicts suboptimal resection and poor survival [J]. Gynecologic Oncology, 2014, 132(3): 556-559

[17] Gerestein C G, Eijkemans M J, De J D, et al. The prediction of progression-free and overall survival in women with an advanced stage of epithelial ovarian carcinoma[J]. Bjog-an International Journal of Obstetrics And Gynaecology, 2009, 116(3): 372-380

[18] Bakkumgamez J N, Langstraat C L, Martin J R, et al. Incidence of and risk factors for postoperative ileus in women undergoing primary staging and debulking for epithelial ovarian carcinoma [J]. Gynecologic Oncology, 2012, 125(3): 614-616

[19] Karl E, Darragh C, Paul S, et al. Platelet Adhesion and Degranulation Induce Pro-Survival and Pro-Angiogenic Signalling in Ovarian Cancer Cells[J]. Plos One, 2011, 6(10): 125-126

[20] Coward J, Kulbe H, Chakravarty P, et al. Interleukin-6 as a therapeutic target in human ovarian cancer [J]. Clinical Cancer Research An Official Journal of the American Association for Cancer Research, 2011, 17(18): 6083-6096

[21] Xu J, Zhang W, Lv Q, et al. Overexpression of miR-21 promotes the proliferation and migration of cervical cancer cells via the inhibition of PTEN[J]. Oncology Reports, 2015, 33(6): 3108-3116

[22] Zhao K, Deng H, Yan Q, et al. Prognostic Significance of Pretreatment Plasma Fibrinogen and Platelet Levels in Patients with Early-Stage Cervical Cancer [J]. Gynecologic and Obstetric Investigation, 2015, 79(1): 25-33

[23] 申太峰, 王悦, 杨帆. 子宫颈浸润癌与血小板增多的临床分析[J]. 中国妇产科临床杂志, 2014(4): 295-297

[24] Hernandez E, Lavine M, Dunton C J, et al. Poor prognosis associated with thrombocytosis in patients with cervical cancer[J]. Cancer, 1992, 69(12): 2975-2977

[25] Hernandez E, Donohue K A, Anderson L L, et al. The significance of thrombocytosis in patients with locally advanced cervical carcinoma: a Gynecologic Oncology Group study [J]. Gynecologic Oncology, 2000, 78(2): 137-142

[26] Zhao K, Deng H, Qin Y, et al. Prognostic significance of pretreatment plasma fibrinogen and platelet levels in patients with early-stage cervical canc- er[J]. Gynecol Obstet Invest, 2015, 79(1): 25-33

[27] Rodriguez G C, Clarke-Pearson D L, Soper J T, et al. The negative prognostic implications of thrombocytosis in women with stage IB cervical cancer[J]. Obstetrics And Gynecology, 1994, 83(3): 445-448

[28] Lopes A, Daras V, Cross P A, et al. Thrombocytosis as a prognostic factor in women with cervical cancer[J]. Cancer, 1994, 74(1): 90-92

[29] De Jonge E T, Viljoen E, Lindeque B G, et al. The prognostic significance of p53, mdm2, c-erbB-2, cathepsin D, and thrombocytosis in stage IB cervical cancer treated by primary radical hysterectomy [J]. International Journal of Gynecological Cancer, 1999, 9(3): 198-205

[30] 王菊萍, 刘秀兰. 妇科恶性肿瘤与血小板升高相关性的研究进展[J]. 世界最新医学信息文摘, 2017(52): 121-122

(下转第 592 页)

[48] Liu CP, Wang SH, Wang WQ, et al. Long Noncoding RNA-Sox2OT Knockdown Alleviates Diabetes Mellitus-Induced Retinal Ganglion Cell (RGC) injury[J]. Cell Mol Neurobiol, 2016, 18: 1-9

[49] Tong Y, Zhou YL, Wang YX, et al. Retinal pigment epithelium cell-derived exosomes: Possible relevance to CNV in wet-age related macular degeneration[J]. Medical Hypotheses, 2016, 97: 98-101

[50] Xu XD, Li KR, Li XM, et al. Long non-coding RNAs: New players in ocular neovascularization[J]. Mol Biol Rep, 2014, 41(7): 4493-4505

[51] Sjakste N, Bielskiene K, Bagdoniene L, et al. Tightly bound to DNA proteins: Possible universal substrates for intranuclear processes [J]. Gene, 2012, 492(1): 54-64

[52] Scheller N, Resainfante P, De ILS, et al. Identification of PatL1, a human homolog to yeast P body component Pat1 [J]. Biophys Acta, 2007, 1773(12): 1786-1792

[53] Venkatesan N, Deepa PR, Khetan V, et al. Computational and in vitro Investigation of miRNA-Gene Regulations in Retinoblastoma Pathogenesis: miRNA Mimics Strategy [J]. Bioinform Biol Insights, 2015, 9: 89-101

[54] Gao YL, Lu XH. Erratum to: Decreased expression of MEG3 contributes to retinoblastoma progression and affects retinoblastoma cell growth by regulating the activity of Wnt/β-catenin pathway [J]. Tumour Biol, 2016, 37(4): 5655

[55] Kruer TL, Dougherty SM, Reynolds L, et al. Expression of the LncRNA Maternally Expressed Gene 3 (MEG3) Contributes to the Control of Lung Cancer Cell Proliferation by the Rb Pathway [J]. PLOS ONE, 2016, 11(11): e0166363

