

· 临床研究 ·

中性粒细胞/淋巴细胞比值与不稳定型心绞痛行经皮冠状动脉介入治疗的关系

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【摘要】目的 探讨中性粒细胞/淋巴细胞比值(NLR)与不稳定型心绞痛(UAP)患者需行经皮冠状动脉介入(PCI)治疗的关系。**方法** 选择2018年1月至2019年6月河南科技大学第一附属医院心血管内科收治的260例UAP患者为研究对象,根据冠状动脉造影结果,分为需行PCI组167例和无需行PCI组93例。收集2组患者的临床资料并进行比较。采用SPSS 24.0软件进行数据处理。采用logistic回归法分析UAP患者需行PCI治疗的危险因素。受试者工作特征(ROC)曲线分析NLR对UAP患者需行PCI治疗的诊断价值。**结果** 2组患者年龄、糖尿病史、中性粒细胞、总胆固醇(TC)、高密度脂蛋白胆固醇(HDL-C)、低密度脂蛋白胆固醇(LDL-C)、NLR水平比较,差异均有统计学意义($P<0.05$)。Spearman相关性分析显示,NLR与UAP患者需行PCI治疗呈正相关($r=0.353, P<0.001$)。多因素logistic回归分析显示NLR是UAP患者需行PCI治疗的独立危险因素($OR=1.982, 95\%CI 1.168 \sim 3.362$)。ROC曲线分析显示,NLR预测UAP患者需行PCI治疗的曲线下面积为0.713(95%CI 0.651~0.776)。**结论** NLR可作为UAP患者需行PCI治疗的预测指标之一。

【关键词】 中性粒细胞/淋巴细胞比值;不稳定型心绞痛;经皮冠状动脉介入;相关性

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Relationship between neutrophil-to-lymphocyte ratio and unstable angina during percutaneous coronary intervention

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【Abstract】 Objective To explore the relationship between neutrophil-to-lymphocyte ratio (NLR) and percutaneous coronary intervention (PCI) in the patients with unstable angina pectoris (UAP). **Methods** A total of 260 UAP patients admitted to the Department of Cardiology of the First Affiliated Hospital of Henan University of Science and Technology from January 2018 to June 2019 were enrolled in this study. According to the results of coronary angiography, they were divided into PCI group ($n=167$) and the group without the need for the procedure ($n=93$). The clinical data were collected and compared between the two groups. SPSS statistics 24.0 was used for data processing. Logistic regression analysis was employed to analyze the risk factors for PCI in UAP patients. Receiver operating characteristic (ROC) curve was plotted to analyze the diagnostic value of NLR for UAP patients who needed PCI. **Results** There were statistical differences between the two groups in age, gender, history of diabetes mellitus, neutrophil count, levels of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C), and NLR ($P<0.05$). Spearman correlation analysis showed that NLR was positively correlated to the necessity of PCI in UAP patients ($r=0.353, P<0.001$). Multivariate logistic regression analysis indicated that NLR was independent risk factor for PCI in UAP patients ($OR=1.982, 95\%CI 1.168 \sim 3.362$). ROC curve showed that the area under the curve of NLR in the diagnosis of unstable angina requires PCI treatment was 0.719 (95%CI 0.651~0.776). **Conclusion** NLR can be regarded as one of the predictors for PCI in UAP patients.

【Key words】 neutrophil-to-lymphocyte ratio; unstable angina pectoris; percutaneous coronary intervention; correlation

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不稳定型心绞痛(unstable angina pectoris, UAP)是介于急性心肌梗死和稳定型心绞痛之间的临床冠脉综合征^[1],是多种危险因素作用下,在冠状动脉粥

样硬化基础上形成的炎性不稳定斑块所致,属于冠心病中急性冠状动脉综合征的一种,需尽早治疗。中性粒细胞/淋巴细胞比值(neutrophil-to-lymphocyte

