

子宫腺肌病患者外周血红细胞分布宽度水平检测的临床诊断价值研究

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摘要: 目的 探讨子宫腺肌病患者外周血红细胞分布宽度 (red blood cell distribution width, RDW) 的变化及临床意义。方法 对2020年1月~2022年12月于广西壮族自治区妇幼保健院收治的300例子宫腺肌病患者和250例健康体检者进行回顾性研究。Mann-Whitney U 检验用于比较患者组 (包括治疗前与治疗后) 和健康对照组的血细胞检测参数水平。采用 Spearman 相关分析评估 RDW 与其他血液炎症参数的相关性; 采用 ROC 评估 RDW 在子宫腺肌病中的诊断效能。此外, Logistic 多因素分析子宫腺肌病的独立危险因素。结果 与健康对照组相比, 子宫腺肌病患者的 RDW 水平 [14.60%(13.20% ~ 18.65%) vs 13.00%(12.40% ~ 13.80%)] 升高, 差异具有统计学意义 ($Z=11.396, P=0.001$), 治疗后患者的 RDW 水平 [14.10%(12.10% ~ 15.90%) vs 14.60%(13.20% ~ 18.65%)] 降低, 差异具有统计学意义 ($Z=8.339, P=0.001$)。相关分析结果显示, RDW 与血红蛋白、红细胞压积、平均红细胞体积和绝对淋巴细胞计数呈负相关 ($r=-0.709, -0.614, -0.801, -0.131$, 均 $P < 0.05$), 但与红细胞、血小板和血小板淋巴细胞比率呈正相关 ($r=0.184, 0.439, 0.406$, 均 $P < 0.05$)。ROC 曲线分析显示, RDW 诊断子宫腺肌病的敏感度和特异度分别为 63.0%, 97.6%, 曲线下面积为 0.782, 95% 可信区间为 0.745 ~ 0.819。Logistic 回归分析显示, RDW 和 CA125 是子宫腺肌病发生的独立危险因素 (均 $P < 0.05$)。结论 子宫腺肌病患者的 RDW 升高, 提示 RDW 是子宫腺肌病的潜在辅助诊断指标。

关键词: 子宫腺肌病; 红细胞分布宽度

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Clinical Diagnostic Value of Red Blood Cell Distribution Width in Peripheral Blood of Adenomyosis Patients

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Abstract: Objective To investigate the changes and clinical significance of red blood cell distribution width (RDW) in peripheral blood of patients with adenomyosis. **Methods** A retrospective study was performed on 300 adenomyosis patients and 250 age-matched individuals who were admitted to the Maternal & Child Health Hospital of Guangxi Zhuang Autonomous Region from January 2020 to December 2022. Mann-Whitney U test was used to compare blood parameters between the patient group (including before and after treatment) and the healthy control group. The diagnostic efficacy of RDW in adenomyosis was evaluated by ROC. Spearman correlation method was used to analyze RDW's association with other blood inflammatory parameters. Logistic multivariate analysis was applied to analyze the independent risk factors for adenomyosis. **Results** Compared with healthy control group, RDW values were in patients with adenomyosis [14.60%(13.20% ~ 18.65%) vs 13.00%(12.40% ~ 13.80%)], and the difference was statistically significant ($Z=11.396, P=0.001$). In addition, the RDW levels of patients after treatment were reduced compared with healthy control group [14.10%(12.10% ~ 15.90%) vs 14.60%(13.20% ~ 18.65%)], and the difference was statistically significant ($Z=8.339, P=0.001$). Correlation analysis results showed that RDW was negatively correlated with hemoglobin, hematocrit, mean corpuscular volume and absolute lymphocyte count ($r=-0.709, -0.614, -0.801, -0.131$, all $P < 0.05$), but positively correlated with red blood cell, platelet and platelet lymphocyte ratio ($r=0.184, 0.439, 0.406$, all $P < 0.05$). ROC curve analysis showed that the sensitivity and specificity of RDW for diagnosing adenomyosis were 63.0% and 97.6%, the area under the curve was 0.782, 95% confidence interval was 0.745 ~ 0.819, respectively. Logistic regression analysis showed that RDW was independently associated with adenomyosis (OR=0.755, 95% CI=0.677 ~ 1.347, $P=0.012$). **Conclusion** RDW was elevated in patients with

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adenomyosis, suggesting that RDW may be a potential auxiliary diagnostic marker for adenomyosis.

