

# 首次发作的儿童青少年抑郁障碍患者中性粒细胞与淋巴细胞比值和自杀意念的关系

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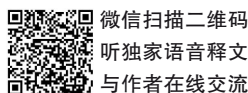
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**【摘要】** 背景 自杀是全球严重的公共卫生问题之一。自杀与中性粒细胞与淋巴细胞比值(NLR)的关系可能在不同地区和不同年龄的人群中存在差异,有必要进一步研究NLR与我国儿童青少年抑郁障碍患者自杀意念之间的关系。**目的** 探讨儿童青少年抑郁障碍患者NLR与自杀意念的相关性,为探寻自杀的生物学指标提供线索。**方法** 回顾性纳入2020年1月-2022年12月在阜阳市第三人民医院住院治疗的536例符合《国际疾病分类(第10版)》(ICD-10)诊断标准的儿童青少年抑郁障碍患者,根据患者是否报告存在自杀意念,将患者分为两组。从病历中收集患者的人口学资料、出院诊断以及入院第二天的汉密尔顿抑郁量表17项版(HAMD-17)评分和血液学检验数据(中性粒细胞计数、淋巴细胞计数)。使用受试者操作特征曲线(ROC)测定NLR预测儿童青少年抑郁障碍患者自杀意念的最佳临界点,采用二元Logistic回归分析探索患者自杀意念的危险因素。**结果** 在536例患者中,无自杀意念者429例(80.04%),有自杀意念者107例(19.96%)。与无自杀意念组相比,有自杀意念组HAMD-17评分更高[(25.28±8.86)分 vs. (21.21±8.46)分,  $F=19.400, P<0.01$ ],中性粒细胞水平更高[(3.85±1.68)×10<sup>9</sup>/L vs. (3.15±1.14)×10<sup>9</sup>/L,  $Z=-4.073, P<0.01$ ],NLR更高[(1.96±1.50) vs. (1.52±0.71),  $Z=-3.532, P<0.01$ ]。ROC曲线确定的最佳临界NLR值是1.52(敏感度为59.80%,特异度为58.50%),曲线下面积为0.610。Logistic回归分析显示,在控制年龄、性别、发病年龄、病程和HAMD-17评分后,高NLR者发生自杀意念的风险是低NLR者的1.94倍( $OR=1.940, 95\% CI: 1.251-3.009, P=0.003$ )。**结论** NLR可能是影响首次发作的儿童青少年抑郁障碍患者自杀意念的危险因素及潜在生物标志物。

**【关键词】** 抑郁障碍;自杀意念;儿童;青少年;中性粒细胞与淋巴细胞比值

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## Association between neutrophil-to-lymphocyte ratio and suicidal ideation in children and adolescents with first-episode depression

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**【Abstract】** **Background** Suicide is one of the serious public health problems worldwide. The relationship between suicide and neutrophil-to-lymphocyte ratio (NLR) may vary in different regions and different age. It is necessary to further investigate the relationship between NLR and suicidal ideation in Chinese children and adolescents with depression. **Objective** To explore the correlation between NLR and suicidal ideation in children and adolescents with depression, so as to provide clues for exploring the biomarkers of suicide. **Methods** A retrospective analysis of 536 children and adolescents with depression who were hospitalized in the Third People's Hospital of Fuyang from January 2020 to December 2022 and met the diagnostic criteria of the International Classification of Diseases, tenth edition (ICD-10) was performed. Patients were divided into two groups according to whether they reported suicidal ideation. Demographic data, discharge diagnosis, Hamilton Depression Scale-17 item (HAMD-17) score and

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hematological test data (neutrophil counts, lymphocyte counts) on the second day were collected from medical records. Receiver operating characteristic (ROC) curve was used to determine the optimal cut-off point of NLR for predicting suicidal ideation in children and adolescents with depression, and binary Logistic regression was used to analyze the risk factors for suicidal ideation.

**Results** Among the 536 patients, 429 cases (80.04%) had no suicidal ideation, and 107 cases (19.96%) had suicidal ideation. Compared with patients without suicidal ideation, the HAMD-17 score [ $(25.28 \pm 8.86)$  vs.  $(21.21 \pm 8.46)$ ,  $F=19.400$ ,  $P<0.01$ ], neutrophil level [ $(3.85 \pm 1.68) \times 10^9/L$  vs.  $(3.15 \pm 1.14) \times 10^9/L$ ,  $Z=4.073$ ,  $P<0.01$ ], and NLR level [ $(1.96 \pm 1.50)$  vs.  $(1.52 \pm 0.71)$ ,  $Z=3.532$ ,  $P<0.01$ ] in the suicidal ideation patients were significantly higher. The optimal critical NLR value determined by the ROC curve was 1.52 (59.80% sensitivity, 58.50% specificity), with an area under the curve of 0.610. Logistic regression analysis showed that the risk of suicidal ideation was 1.94 times higher in those with high NLR than in the low NLR after controlling for age, sex, age at onset, duration of illness, and HAMD-17 score ( $OR=1.940$ , 95%  $CI: 1.251 \sim 3.009$ ,  $P=0.003$ ).