ratio, NLR)是中性粒细胞数目与淋巴细胞数目的比值。中性粒细胞可以分泌炎症介质,导致血管壁变性,而淋巴细胞调节炎症反应,具有抗动脉粥样硬化作用。因此,NLR 被作为炎症生物标志物并且可能预测心血管疾病的风险和预后^[2]。有研究表明,心血管风险与 NLR 之间存在显著相关性^[3]。另有研究提示,NLR 与冠状动脉狭窄的严重程度、心肌损伤的程度和冠心病的临床结果有关^[4,5]。经皮冠状动脉介入(percutaneous coronary intervention, PCI)治疗是 UAP 的一种有效治疗方案,有学者认为 PCI 治疗对中重度缺血患者有益,但是对于动脉粥样硬化斑块<50%甚至正常的 UAP 患者,考虑主要由冠状动脉痉挛所致,不推荐行 PCI 治疗^[6]。因此,若能利用 NLR 指导 UAP 患者是否需行 PCI 治疗,可减少不必要的支架植入术,减少资源浪费。笔者旨在探讨 NLR 与 UAP 患者需行 PCI 治疗的相关性,以期为临床中判断 UAP 患者是否需行 PCI 治疗提供科学依据。

1 对象与方法

1.1 研究对象

选择 2018 年 1 月至 2019 年 6 月河南科技大学第一附属医院心血管内科收治的 UAP 患者 260 例,根据冠状动脉造影结果,分为需行 PCI 组 167 例和无需行 PCI 组 93 例。纳入标准:(1)UAP 的诊断参照《内科学》第 9 版诊断标准^[7]; (2)患者是否需行 PCI 治疗参考《中国经皮冠状动脉介入治疗指南(2016)》^[8]。排除标准:(1)已明确诊断有急性或慢性感染性疾病、肿瘤、代谢性疾病(糖尿病除外);(2)肝肾疾病病史;(3)严重的其他脏器功能衰退;(4)使用影响白细胞水平的药物,近 3 个月使用过糖皮质激素、免疫抑制剂;(5)既往行支架植入术或心脏手术;(6)临床信息资料缺失。本研究经医院医学伦理委员会批准,所有检查均获得患者知情同意。

1.2 方法

1.2.1 资料采集 调取入选患者病历。收集患者基线资料,包括年龄、性别、吸烟史、饮酒史、高血压史、糖尿病史等。记录患者入院第一次血常规及生化检查结果(禁食 8 h 后采集静脉血),包括:中性粒细胞、淋巴细胞、总胆固醇(total cholesterol, TC)、甘油三酯(triglyceride, TG)、高密度脂蛋白胆固醇(high-density lipoprotein cholesterol, HDL-C)、低密度脂蛋白胆固醇(low-density lipoprotein cholesterol, LDL-C)、空腹血糖(fasting blood glucose, FBG)、血肌

酐(serum creatinine, SCr)等指标,计算 NLR。

1.2.2 冠状动脉造影检查 由 2 名经验丰富的医师行冠状动脉造影术并严格规范操作流程。采用 Gensini 评分^[9]确定冠状动脉粥样硬化的严重程度。

1.3 统计学处理

采用 SPSS 24.0 统计软件进行数据处理。计量资料呈正态分布者以均数±标准差($\bar{x}\pm s$)表示,组间比较采用独立样本 t 检验;呈偏态分布者以中位数(四分位间距) [$M(Q_1, Q_3)$] 表示,组间比较采用 Mann-Whitney U 检验。计数资料以例数(百分率)表示,组间比较采用 χ^2 检验。相关性分析采用 Spearman 相关分析法。利用受试者工作特征(receiver operating characteristic, ROC) 曲线评价 NLR 对 UAP 患者需行 PCI 治疗的诊断价值。对单因素 logistic 回归分析中 $P<0.15$ 的指标进行多因素 logistic 回归分析,评估 UAP 患者需行 PCI 治疗的独立危险因素。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 2 组患者基线资料比较

2 组患者年龄、糖尿病史、中性粒细胞、TC、HDL-C、LDL-C、NLR 水平比较,差异均有统计学意义($P<0.05$;表 1)。

2.2 Spearman 相关性分析

相关性分析结果显示,UAP 需行 PCI 治疗与男性性别($r=0.177$)、年龄($r=0.199$)、糖尿病史($r=0.258$)、中性粒细胞($r=0.333$)、NLR($r=0.353$)、Gensini 评分($r=0.785$)呈正相关,与 TC($r=-0.182$)、HDL-C($r=-0.237$)、LDL-C($r=-0.179$)呈负相关(均 $P<0.01$)。