Keywords: adenomyosis; red blood cell distribution width

子宫腺肌病是一种子宫内膜腺体和间质浸润到子宫内壁的疾病^[1]。由于无症状患者的存在,子宫腺肌病的患病率难以估计^[2],约20%~30%的患者通过影像学诊断为腺肌病^[3-4]。子宫腺肌病过去多发生于40岁以上的经产妇,但近年来有年轻化趋势。据报道,约30%的子宫腺肌病患者没有明显的临床症状,但临床表现如月经紊乱、子宫异常出血、盆腔疼痛或不孕等可对女性身心健康产生严重的负面影响^[5-6]。因此,寻找合适的标记物对于子宫腺肌病快速准确的筛查和提高临床疗效至关重要。

红细胞分布宽度(red blood cell distribution width, RDW)是血细胞检测指标之一,反映了红细胞体积的异质性^[7]。RDW的临床应用主要是作为贫血相关疾病的辅助诊断指标^[8]。近年来文献报道RDW升高反映了机体的炎症状态。研究显示,冠心病^[9]、感染性休克^[10]、子宫内膜癌^[11]和卵巢癌^[12]患者的RDW水平升高。目前尚无RDW与子宫腺肌病的相关性研究,故本文旨在探讨RDW对子宫腺肌病的临床意义。

1 材料与方法

1.1 研究对象 对2020年1月~2022年12月于广西壮族自治区妇幼保健院首次诊断为子宫腺肌病的300例患者的临床资料进行回顾性分析。采用同期体检的250例受试者作为健康对照组。患者组平均年龄40.00(35.00~44.00)岁,对照组平均年龄40.00(35.00~45.00)岁,两组年龄比较差异无统计学意义($Z=-0.359$, $P=0.719$),具有可比性。所有子宫腺肌病患者均未经治疗,并根据国际诊断标准进行诊断。本研究经广西壮族自治区妇幼保健院伦理委员会批准。根据排除和纳入标准,排除有肝炎、心血管疾病、糖尿病、肾脏疾病、血液疾病或曾接受可能干扰血液学治疗的患者。

表1 子宫腺肌病患者与健康对照组血液参数的比较[M(P_{25} , P_{75})]

项目	患者组($n=300$)	健康对照组($n=250$)	Z值	P值
WBC($\times 10^9/L$)	6.35(5.20, 7.60)	5.75(4.90, 6.63)	4.067	0.001
RBC($\times 10^{12}/L$)	4.50(4.10, 4.80)	4.40(4.20, 4.60)	0.704	0.482
Hb(g/L)	115.00(95.25, 130.00)	135.00(130.00, 140.00)	-13.685	0.001
HCT(%)	35.80(31.50, 39.48)	41.00(39.50, 42.33)	-13.016	0.001
MCV(fl)	83.15(69.48, 89.98)	92.80(90.90, 95.23)	-15.075	0.001
PLT($\times 10^9/L$)	291.00(242.25, 356.75)	263.50(230.75, 301.00)	4.793	0.001
LYM#($\times 10^9/L$)	1.75(1.41, 2.14)	1.91(1.64, 2.33)	-4.542	0.001
NEU#($\times 10^9/L$)	3.84(3.04, 5.06)	3.23(2.67, 4.02)	5.991	0.001
RDW(%)	14.60(13.20, 18.65)	13.00(12.40, 13.80)	11.396	0.001
CA125(U/L)	57.79(23.92, 135.90)	13.63(10.07, 18.31)	15.561	0.001
NLR	2.24(1.69, 2.92)	1.67(1.27, 2.16)	8.097	0.001
PLR	165.47(131.51, 230.30)	137.87(112.07, 170.16)	6.856	0.001

1.2 仪器与试剂 迈瑞CAL8000血液分析仪,罗氏E601电化学发光分析仪。此外,本实验室采用Westgard室内质控规则,仪器均进行每日质控监测,所有项目均在控。

1.3 方法 收集每位首次诊断为子宫腺肌病患者的静脉血样(包括治疗前和治疗后)两管。其中一管抽取2ml置于EDTA-K₂抗凝管中,30min内上机检测白细胞计数(white blood cell, WBC)、红细胞计数(red blood cell, RBC)、血红蛋白(hemoglobin, Hb)、红细胞压积(hematokrit, HCT)、平均红细胞体积(mean corpuscular volume, MCV)、血小板计数(platelet, PLT)、RDW,绝对中性粒细胞计数(neutrophil, NEU#)和绝对淋巴细胞计数(lymphocyte, LYM#),计算NLR=NEU#/LYM#, PLR=PLT/LYM#;另一管4ml置于干燥管内,3000r/min离心5min,2h内取血清检测CA125,具体操作严格按照操作说明进行。本院使用的RDW参考范围为11.6%~14.6%。

