

DOI: 10.16781/j.0258-879x.2019.07.0754

· 专题报道 ·

中性粒细胞与淋巴细胞比值、血小板与淋巴细胞比值诊断强直性脊柱炎的价值

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[摘要] **目的** 评估中性粒细胞与淋巴细胞比值(NLR)、血小板与淋巴细胞比值(PLR)在强直性脊柱炎(AS)诊断中的价值。**方法** 纳入海军军医大学(第二军医大学)长海医院收治的AS患者80例(AS组)及健康体检者100例(健康对照组)作为研究对象。采集研究对象清晨空腹静脉血进行血常规检查并计算NLR和PLR, 比较两组NLR和PLR的差异, 采用受试者工作特征(ROC)曲线评价NLR、PLR诊断AS的灵敏度和特异度并进行联合诊断试验。**结果** 与健康对照组相比, AS组NLR、PLR均增高, 差异均有统计学意义[2.25(1.66, 3.35) vs 1.50(1.23, 2.09), $P < 0.01$; 147.94(104.11, 188.80) vs 105.75(89.55, 148.02), $P < 0.01$]。ROC曲线分析显示, NLR诊断AS的曲线下面积(AUC)为0.694[95%置信区间(CI): 0.615~0.772, $P < 0.01$], 以最佳截断值(1.64)为诊断标准时其灵敏度和特异度分别为77.5%和58.0%; PLR诊断AS的AUC为0.662(95% CI: 0.580~0.756), 以最佳截断值(120.91)为诊断标准时其灵敏度和特异度分别为66.2%和63.0%。联合诊断试验结果显示, NLR与PLR并联试验(NLR/PLR)诊断AS的灵敏度和特异度分别为83.8%和50.0%, NLR与PLR串联试验(NLR+PLR)诊断AS的灵敏度和特异度分别为61.2%和75.0%。**结论** NLR和PLR对AS具有一定的诊断价值, 二者联合诊断可提高诊断的灵敏度和特异度。

[关键词] 强直性脊柱炎; 中性粒细胞与淋巴细胞比值; 血小板与淋巴细胞比值; 诊断**[中图分类号]** R 593.23 **[文献标志码]** A **[文章编号]** 0258-879X(2019)07-0754-05

Clinical value of neutrophil-lymphocyte ratio and platelet-lymphocyte ratio in diagnosis of ankylosing spondylitis

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[Abstract] **Objective** To assess the clinical value of neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) in diagnosis of ankylosing spondylitis. **Methods** Eighty patients with ankylosing spondylitis and 100 normal controls from Changhai Hospital, Naval Medical University (Second Military Medical University) were enrolled in our study. The fasting venous blood samples were collected in the morning for routine blood examination. The differences of NLR and PLR between the two groups were analyzed. The receiver operating characteristic (ROC) curve was used to evaluate the sensitivity and specificity of NLR and PLR, and combined diagnostic test was performed. **Results** The levels of NLR and PLR in ankylosing spondylitis patients were significantly higher than those in the control group [2.25 [1.66, 3.35] vs 1.50 [1.23, 2.09], $P < 0.01$; 147.94 [104.11, 188.80] vs 105.75 [89.55, 148.02], $P < 0.01$]. ROC curve analysis showed that the area under curve (AUC) of NLR in diagnosis of ankylosing spondylitis was 0.694 (95% confidence interval [CI]: 0.615-0.772, $P < 0.01$), and the sensitivity and specificity of NLR were 77.5% and 58.0%, respectively, when the cut-off value was 1.64. The AUC of PLR in diagnosis of ankylosing spondylitis was 0.662 (95% CI: 0.580-0.756), and the sensitivity and specificity of PLR were 66.2% and 63.0%, respectively, when the cut-off value was 120.91. The sensitivity and specificity of NLR and

[收稿日期] 2019-02-08 **[接受日期]** 2019-06-21**[作者简介]** 景丽玲, 硕士, 技师. E-mail: iamjing329@163.com; 刘云龙, 主治医师. E-mail: iamlong329@163.com

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PLR parallel testing (NLR/PLR) were 83.8% and 50.0%, and the sensitivity and specificity of the NLR and PLR tandem testing (NLR+PLR) were 61.2% and 75.0%, respectively. **Conclusion** NLR and PLR both have clinical value for the diagnosis of ankylosing spondylitis, and the combination of the two can improve the diagnostic sensitivity and specificity.