2.3 logistic 回归分析

单因素 logistic 回归分析显示,中性粒细胞、NLR 是 UAP 患者需行 PCI 治疗的危险因素(均 $P<0.001$;表 2)。多因素 logistic 回归分析校正了 TC、HDL-C、LDL-C 后显示,男性性别、年龄、糖尿病史、中性粒细胞、NLR 是 UAP 患者需行 PCI 治疗的独立危险因素(均 $P<0.05$;表 3)。

2.4 ROC 曲线分析

NLR 对 UAP 患者需行 PCI 治疗具有一定预测价值,曲线下面积为 0.713(95%CI 0.651~0.776),最佳截断点为 2.257,灵敏度为 61.7%,特异度为 72.0%(图 1)。

表1 2组患者基线资料比较

Table 1 Comparison of baseline data between two groups

Item	PCI group (n=167)	Non-PCI group (n=93)	t/X ² /U	P value
Age (years, $\bar{x}\pm s$)	59.31±9.41	55.61±7.35	-3.509	0.001
Male [n (%)]	116 (69.5)	48 (51.6)	8.170	0.004
Smoking history [n (%)]	49 (29.3)	22 (23.7)	0.973	0.324
Drinking history [n (%)]	35 (21.0)	19 (20.4)	0.010	0.920
Hypertension [n (%)]	99 (59.3)	44 (47.3)	3.458	0.063
Diabetes mellitus [n (%)]	47 (28.1)	6 (6.5)	17.319	<0.001
Neutrophil ($\times 10^9/L$, $\bar{x}\pm s$)	4.25±1.17	3.42±0.95	-5.910	<0.001
Lymphocyte ($\times 10^9/L$, $\bar{x}\pm s$)	1.81±0.53	1.92±0.47	1.701	0.090
TC (mmol/L, $\bar{x}\pm s$)	4.05±1.00	4.43±1.00	2.996	0.003
TG (mmol/L, $M(Q_1, Q_3)$)	1.39 (1.06, 2.24)	1.33 (1.03, 1.77)	1.709	0.087
HDL-C (mmol/L, $M(Q_1, Q_3)$)	1.04 (0.92, 1.22)	1.19 (1.00, 1.39)	-3.651	<0.001
LDL-C (mmol/L, $\bar{x}\pm s$)	2.34±0.78	2.59±0.74	2.550	0.011
FBG (mmol/L, $M(Q_1, Q_3)$)	4.92 (4.44, 5.86)	4.77 (4.41, 5.58)	1.005	0.315
SCr ($\mu\text{mol}/\text{L}$, $\bar{x}\pm s$)	66.92±15.69	64.05±13.66	-1.488	0.138
NLR ($\bar{x}\pm s$)	2.50±0.84	1.88±0.64	-6.696	0.001

PCI: percutaneous coronary intervention; TC: total cholesterol; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; FBG: fasting blood glucose; SCr: serum creatinine; NLR: neutrophil-to-lymphocyte ratio.

表2 UAP患者需行PCI治疗的单因素logistic回归分析

Table 2 Univariate logistic regression analysis of PCI necessity in patients with UAP

Item	B	SE	Wald	OR	95%CI	P value
Male	0.757	0.267	8.044	2.132	1.264~3.599	0.005
Age	0.048	0.015	10.002	1.050	1.019~1.082	0.002
Diabetes mellitus	-1.737	0.456	14.518	0.176	0.072~0.430	<0.001
Neutrophil	0.733	0.139	27.722	2.080	1.584~2.732	<0.001
TC	-0.333	0.132	8.455	0.682	0.527~0.883	0.004
HDL-C	-1.368	0.468	8.559	0.255	0.102~0.637	0.003
LDL-C	-0.428	0.172	6.193	0.652	0.466~0.913	0.013
NLR	1.103	0.202	29.906	3.012	2.029~4.472	<0.001

UAP: unstable angina pectoris; PCI: percutaneous coronary intervention; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; NLR: neutrophil-to-lymphocyte ratio.

表3 UAP患者需行PCI治疗的多因素logistic回归分析

Table 3 Multivariate logistic regression analysis of PCI necessity in patients with UAP

Item	B	SE	Wald	OR	95%CI	P value
Male	0.854	0.332	6.594	2.348	1.224~4.505	0.010
Age	0.056	0.019	9.030	1.058	1.020~1.097	0.003
Diabetes mellitus	-1.775	0.517	11.788	0.169	0.062~0.467	0.001
Neutrophil	0.433	0.184	5.510	1.542	1.074~2.013	0.019
TC	-0.214	0.332	0.416	0.807	0.421~1.548	0.519
HDL-C	-0.971	0.632	2.364	0.378	0.110~1.306	0.124
LDL-C	-0.006	0.415	0.000	0.994	0.441~2.243	0.989
NLR	0.684	0.270	6.429	1.982	1.168~3.362	0.011

UAP: unstable angina pectoris; PCI: percutaneous coronary intervention; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; NLR: neutrophil-to-lymphocyte ratio.