1.4 统计学分析 SPSS软件用于统计分析,Graphpad Prism 5用于绘图。非正态分布的计量资料用中位数(四分位间距)[M(P_{25} , P_{75})]表示。两组之间的比较采用Mann-Whitney U检验。Spearman用于分析各参数之间的相关性。ROC用于评估曲线下面积(AUC)和95%置信区间(95% CI)。采用Logistic分析子宫腺肌病的独立危险因素。 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 子宫腺肌病患者与健康对照组血液学参数的比较 见表1。与健康对照组比较,子宫腺肌病患者的WBC, PLT, NEU#, RDW, CA125, NLR和PLR水平显著升高,而Hb, HCT, MCV和LYM#水平显著降低,差异具有统计学意义(均 $P<0.05$)。

2.2 子宫腺肌病患者治疗前后血液学参数的比较 见表2。与治疗前组比较,治疗后子宫腺肌病患者的RBC, Hb, HCT, MCV和LYM#水平明显

升高;而NEU#, RDW, CA125, NLR和PLR水平明显降低,差异具有统计学意义(均 $P < 0.05$)。

表2 子宫腺肌病患者治疗前后各项参数比较 [M (P₂₅, P₇₅)]

项目	治疗前组	治疗后组	Z值	P值
WBC (×10 ⁹ /L)	6.35 (5.20, 7.60)	6.10 (5.30, 7.20)	1.124	0.261
RBC (×10 ¹² /L)	4.50 (4.10, 4.80)	4.70 (4.50, 5.70)	-10.221	0.001
Hb (g/L)	115.00 (95.25, 130.00)	131.00 (126.00, 136.00)	-11.915	0.001
HCT (%)	35.80 (31.50, 39.48)	40.50 (39.13, 42.20)	-13.248	0.001
MCV (fl)	83.15 (69.48, 89.98)	83.60 (71.10, 91.08)	-2.018	0.044
PLT (×10 ⁹ /L)	291.00 (242.25, 356.75)	293.00 (243.50, 342.75)	-0.982	0.326
LYM# (×10 ⁹ /L)	1.75 (1.41, 2.14)	2.00 (1.71, 2.40)	-6.679	0.001
NEU# (×10 ⁹ /L)	3.84 (3.04, 5.06)	3.45 (2.76, 4.34)	3.673	0.001
RDW (%)	14.60 (13.20, 18.65)	14.10 (12.10-15.90)	8.339	0.001
CA125 (U/L)	57.79 (23.92, 135.90)	33.22 (10.81, 42.09)	12.817	0.001
NLR	2.24 (1.69, 2.92)	1.68 (1.33, 2.15)	7.917	0.001
PLR	165.47 (131.51, 230.30)	142.56 (111.09, 180.30)	6.201	0.001

2.3 RDW与其他血液参数的相关性分析 相关分析结果显示, RDW与Hb, HCT, MCV和LYM#呈负相关($r=-0.709, -0.614, -0.801, -0.131$, 均 $P < 0.05$),但与RBC, PLT和PLR呈正相关($r=0.184, 0.439, 0.406$, 均 $P < 0.05$)。

2.4 RDW对子宫腺肌病的诊断价值 见图1, 表3。ROC曲线分析评价了RDW及CA125单独或联合检测对子宫腺肌病的诊断效能。值得注意的是, RDW和CA125联合诊断子宫腺肌病均优于单一指标的应用。

表3 不同指标对子宫腺肌病的预测值比较

项目	约登指数	截断值	敏感度 (%)	特异度 (%)	曲线下面积 (95%CI)
RDW	0.406	15.65	63.0	97.6	0.782 (0.745 ~ 0.819)
CA125	0.670	34.06	67.0	99.6	0.885 (0.857 ~ 0.913)
RDW+CA125	0.767	0.44	82.3	94.4	0.927 (0.905 ~ 0.950)