[56] Wang D, Wang D, Wang N, et al. Long Non-Coding RNA BANCR Promotes Endometrial Cancer Cell Proliferation and Invasion by Regulating MMP2 and MMP1 via ERK/MAPK Signaling Pathway[J]. Cell Physiol Biochem, 2016, 40(3-4): 644-656

[57] Zhang ZX, Liu ZQ, Jiang B, et al. BRAF activated non-coding RNA (BANCR) promoting gastric cancer cells proliferation via regulation of NF-kB1[J]. Biochem Biophys Res Commun, 2015, 465(2): 225-231

[58] Su S, Gao J, Wang T, et al. Long non-coding RNA BANCR regulates growth and metastasis and is associated with poor prognosis in retinoblastoma[J]. Tumour Biol, 2015, 36(9): 7205-7211

[59] Kaliki S, Shields CL. Uveal melanoma: relatively rare but deadly cancer[J]. Eye (London, England), 2016, 30(12): 1527-1530

[60] Loewer S, Cabili MN, Guttman M, et al. Large intergenic non-coding RNA-RoR modulates reprogramming of human induced pluripotent stem cells[J]. Nat Genet, 2010, 42(12): 1113-1117

[61] Fan J, Xing Y, Wen X, et al. Long non-coding RNA ROR decoys gene-specific histone methylation to promote tumorigenesis [J]. Genome Biol, 2015, 16(1): 139

[62] Sun L, Sun P, Zhou QY, et al. Long noncoding RNA MALAT1 promotes uveal melanoma cell growth and invasion by silencing of miR-140[J]. Am J Transl Res, 2016, 8(9): 3939-3946

[63] Pan H, Ni H, Zhang L, et al. P2RX7-V3 is a novel oncogene that promotes tumorigenesis in uveal melanoma [J]. Tumour Biol, 2016, 37(10): 13533-13543

[64] Furney SJ, Pedersen M, Gentien D, et al. SF3B1 mutations are associated with alternative splicing in uveal melanoma [J]. Cancer Discov, 2013, 3(10): 1122-1129

[65] Wang Y, Wang Y, Li J, et al. CRNDE, a long-noncoding RNA, promotes glioma cell growth and invasion through mTOR signaling [J]. Cancer Lett, 2015, 367(2): 122-128

[66] Chen Z, Yu C, Zhan L, et al. LncRNA CRNDE promotes hepatic carcinoma cell proliferation, migration and invasion by suppressing miR-384[J]. Am J Cancer Res, 2016, 6(10): 2299-2309

[67] Ding X, Wang X, Lin M, et al. PAUPAR LncRNA suppresses tumourigenesis by H3K4 demethylation in uveal melanoma[J]. FEBS Lett, 2016, 590(12): 1729-1738

（上接第 582 页）

[31] 梁承蓉. 子宫内膜癌患者手术前后血小板参数变化的临床意义[J]. 血栓与止血学, 2017, 23(2): 313-315

[32] Menczer J, Geva D, Schejter E, et al. Elevated platelet count in patients with endometrial carcinoma: correlation with selected prognostic factors and with survival [J]. International Journal of Gynecological Cancer, 2010, 6(6): 463-466

[33] Gü cer F, Moser F, Tamussino K, et al. Thrombocytosis as a Prognostic Factor in Endometrial Carcinoma [J]. Gynecologic Oncology, 1998, 70(2): 210-214

[34] Gorelick C, Andikyan V, Mack M, et al. Prognostic significance of preoperative thrombocytosis in patients with endometrial carcinoma in an inner-city population[J]. International Journal of Gynecological Cancer, 2010, 19(8): 1384-1389

[35] Heng S, Benjapibal M. Preoperative thrombocytosis and poor prognostic factors in endometrial cancer [J]. Asian Pacific Journal of Cancer Prevention, 2014, 15(23): 10231-10236

[36] Scholz H S, Petru E, Gü cer F, et al. Preoperative thrombocytosis is an independent prognostic factor in stage III and IV endometrial cancer[J]. Anticancer Research, 2000, 20(5C): 3983-3985

[37] Kaloglu S, Guraslan H, Tekirdag A I, et al. Relation of Preoperative Thrombocytosis between Tumor Stage and Grade in Patients with Endometrial Cancer[J]. Eurasian J Med, 2014, 46(3): 164-168

[38] Ding D, Liu X, Duan J, et al. Platelets are an unindicted culprit in the development of endometriosis: clinical and experimental evidence[J]. Human Reproduction, 2015, 30(4): 812-832

[39] 侯佳佳, 倪妍. 外阴鳞癌腹股沟淋巴结清扫术的研究进展[J]. 实用医技杂志, 2017, 24(1): 60-63

[40] Sang X B, Zong Z H, Wang L L, et al. E2F-1 targets miR-519d to regulate the expression of the ras homolog gene family member C[J]. Oncotarget, 2017, 8(9): 14777-14793

[41] Lavie O, Comerci G, Daras V, et al. Thrombocytosis in women with vulvar carcinoma[J]. Gynecologic Oncology, 1999, 72(1): 82-86

[42] Li Z L, Liu N, Zhang J, et al. Effect of Shexiang baoxin pills on clopidogrel resistance in patients with acute coronary syndrome [J]. Pakistan Journal of Pharmaceutical Sciences, 2016, 29(6): 2303-2306

[43] Menczer J. Preoperative elevated platelet count and thrombocytosis in gynecologic malignancies [J]. Archives of Gynecology & Obstetrics, 2017, 295(1): 9-15