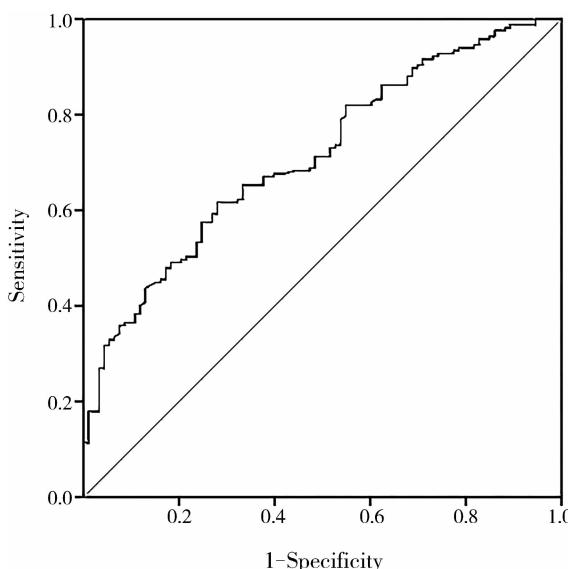


图1 NLR预测UAP患者需行PCI治疗的ROC曲线

Figure 1 ROC curve of NLR in predicting PCI necessity in patients with UAP

NLR: neutrophil-to-lymphocyte ratio; UAP: unstable angina pectoris; PCI: percutaneous coronary intervention; ROC: receiver operating characteristic.

3 讨论

炎症在动脉粥样硬化的进化中起重要作用, NLR 综合了中性粒细胞及淋巴细胞的平衡状态, 是一种测量简单、稳定性高的炎症标志物^[10]。UAP 为冠心病常见类型之一, 其发病机制是在动脉粥样硬化基础上, 继发的冠状动脉粥样硬化斑块破裂、血栓形成, 导致冠状动脉狭窄、急性或亚急性心肌缺血缺氧。冠状动脉狭窄的严重程度是 UAP 患者选择治疗方案、评估疾病预后的标准之一。冠状动脉有严重病变或血管内皮严重损伤时, 会使耗氧量增加、促炎症因子释放增加、皮质类固醇激素水平升高, 导致交感神经紧张性增加, NLR 可通过反映交感神经活跃程度进一步反应冠状动脉病变的严重程度^[11-13]。多项研究发现, NLR 与冠心病冠状动脉病变程度存在相关性且对其具有重要的预测价值^[14,15]。本研究显示, NLR 与 UAP 患者需行 PCI 治疗呈正相关, $OR = 1.982, 95\% CI 1.168 \sim 3.362$ 是 UAP 患者需行 PCI 治疗的独立危险因素, 其预测 UAP 患者需行 PCI 治疗的曲线下面积为 0.713(95%CI 0.651~0.776), 提示 NLR 对 UAP 患者需行 PCI 治疗具有一定的预测价值, 值得在临床工作中高度重视。

此外, 有研究表明, 糖尿病患者处于轻度慢性炎症状态, 可诱导 C-反应蛋白等炎症因子过

度分泌, 导致中性粒细胞计数不断升高, 而中性粒细胞数量的增加与血栓形成、冠状动脉狭窄有关^[16]。因此, 糖尿病患者 NLR 相对偏高。本研究显示, 糖尿病史与 UAP 患者需行 PCI 治疗呈正相关, 且为 UAP 患者需 PCI 治疗的独立危险因素。

综上所述, NLR 是 UAP 患者需行 PCI 治疗的独立危险因素, 与 UAP 患者需 PCI 治疗呈显著正相关, 可作为 UAP 患者需行 PCI 治疗的初步筛查因素, 预测疾病风险。本研究存在一定局限性, 除了是小样本、单中心的回顾性研究外, 没有联合 C-反应蛋白等其他炎症因子进行探讨。今后仍需多中心、大规模、前瞻性研究来进一步证实该结论。

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