2.5 Logistic模型对子宫腺肌病血液学独立危险因素分析 见表4。以患者是否发生子宫腺肌病为因变量(是=1, 否=0), 以PLT, RDW, CA125,

NLR, PLR为自变量进行多因素Logistic回归分析显示, RDW和CA125是子宫腺肌病发生的独立危险因素(均 $P < 0.05$)。

表4 子宫腺肌病危险因素的Logistic回归分析

因素	β	SE	P值	OR	95%CI
PLT (×10 ⁹ /L)	0.003	0.011	0.810	1.003	0.981 ~ 1.025
RDW (%)	-0.046	0.176	0.012	0.755	0.677 ~ 1.347
CA125 (U/L)	-0.107	0.016	0.001	0.899	0.871 ~ 0.927
NLR	-0.041	0.868	0.962	0.960	0.175 ~ 5.261
PLR	0.024	0.018	0.190	1.024	0.988 ~ 1.061

3 讨论

子宫腺肌病的病因尚不清楚, 但可能与遗传、激素和宫内操作(如刮宫、流产、分娩等)有关。如果子宫增大、月经出血、盆腔疼痛等临床症状不能通过药物控制, 最终可进行子宫切除^[13-14]。目前,

子宫腺肌病的诊断多从临床怀疑开始, 最终通过病理、阴道超声和盆腔磁共振证实^[15]。影像学技术易受环境因素影响, 且具有较高的放射学和医疗成本; 而病理检查是确定肿瘤具体位置和体积的一种有创检测方法。因此, 一种简单、快速、有效的血液学

检测方法对于子宫腺肌病的早期诊断和及时治疗具有重要的临床意义。

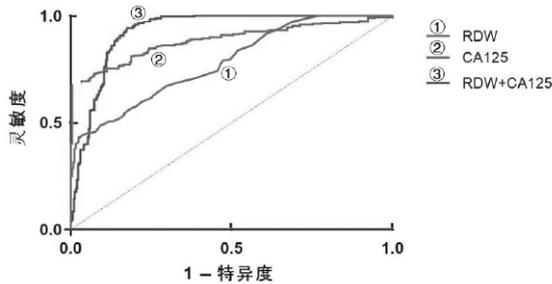


图1 RDW与CA125单独或联合检测对子宫腺肌病诊断效能的ROC曲线

RDW作为一种低成本的测试,通常报告于全血细胞计数中。据文献报道,升高的RDW与许多自身免疫性疾病(如系统性红斑狼疮、桥本氏甲状腺炎、自身免疫性肝炎)等的发生及疾病活动程度相关^[16]。RDW在反映炎症方面有重要意义。基于对年龄和血液学参数的多元分析,我们观察到子宫腺肌病患者RDW与疾病活动之间的关联。在这项回顾性研究中,子宫腺肌病患者的RDW水平明显高于健康对照组,治疗后腺肌病患者的RDW水平显著降低。Logistic回归分析也表明RDW该病的独立危险因素。这提示RDW对子宫腺肌病的疾病进展具有一定的诊断价值。类似,ZHANG等^[17]发现侵袭性葡萄胎患者的RDW明显高于健康对照组。KEMAL等^[18]回顾性分析了113例子宫内膜癌患者的血液学参数,发现RDW水平显著高于良性组;此外,RDW与子宫内膜癌的临床病理特征显著相关。张玲玲等^[19]观察到Ⅲ期和Ⅳ期绒毛膜癌患者的RDW水平高于Ⅰ期和Ⅱ期患者,且RDW与癌症分期呈正相关。这些国内外的报道与我们的研究结果相符合。由此可推测,若RDW升高是炎症状态的指标,那么炎症状态更明显的疾病或更具侵袭性的肿瘤将导致更高水平的RDW。此外,本研究发现RDW与Hb和MCV呈负相关,与其它炎症参数(PLT和NLR)呈正相关,这提示RDW不仅与子宫腺肌病患者出血情况密切相关,也进一步确认了RDW与炎症状态之间的密切作用。

RDW在炎症中的机制尚未完全明确,但可能存在与机体在疾病状态下释放的炎症因子(如白细胞介素、肿瘤坏死因子)有关^[20]。炎症因子可抑制促红细胞生成素对骨髓红细胞干细胞的刺激作用、抗凋亡作用和细胞成熟作用,使更多未成熟红细胞释放到外周血循环从而引起RDW升高^[21]。此外,HUNZIKER等^[22]研究表明,炎症反应和氧化应激可影响红细胞生成,改变血细胞膜变形能力和红细

