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血小板 / 淋巴细胞比值评估急性冠脉综合征冠脉病变严重程度 的临床价值 *

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摘要 目的:探讨血小板淋巴细胞比值(platelet-to-lymphocyte ratio, PLR)评估急性冠脉综合征(acute coronary syndrome, ACS)冠脉病变严重程度中的临床价值。**方法:**回顾性分析 2015 年 3 月至 2017 年 3 月在南京市第一医院心血管内科行冠脉造影的 168 例 ACS 患者的临床资料,其中不稳定型心绞痛(unstable angina, UA) 52 例,非 ST 段抬高型心肌梗死(non-ST-segment elevation myocardial infarction, NSTEMI) 54 例,ST 段抬高型心肌梗死(ST-segment elevation myocardial infarction, STEMI) 62 例,根据冠脉造影结果进行 Gensini 评分,采用 Spearman 相关分析对 PLR 和 Gensini 评分进行相关性分析。**结果:**三组白细胞总数、淋巴细胞计数以及 LDL 比较差异均有统计学意义($P < 0.05$),STEMI 组白细胞总数、淋巴细胞计数明显高于 UA 组及 NSTEMI 组,LDL 显著低于 UA 组及 NSTEMI 组,且 NSTEMI 组白细胞总数、淋巴细胞计数明显高于 UA 组,LDL 显著低于 UA 组。此外,NSTEMI 和 STEMI 组 PLR 和 Gensini 评分显著均高于 UA 组 ($P < 0.05$)。Spearman 相关性分析显示 PLR 与 Gensini 评分呈正相关($r = 0.2205, P = 0.0114$)。多元逐步回归分析结果显示 PLR 和白细胞总数均是 Gensini 评分的影响因素。**结论:**PLR 在评估 ACS 患者冠脉病变严重程度中具有一定的价值,其值越高,冠脉病变越重。

关键词:急性冠脉综合征;血小板 / 淋巴细胞比值;Gensini 评分

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Clinical Significance of Platelet-to-Lymphocyte Ratio for the Severity Evaluation of Coronary Artery Disease in Patients with Acute Coronary Syndrome*

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ABSTRACT Objective: To explore the role of platelet-to-lymphocyte ratio (PLR) in evaluating the severity of coronary lesion in patients with acute coronary syndrome (ACS). **Methods:** A total of 168 patients with ACS who undergoing coronary angiography in department of cardiovascular medicine of Nanjing First Hospital were included in this study from March 2015 to March 2017. The severity of coronary artery was evaluated using Gensini score. A Spearman correlation analysis was used for the relationship between PLR and Gensini score. **Results:** There were significant differences in the white blood cells, lymphocyte and low density lipoprotein between UA, NSTEMI and STEMI groups ($P < 0.05$). White blood cells and lymphocyte were higher in STEMI group compared to that of UA and NSTEMI, and serum LDL level was significant lower than that of UA and NSTEMI groups. Further analysis showed that white blood cells and lymphocyte in NSTEMI group were significantly higher than UA group, but LDL was lower than UA group. Moreover, the PLR and Gensini score in NSTEMI and STEMI groups were significantly higher than in UA group ($P < 0.05$). There was a positive significant correlation between PLR and Gensini score ($r = 0.2205, P = 0.0114$). Multiple stepwise regression analysis showed that both PLR and white blood cells are influence factors for Gensini score. **Conclusions:** PLR is significantly related to the severity of coronary lesion. Higher level of PLR indicated more serious artery lesion in patients with ACS.