[Key words] ankylosing spondylitis; neutrophil to lymphocyte ratio; platelet to lymphocyte ratio; diagnosis

[Acad J Sec Mil Med Univ, 2019, 40(7): 754-758]

强直性脊柱炎 (ankylosing spondylitis, AS) 是一种慢性自身免疫性炎症疾病, 以中轴关节受累为主, 伴发关节外表现, 全球发病率为 0.1%~1.4%^[1-2]。C-反应蛋白 (C-reactive protein, CRP) 和红细胞沉降率 (erythrocyte sedimentation rate, ESR) 是临床上常用的 AS 检测项目, 可用于评估患者是否存在炎症、早期筛查疾病和监测疾病活动度, 但这些生物标志物已被证实特异度和灵敏度较低, 只有 40%~50% 的 AS 患者存在 CRP 和 (或) ESR 升高^[3-4]。实验室检测有助于疾病的快速诊断和恰当管理, 因此, 有必要寻找特异度和灵敏度更高的指标, 为临床上 AS 的诊断提供实验室依据。

系统性炎症与循环血细胞数量及组成的变化密切相关^[5]。中性粒细胞与淋巴细胞比值 (neutrophil-lymphocyte ratio, NLR) 和血小板与淋巴细胞比值 (platelet-lymphocyte ratio, PLR) 是重要的全身炎症指标, 研究发现其可用于评估系统性红斑狼疮、干燥综合征、骨关节炎和多发性肌炎等的疾病活动度和严重程度^[6-9]。本研究以 AS 患者和健康对照者为研究对象, 分析 NLR 和 PLR 诊断 AS 的灵敏度和特异度, 评估其潜在的临床诊断价值。

1 资料和方法

1.1 研究对象 AS 组: 2016 年 1 月至 2019 年 2 月海军军医大学 (第二军医大学) 长海医院收治的 AS 患者 80 例, 其中男 61 例、女 19 例, 平均年龄为 (47.40±12.05) 岁。AS 诊断符合 1984 年修订的纽约标准^[10]: (1) 腰背痛和僵硬超过 3 个月; (2) 腰椎前屈和侧弯受限; (3) 胸廓扩展范围/胸廓活动度小于同年龄和性别者的正常值; (4) 双侧骶髂关节炎 2~4 级或单侧骶髂关节炎 3~4 级。符合上述条件 (4) 加上 (1)~(3) 中任何一项即可诊断 AS。健康对照组: 选择健康体检者 100 例, 其中男 70 例、女 30 例, 平均年龄为 (54.51±11.38) 岁。健康对照组年龄和性别与 AS

组差异均无统计学意义 ($P=0.170$ 、 0.349), 具有可比性。排除标准: 两组研究对象近期内均未接受抗炎或免疫抑制治疗, 排除合并恶性肿瘤、严重肝肾功能障碍、糖尿病、炎症性肠病等慢性消耗性及免疫系统疾病患者。本研究方案经海军军医大学 (第二军医大学) 长海医院伦理委员会审批。

1.2 研究方法 采集研究对象清晨空腹静脉血 (AS 患者于入院后次日采血), 采用 Sysmex XN-9000 血液分析仪 (日本希森美康公司) 进行血液常规检查, 记录白细胞计数、中性粒细胞计数、淋巴细胞计数、血小板计数, 计算 NLR 和 PLR; 采用散射比浊法 (试剂购自深圳国赛生物技术有限公司) 检测 CRP, Sysmex Monitor-100 全自动 ESR 检测仪 (日本希森美康公司) 检测 ESR。标本采集、处理、测定步骤和含量计算均按照仪器操作规范进行。所有样品均由专业的实验室技术人员检测和分析。

1.3 统计学处理 采用 SPSS 22.0 软件进行统计分析。计数资料以例数和百分数表示, 两组间比较采用 χ^2 检验。符合正态分布的计量资料以 $\bar{x}\pm s$ 表示, 两组间比较采用独立样本 t 检验; 不符合正态分布的计量资料以中位数 (下四分位数, 上四分位数) 表示, 两组间比较采用 Mann-Whitney U 检验。采用受试者工作特征 (receiver operating characteristic, ROC) 曲线评估 NLR 和 PLR 对 AS 的诊断价值, 通过约登指数确定最佳截断值, 并计算灵敏度和特异度。采用 Spearman 秩相关分析研究非参数变量之间的相关性。检验水准 (α) 为 0.05。

2 结果

2.1 两组血液分析结果比较 由图 1 可见, AS 组血 CRP 水平和 ESR 均高于健康对照组, 差异均有统计学意义 [CRP: 10.60 (5.78, 26.90) mg/L vs 6.00 (4.00, 8.00) mg/L, $P<0.01$; ESR: 19.00 (10.25, 34.00) mm/1 h vs 9.00 (7.00, 13.75)

mm/1 h, $P<0.01$]; AS 组患者血 NLR 和 PLR 均高于健康对照组, 差异均有统计学意义 [2.25 (1.66, 3.35) vs 1.50 (1.23, 2.09), $P<0.01$; 147.94