胞半衰期升高RDW水平。最后,炎症会导致机体营养消耗增加和吸收不良,在缺乏铁、叶酸和维生素B12的情况下容易诱发贫血导致RDW增加。研究表明,子宫腺肌病与慢性炎症互为因果^[23]。由黄体酮水平上升驱动的人类去个体化过程促进了腺肌瘤细胞血管生成和纤维生成因子的产生,这种持续的炎症与子宫腺肌病的发病机制密切相关。本研究的对象为子宫腺肌病患者,大部分具有子宫异常出血病史,机体慢性失血和营养不良也可引起RDW的增加。

综上,本研究首次揭示了RDW在子宫腺肌病诊断中的潜在价值,提示这种简单、通用且易于测量的测试可作为辅助诊断子宫腺肌病的新标志物。本研究有一些局限性:首先,我们排除了有可能影响RDW病史的患者,这导致本研究的样本量较小。其次,虽然调整了多种影响RDW水平的危险因素和疾病,但可能存在其他混杂因素。在未来,仍需要大规模的前瞻性研究来证实RDW在子宫腺肌病患者中的重要性。

参考文献:

- [1] CHAPRON C, VANNUCCINI S, SANTULLI P, et al. Diagnosing adenomyosis: an integrated clinical and imaging approach[J]. Human Reproduction Update, 2020, 26(3): 392-411.
- [2] BOURDON M, SANTULLI P, MARCELLIN L, et al. Adenomyosis: an update regarding its diagnosis and clinical features[J]. Journal of Gynecology Obstetrics and Human Reproduction, 2021, 50(10): 102228.
- [3] CHAPRON C, TOSTI C, MARCELLIN L, et al. Relationship between the magnetic resonance imaging appearance of adenomyosis and endometriosis phenotypes[J]. Human Reproduction, 2017, 32(7): 1393-1401.
- [4] PINZAUTI S, LAZZERI L, TOSTI C, et al. Transvaginal sonographic features of diffuse adenomyosis in 18-30-year-old nulligravid women without endometriosis: association with symptoms[J]. Ultrasound in Obstetrics & Gynecology, 2015, 46(6): 730-736.
- [5] MOAWAD G, KHEIL M H, AYOUBI J M, et al. Adenomyosis and infertility[J]. Journal of Assisted Reproduction and Genetics, 2022, 39(5): 1027-1031.
- [6] ZHAI Junyu, VANNUCCINI S, PETRAGLIA F, et al. Adenomyosis: mechanisms and pathogenesis[J]. Seminars in Reproductive Medicine, 2020, 38(2-03): 129-143.
- [7] SALVAGNO G L, SANCHIS-GOMAR F, PICANZA A, et al. Red blood cell distribution width: a simple parameter with multiple clinical applications[J]. Critical Reviews in Clinical Laboratory Sciences, 2015, 52(2): 86-105.
- [8] MARZOUK H, MOSTAFA N, KHALIFA I, et al. Red cell distribution width(RDW)as a marker of subclinical