Key words: Acute coronary syndrome; Platelet-to-lymphocyte ratio; Gensini score

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前言

急性冠脉综合征(Acute coronary syndrome, ACS)是冠心病

的最主要表现,包括不稳定型心绞痛(unstable angina, UA)、非 ST 段抬高型心肌梗死(non-ST-segment elevation myocardial infarction, NSTEMI)和 ST 段抬高型心肌梗死(ST-segment eleva

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tion myocardial infarction, STEMI)。尽管经过抗凝、扩冠等药物治疗和积极的经皮腔内冠状动脉成形术等介入治疗, ACS 的病死率仍然较高。目前,除了心电图、心肌酶谱以及肌钙蛋白等指标,评价 ACS 病情严重程度的金标准仍然是冠状动脉造影,但是由于其操作的有创性及风险,筛选新的无创性损伤标记物显得尤为必要。

血小板和淋巴细胞的变化均可体现炎症的程度,既往研究表明血小板计数增高和淋巴细胞计数降低与心血管疾病相关^[1,2]。而近年来血小板淋巴细胞比值(platelet-to-lymphocyte ratio, PLR)被认为是多种心血管疾病的炎症标志物和不良预后的预测指标^[3-5],但其在评价不同类型急性冠脉综合征冠脉病变严重程度中的意义尚不完全明确。因此,本研究主要探讨了 PLR 与急性冠脉综合征患者 Gensini 评分的相关性,旨在评价其在 ACS 患者冠脉病变程度中的预测价值。

1 资料与方法

1.1 研究对象

选择 2015 年 3 月至 2017 年 3 月年在南京市第一医院心血管内科住院行冠状动脉造影的急性冠脉综合征患者 168 例,其中男性 138 例,女性 26 例,平均(61.2±11.5)岁。根据 ACS 诊断标准,分为 UA 52 例, NSTEMI 54 例, STEMI 62 例。排除标准:血流动力学障碍、急慢性感染性疾病、风湿性疾病、严重肾脏或肝脏疾病、血液系统疾病、恶性肿瘤、既往曾行冠状动脉介入治疗或冠状动脉搭桥术者。

1.2 研究方法

采用回顾性病例分析方法,通过医院病历系统收集研究对象的临床资料,一般情况如年龄、性别、吸烟史、既往病史(高血

压病、糖尿病);入院后的血常规检查包括白细胞计数(white blood cell, WBC)、血小板计数、淋巴细胞计数;低密度脂蛋白胆固醇(low density lipoprotein, LDL)。冠状动脉造影结果根据美国心脏协会规定的冠状动脉血管图像积分评分标准,采用 Gensini 评分系统评价冠脉病变的严重程度^[6]。

1.3 统计学方法

采用 SPSS19.0 统计软件进行数据的统计分析。计量资料符合正态分布者以均数±标准差($\bar{x} \pm s$)表示,多组间比较采用单因素方差分析或秩和检验。计数资料采用百分率表示(%),组间比较采用卡方检验。Gensini 评分与 PLR 之间的相关性分析采用 Spearman 相关性检验进行评估。采用多元逐步回归分析影响 Gensini 评分的因素。P<0.05 为差异有统计学意义。

2 结果

2.1 各组患者基线资料和实验室结果的比较

UA 组、NSTEMI 和 STEMI 三组患者性别构成、糖尿病、高血压以及血小板计数比较差异均无统计学意义(P 均>0.05)。UA 组及 NSTEMI 组患者年龄大于 STEMI 组(P<0.05)。三组吸烟患者所占比例方面差异有统计学意义(P<0.05), STEMI 组(79.0%)和 NSTEMI(81.8%)吸烟患者所占比例明显高于 UA 组(61.9%)。三组白细胞总数、淋巴细胞计数以及 LDL 比较差异均有统计学意义(P<0.05), STEMI 组白细胞总数、淋巴细胞计数明显高于 UA 组及 NSTEMI 组, LDL 显著低于 UA 组及 NSTEMI 组,且 NSTEMI 组白细胞总数、淋巴细胞计数明显高于 UA 组, LDL 显著低于 UA 组。此外, NSTEMI 和 STEMI 组 PLR 和 Gensini 评分显著均高于 UA 组(P<0.05)。详见表 1。

表 1 三组患者基线资料和实验室结果比较

Table 1 Comparison of the baseline characteristics and laboratory results between three groups