(104.11, 188.80) vs 105.75 (89.55, 148.02), $P<0.01$]

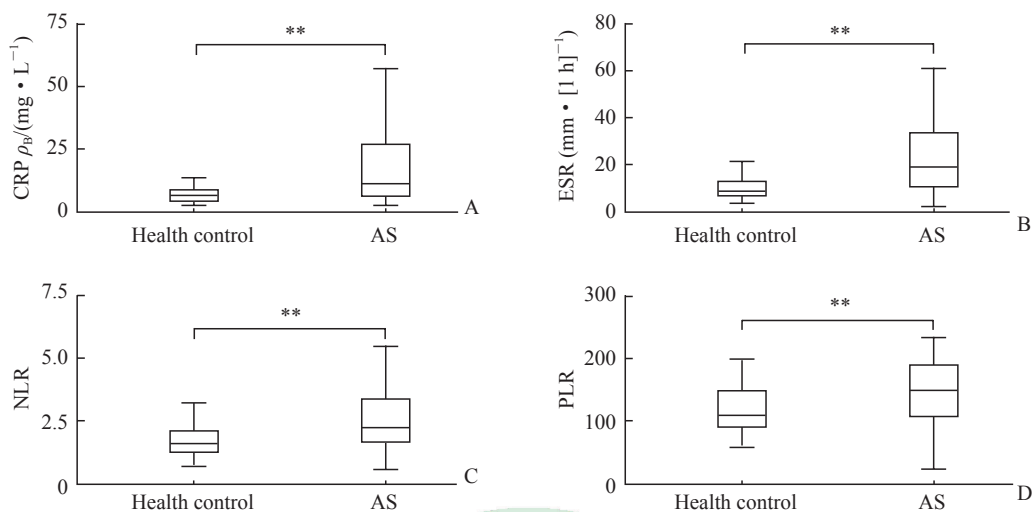


图1 AS 组和健康对照组血 CRP、ESR、NLR 和 PLR 的比较

Fig 1 Comparison of blood CRP, ESR, NLR and PLR between AS and healthy control groups

AS: Ankylosing spondylitis; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio. ** $P<0.01$. $n=80$ in AS group, $n=100$ in healthy control group

2.2 血 NLR 和 PLR 对 AS 的诊断价值 ROC 曲线分析结果 (图 2) 显示, NLR 诊断 AS 的曲线下面积 (area under curve, AUC) 为 0.694 [95% 置信区间 (confidence interval, CI): 0.615~0.772; $P<0.01$], 最佳截断值为 1.64; 以 1.64 为诊断标准时, NLR 诊断 AS 的灵敏度和特异度分别为 77.5% 和 58.0%。PLR 诊断 AS 的 AUC 为 0.662 (95% CI: 0.580~0.745; $P<0.001$), 最佳截断值为 120.91; 以 120.91 为诊断标准时, PLR 诊断 AS 的灵敏度和特异度分别为 66.2% 和 63.0%。

以 NLR 和 PLR 的最佳截断值为标准, 按并联试验、串联试验原则分析 NLR、PLR 单独试验及联合试验诊断 AS 的灵敏度、特异度、准确度, 结果显示 NLR 与 PLR 并联试验 (NLR/PLR) 诊断灵敏度最高, NLR 与 PLR 串联试验 (NLR+PLR) 诊断特异度最高 (表 1)。

2.3 血 NLR 和 PLR 与传统炎症标志物的相关性分析 180 例研究对象中, 血 NLR 与 CRP 呈正相关 ($r_s=0.339$, $P<0.001$), PLR 与 CRP 呈正相关 ($r_s=0.642$, $P<0.001$); NLR 和 PLR 均与 ESR 呈正相关 ($r_s=0.393$, $P<0.001$; $r_s=0.662$, $P<0.001$)。

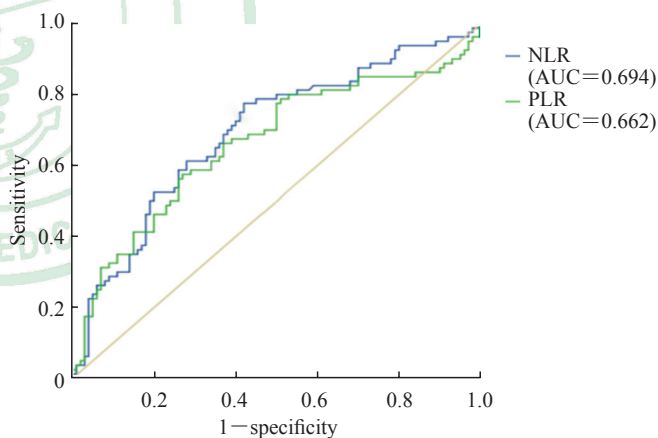


图2 NLR、PLR 诊断 AS 的 ROC 曲线
Fig 2 ROC curve of NLR and PLR levels for diagnosis of AS

NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; AS: Ankylosing spondylitis; ROC: Receiver operating characteristic

3 讨论

AS 是脊柱关节炎的主要亚型, 以炎性背痛、非对称外周性小关节炎、附着点炎和特定器官受累为主要特征, 可导致结构和功能损伤, 使患者生活质量下降^[11]。临床实践中, CRP 和 ESR 经常被用于

评估 AS 患者急性或慢性全身炎症反应状态^[4]。本研究发现 AS 患者与健康对照组相比 CRP 和 ESR 水平均升高, 与既往研究结果^[12]一致。但是, CRP

和 ESR 的灵敏度和阳性预测值均较低, 不适合用于评估 AS 的疾病活动度^[4]。

表 1 NLR 和 PLR 单独试验与联合试验诊断 AS 的准确度分析

Tab 1 Accuracy analysis of NLR and PLR alone and combined for the diagnosis of AS

Index	AS <i>n</i>		Healthy control <i>n</i>		Sensitivity (%)	Specificity (%)	Accuracy (%)
	Positive	Negative	Positive	Negative			
NLR	62	18	42	58	77.5	58.0	66.7
PLR	53	27	37	63	66.2	63.0	64.4
NLR/PLR	67	13	50	50	83.8	50.0	65.0
NLR+PLR	49	31	25	75	61.2	75.0	68.9

NLR: Neutrophil-lymphocyte ratio; PLR: Platelet-lymphocyte ratio; AS: Ankylosing spondylitis

NLR 和 PLR 是全身炎症标志物, 容易从全血细胞计数检测中获得, 已被用于心血管系统疾病和溃疡性结肠炎等疾病的评估^[13-15], 并且能够反映系统性红斑狼疮、干燥综合征、骨关节炎和多发性肌炎等自身炎症性疾病的活动度和严重程度^[6-9]。AS 的病程进展与炎症密切相关, 近年来也有学者探讨了 NLR 和 PLR 与 AS 的关系。Gökmen 等^[16]研究发现 AS 患者 NLR 高于健康对照组, 并且与抗炎药物治疗有关; Xu 等^[17]通过对既往发表的研究进行 meta 分析发现, AS 患者 NLR 明显高于健康对照组, 并且与 AS 患者疾病活动指数和 CRP 有关。Boyraz 等^[18]发现, AS 患者接受抗肿瘤坏死因子治疗获得疾病控制后, PLR 与健康对照组相比明显降低, 而 NLR 与健康对照组相比无明显差异, 认为 PLR 可作为监测 AS 病情进展和亚临床炎症的指标。

本研究发现, AS 患者 NLR 和 PLR 均高于健康对照组, 并且 NLR 和 PLR 均分别与 CRP 和 ESR 呈正相关, 表明炎症在 AS 复杂的病理生理过程中发挥重要作用, NLR 和 PLR 可用于评估 AS 的炎症状态。ROC 曲线分析结果显示, NLR 和 PLR 诊断 AS 的 AUC 分别为 0.694 和 0.662, 最佳截断值分别为 1.64 和 120.91; 以最佳截断值为诊断标准, NLR 诊断 AS 的灵敏度和特异度分别为 77.5% 和 58.0%, PLR 诊断 AS 的灵敏度和特异度分别为 66.2% 和 63.0%。联合诊断试验结果显示, NLR 与 PLR 并联试验 (NLR/PLR) 诊断 AS 的灵敏度和特异度分别为 83.8% 和 50.0%, NLR 与 PLR 串联试验 (NLR+PLR) 诊断 AS 的灵敏度和特异度分别为 61.2% 和 75.0%。上述结果表明

NLR 和 PLR 对 AS 具有一定的诊断价值, 二者联合诊断可提高诊断的灵敏度和特异度。

综上所述, NLR 和 PLR 作为简单、可重复性、价廉且灵敏的炎症指标, 对 AS 的诊断具有一定临床价值。由于 AS 缺乏符合要求的鉴别诊断病例, 本研究参考既往研究^[16-18]选择健康体检者作为对照组。本研究的不足之处在于: (1) 样本量相对较小且为单中心回顾性研究, 相关结论需更大规模的前瞻性临床研究证实; (2) 因样本量小, 未根据 AS 分型进行分层分析, 这可能是导致 NLR 和 PLR 灵敏度和特异度偏低的原因之一; (3) 本研究为横截面设计, 未能对 NLR、PLR 和 AS 疾病活动之间的因果关系进行研究, 今后需要设计纵向研究进一步探索。

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[本文编辑] 孙岩