- inflammation in children with familial mediterranean fever[J]. *Current Rheumatology Reviews*, 2020, 16(4): 298-303.
- [9] 罗金, 蓝柳萍. 血液 RDW, Hcy 和 NEFA 水平联合检测在冠心病诊断中的应用 [J]. *现代检验医学杂志*, 2020, 35 (3) : 62-65, 80.
- LUO Jin, LAN Liuping. Application of combined detection of blood RDW, Hcy and NEFA levels in the diagnosis of coronary heart disease[J]. *Journal of Modern Laboratory Medicine*, 2020, 35(3): 62-65, 80.
- [10] GUPTA M K, YADAV G, SINGH Y, et al. Correlation of the changing trends of red cell distribution width and serum lactate as a prognostic factor in sepsis and septic shock[J]. *Journal of Anaesthesiology Clinical Pharmacology*, 2020, 36(4): 531-534.
- [11] 张红雨, 陆奉科, 李山, 等. 子宫内膜癌患者血清 CA125 水平与外周血 RDW 检测在临床病理分期中的应用价值 [J]. *现代检验医学杂志*, 2020, 35 (1) : 94-96, 100.
- ZHANG Hongyu, LU Fengke, LI Shan, et al. Value of serum CA125 level and peripheral blood RDW detection in clinical pathological staging of patients with endometrial cancer[J]. *Journal of Modern Laboratory Medicine*, 2020, 35(1): 94-96, 100.
- [12] QIN Yuanyuan, WU Yangyang, XIAN Xiaoying, et al. Single and combined use of red cell distribution width, mean platelet volume, and cancer antigen 125 for differential diagnosis of ovarian cancer and benign ovarian tumors[J]. *Journal of Ovarian Research*, 2018, 11(1): 10.
- [13] LACHETA J. Uterine adenomyosis: pathogenesis, diagnostics, symptomatology and treatment[J]. *Ceska Gynekologie*, 2019, 84(3): 240-246.
- [14] SZUBERT M, KOZIRÓG E, OLSZAK O, et al. Adenomyosis and infertility-review of medical and surgical approaches[J]. *International Journal of Environmental Research and Public Health*, 2021, 18(3): 1235.
- [15] SCHRAGER S, YOGENDRAN L, MARQUEZ C M, et al. Adenomyosis: diagnosis and management[J]. *American Family Physician*, 2022, 105(1): 33-38.
- [16] LIU Lingyan, CAO Junying, ZHONG Zhengrong, et al. Noninvasive indicators predict advanced liver fibrosis in autoimmune hepatitis patients[J]. *Journal of Clinical Laboratory Analysis*, 2019, 33(7): e22922.
- [17] ZHANG Lingling, XIE Youjun, ZHAN Lingling. The potential value of red blood cell distribution width in patients with invasive hydatidiform mole[J]. *Journal of Clinical Laboratory Analysis*, 2019, 33(4): e22846.
- [18] KEMAL Y, DEMIRAG G, BAS B, et al. The value of red blood cell distribution width in endometrial cancer[J]. *Clinical Chemistry and Laboratory Medicine*, 2015, 53(5): 823-827.
- [19] 张玲玲, 谢有军, 詹灵凌. 绒毛膜癌患者的红细胞分布宽度及其临床意义 [J]. *广西医学*, 2019, 41 (6) : 665-667.
- ZHANG Lingling, XIE Youjun, ZHAN Lingling. Red blood cell distribution width and its clinical significance in patients with choriocarcinoma[J]. *Guangxi Medical Journal*, 2019, 41(6): 665-667.
- [20] MORENO-TORRES V, SÁNCHEZ-CHICA E, CASTEJÓN R, et al. Red blood cell distribution width as a marker of hyperinflammation and mortality in COVID-19[J]. *Annals of Palliative Medicine*, 2022, 11(8): 2609-2621.
- [21] MAY J E, MARQUES M B, REDDY V V B, et al. Three neglected numbers in the CBC: the RDW, MPV, and NRBC count[J]. *Cleveland Clinic Journal of Medicine*, 2019, 86(3): 167-172.
- [22] HUNZIKER S, CELI L A, LEE J, et al. Red cell distribution width improves the simplified acute physiology score for risk prediction in unselected critically ill patients[J]. *Critical Care*, 2012, 16(3): R89.
- [23] KOBAYASHI H. Endometrial inflammation and impaired spontaneous decidualization: insights into the pathogenesis of adenomyosis[J]. *International Journal of Environmental Research and Public Health*, 2023, 20(4): 3762.

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- [19] ZAMAN V, SHIELDS D C, SHAMS R, et al. Cellular and molecular pathophysiology in the progression of Parkinson's disease[J]. *Metabolic Brain Disease*, 2021, 36(5): 815-827.
- [20] AARSLAND D, BATZU L, HALLIDAY G M, et al. Parkinson disease-associated cognitive impairment[J]. *Nature Reviews Disease Primers*, 2021, 7(1): 47.
- [21] STOKOWSKA A, KÄLL B L, BLOMSTRAND C, et al. Plasma neurofilament light chain levels predict improvement in late phase after stroke[J]. *European Journal of Neurology*, 2021, 28(7): 2218-2228.
- [22] SCHRANZ D, MOLNAR T, ERDO-BONYAR S, et al. Fatty acid-binding protein 3 and CXC-chemokine ligand 16 are associated with unfavorable outcome in aneurysmal subarachnoid hemorrhage[J]. *Journal of Stroke and Cerebrovascular Diseases*, 2021, 30(11): 106068.
- [23] 朱学芳, 朱建建, 沈海清. 基于 TLR4/NF- κ B 信号通路及血清 CXCL16, ACA 评价依达拉奉右莰醇对 ACI 神经功能的保护作用 [J]. *脑与神经疾病杂志*, 2023, 31(7): 401-406.
- ZHU Xuefang, ZHU Jianjian, SHEN Haiqing. Protective effect of edaravone dexbornol on neurological function in patients with acute cerebral infarction through TLR4/NF- κ B signaling pathway and serum CXCL16, ACA[J]. *Journal of Brain and Nervous Diseases*, 2023, 31(7): 401-406.

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