Variables	UA(n=52)	NSTEMI(n=54)	STEMI(n=62)	P value
Age, years	64.6±10.5 ^b	64.3±11.1 ^c	57.9±11.3 ^{bc}	0.004
Male, n(%)	42(80.7%)	44(81.5%)	52(83.9%)	0.921
Smoking, n(%)	32(61.5%) ^{ab}	44(81.5%) ^a	49(79.0%) ^b	0.026
Hypertension, n(%)	28(53.8%)	28(51.9%)	37(59.7%)	0.736
Diabetes mellitus, n(%)	8(15.4%)	10(18.5%)	15(24.2%)	0.251
LDL(mmol/L)	2.35±0.61 ^b	2.71±0.78 ^c	3.19±0.85 ^{bc}	<0.001
WBC(×10 ⁹ /L)	6.58±1.75 ^{ab}	10.06±2.76 ^{ac}	11.78±3.33 ^{bc}	<0.001
Lymphocyte(×10 ⁹ /L)	1.74±0.52 ^{ab}	1.46±0.50 ^a	1.36±0.59 ^b	0.006
Platelet(×10 ⁹ /L)	207±39	208±59	204±57	0.925
PLR	126.8±38.1 ^{ab}	157.2±42.0 ^a	176.7±45.1 ^b	0.002
Gensini score	65±26 ^{ab}	77±28 ^a	91±30 ^b	0.01

Note: ^a, between UA group and USTEMI group, P<0.05; ^b, between UA group and STEMI group, P<0.05; ^c, between USTEMI group and STEMI, P<0.05.

2.2 PLR 与 Gensini 评分的相关性分析

采用 Spearman 相关性分析评估 PLR 与 Gensini 评分的相关关系,结果显示 PLR 与 Gensini 评分呈显著正相关(r=0.2205, P=0.0114),见图 1。

2.3 Gensini 评分影响因素的多元逐步回归分析

为进一步评估影响 Gensini 评分的影响因素,将 Gensini 评

分作为因变量,年龄、白细胞计数、淋巴细胞计数、PLR 和 LDL 作为自变量,选择自变量进入模型的显著水平为 0.05,剔除变量的显著水平为 0.10,进行多元逐步回归分析,如表 2 所示, PLR 和白细胞总数均是 Gensini 评分的影响因素,且与 Gensini 评分呈正相关。

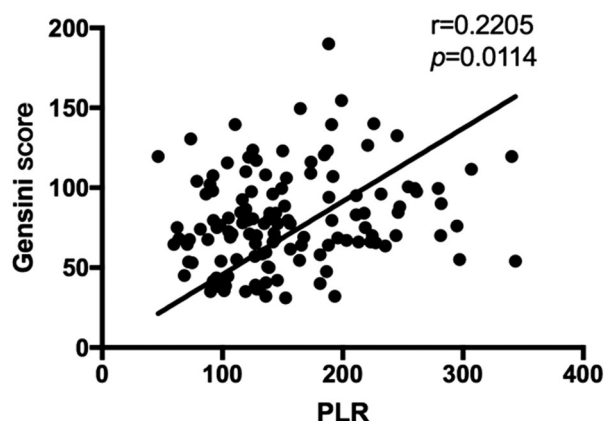


图1 PLR 与 Gensini 评分的相关性

Fig.1 The correlation of PLR with Gensini score

表2 Gensini 评分影响因素的多元逐步回归分析

Table 2 Multiple stepwise regression analysis between variables and Gensini score

Variables	B	SE	β	t	P
Constant	29.957	9.152	-	3.273	0.001
PLR	0.228	0.046	0.397	5.01	0.000
WBC	1.737	0.677	0.204	2.567	0.011

$R^2=0.220$, Adjusted $R^2=0.207$.

ACS 的病理基础是动脉粥样硬化,且炎症在动脉粥样硬化的发病中发挥重要的作用^[8,9]。炎症反应的程度与 ACS 不稳定斑块的形成和变化相关^[10-12]。多种炎症细胞如巨噬细胞、淋巴细胞等均参与斑块的形成。既往研究表明多种炎症反应标记物如基质金属蛋白酶^[13]、白细胞介素 6^[14]、超敏 C-反应蛋白 (high-sensitivity C-reactive protein, hs-CRP)^[15]等均与冠脉病变不稳定斑块的形成和发展相关,因此被认为是 ACS 的生物标记物。但是这些标记物未得到临床的广泛应用,如多项研究对各种炎症指标对 ACS 的预测效能并不一致。因此,探寻研究新型的炎症标记物对于 ACS 的病情评估仍有十分重要的意义。

血细胞计数是一项简便、快速、廉价的常规检测技术,又提供很多信息,包括分类血细胞计数、中性粒细胞/淋巴细胞比值(neutrophil-to-lymphocyte ratio, NLR)和 PLR 等。NLR 在肿瘤以及心血管疾病预后评估中的意义已有较多研究报道^[16-18]。血小板在冠心病的发病中起着重要的作用,包括血小板的活化以及血小板计数的增加等^[19-21]。淋巴细胞在炎症因子的刺激下可以活化,而活化的淋巴细胞又可释放炎症因子如白细胞介素等,参与动脉粥样硬化的发生发展^[22,23]。PLR 是一种新型的、简便可行的炎症标志物,其水平的升高与多种心血管疾病如非勺型高血压、冠状动脉侧支循环形成不良及周围动脉闭塞性疾病相关^[24-26]。Azab 等研究证实 PLR 升高是 NSTEMI 患者长期死亡率的独立危险因素^[27]。郭英杰等人的研究亦表明 PLR 与 NSTEMI 患者的冠脉病变严重程度相关^[28]。Hudzik 等研究发现 PLR 升高对糖尿病合并 STEMI 患者的短期和长期死亡率有较好的预测价值^[29]。李少辉等^[30]研究结果表明 PLR 是急性 STEMI 患者冠脉介入治疗后无复流的预测因素。既往的研究多为 ACS 的某一种类型,无法说明 PLR 在所有 ACS 患者病情评估中的意义,而本研究中纳入的患者包括了三种类型的 ACS 患者,结

3 讨论

ACS 患者冠状动脉病变的严重程度与患者严重并发症的发生率及死亡率密切相关。Gensini 评分是基于冠状动脉造影图像,根据冠脉病变的数目、部位和狭窄程度进行评分,分值越高冠脉病变越严重,能较为客观地评估冠脉病变的严重程度。本研究结果亦显示 STEMI 组和 NSTEMI 组 Gensini 评分高于 UA 组,也提示 Gensini 评分对 ACS 患者病情的评估价值^[7]。虽然,该评分方法能较为准确的反映患者的冠脉病变程度,但是要获得这些资料,需要进行冠脉造影这一侵入性检查。因此,仍需探寻简便、高效的非侵入性方法来评估 ACS 的病变程度和严重性。

果显示三组患者在白细胞总数、淋巴细胞计数以及 LDL 方面存在差异,与既往研究一致。白细胞是非特异性炎症标记物, Gensini 评分在 NSTEMI 和 STEMI 组均高于 UA 组,说明 NSTEMI 和 STEMI 组冠脉病变程度高于 UA 组,且 PLR 的变化趋势与 Gensini 评分一致。进一步通过 Spearman 相关性分析显示 PLR 与 ACS 患者 Gensini 评分呈显著的正相关,表明 PLR 升高,冠脉病变程度越重,与既往 ACS 某一分型中的研究结果基本一致。为进一步探寻影响 ACS 患者 Gensini 评分的因素,我们进行了多元逐步回归分析,结果显示 PLR 和白细胞总数是 ACS 患者冠脉病变程度的危险因素,这也与既往研究结论基本一致。而年龄、淋巴细胞计数以及 LDL 在统计分析中被剔除,说明这些自变量与 Gensini 评分无明显的相关性。而既往研究表明淋巴细胞的下降与心血管疾病相关^[2],可能与本研究样本数量相对较小有关。

综上,PLR 可以从血常规检验中简单、快捷地获取,其水平的升高与冠脉病变严重程度相关,可能在预测 ACS 高危患者以及尽快地选择合适的治疗方案方面具有一定的意义。但是鉴于本研究纳入的研究对象较少,后期需要扩大样本量进一步验证我们的结论,同时需要进行前瞻性的研究以充分的说明问题,以期临床诊治提供简便有效的策略。

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