**Conclusion** NLR may be a risk factor and potential biomarker influencing suicidal ideation in the children and adolescents with first-episode depression. [Funded by Scientific Research Project of Fuyang Municipal Health Commission (number, FY2020xg14)]

**【Keywords】** Depression; Suicidal ideation; Children; Adolescents; Neutrophil-to-lymphocyte ratio

自杀是全球范围内严重的公共卫生问题,多发生在抑郁障碍患者中<sup>[1]</sup>。自杀主要分为自杀完成、自杀企图和自杀意念<sup>[2]</sup>。52.1%的自杀死亡者年龄低于45岁<sup>[3]</sup>,12岁以下儿童自杀意念综合检出率为7.5%<sup>[4]</sup>。在有自杀意念的青少年中,约三分之一在后续12个月内继续尝试自杀<sup>[5]</sup>。自杀的主要危险因素包括内化精神病理、人口学特征、外化精神病理、自杀史和心理社会因素<sup>[6]</sup>。然而,不同性别、年龄和地区人群的自杀风险因素不同<sup>[7-9]</sup>,预测自杀较为困难。

抑郁障碍患者是自杀意念的高危人群,伴有明显的免疫炎症激活<sup>[10-13]</sup>。免疫炎症反应参与抑郁障碍及自杀的病理生理过程。动物实验和临床研究均表明,炎症因子水平升高会导致快感缺失以及抑郁行为<sup>[12-16]</sup>,而抗抑郁药可降低外周血炎症标志物水平<sup>[17-18]</sup>。自杀者血液炎症标志物水平高于非自杀者<sup>[10]</sup>,有自杀倾向的患者血液和死后脑样本中的细胞因子及趋化因子水平均高于无自杀倾向的患者和健康对照者<sup>[19-20]</sup>,炎症和氧化应激引起的神经损伤可能进一步增加自杀风险<sup>[11,21]</sup>。

中性粒细胞与淋巴细胞比值(Neutrophil-to-Lymphocyte Ratio, NLR)是通过计算白细胞分类中的中性粒细胞与淋巴细胞的比值来反映机体炎症状态的指标。一般情况下,中性粒细胞的增加是机体炎症反应的一种表现,而淋巴细胞减少则与机体免疫功能下降有关。因此,NLR增加通常被认为是机体炎症反应和免疫功能下降的指标。NLR可以应用于癌症和心脑血管疾病等多种疾病的预后判断和治疗反应预测<sup>[22-24]</sup>。

已有研究表明,NLR水平与抑郁障碍患病风险存在正向关联<sup>[25]</sup>,NLR可作为抑郁障碍诊断的生物

学指标<sup>[26]</sup>。在有自杀企图家族史的双相情感障碍患者中,NLR可能有助于预测自杀风险,并区分暴力或非暴力自杀企图<sup>[27-28]</sup>。此外,NLR可用于检测成年抑郁障碍患者的自杀脆弱性<sup>[29]</sup>。但如前所述,自杀与NLR的关系可能在不同地区和不同人群中存在差异,故本研究通过探讨NLR与青少年抑郁障碍患者自杀意念的相关性,以期阐明NLR在预测自杀意念方面的可能作用。

## 1 对象与方法

### 1.1 对象

连续纳入2020年1月-2022年12月在安徽省阜阳市第三人民医院住院治疗的儿童和青少年抑郁障碍患者为研究对象。入组标准:①符合《国际疾病分类(第10版)》(International Classification of Diseases, tenth edition, ICD-10)中抑郁障碍的诊断标准;②年龄 $\leq 18$ 岁;③本次发作为首次发病且病程 $\leq 12$ 个月。排除标准:①合并抑郁障碍之外的精神障碍患者;②患有局部或全身急性、慢性炎症性疾病以及其他炎症性免疫疾病,包括病毒性或细菌性感冒等;③合并肿瘤、糖尿病等躯体疾病者。符合入组标准且不符合排除标准共536例。患者及家属均签署知情同意书。本研究符合《赫尔辛基宣言》伦理原则,经阜阳市第三人民医院伦理委员会审批(伦理审批号:2019-340-07)。

### 1.2 资料收集

从病历资料中收集患者的人口学资料,包括年龄、性别和病程,并收集出院诊断、入院第二天的汉密尔顿抑郁量表17项版(Hamilton Depression Scale-17 item, HAMD-17)评分以及血液学检验数

据(中性粒细胞计数和淋巴细胞计数)。

由经过一致性培训的精神科医师进行自杀意念和 HAMD-17 评定。采用单个项目评估患者在过去三个月是否有过自杀意念<sup>[30]</sup>,即“你是否认真地考虑过自杀?”,要求患者以“是”或“否”进行作答。HAMD-17 采用 0~2 分或 0~4 分评分,总评分范围 0~52 分,总评分越高表明抑郁症状越严重。

所有患者均在入院第二天 6:00-8:00 空腹采集外周静脉血,从头静脉中采集 5~10 mL 静脉血液样本,并在 EDTA 管中保存。使用迈瑞 BC-5380/BC-5180 血液学分析仪(中国深圳)分析全血细胞计数,包括中性粒细胞、淋巴细胞和血小板计数。计算公式:NLR=中性粒细胞计数/淋巴细胞计数。

### 1.3 统计方法

采用 SPSS 26.0 进行统计分析。变量正态性检验采用 Shapiro-Wilk 检验。分类变量以[n(%)]表示,连续变量以( $\bar{x}\pm s$ )表示。采用方差分析、Mann-Whitney U 检验或 $\chi^2$ 检验比较组间差异。以参与者自我报告自杀意念为分组标准,绘制入院时 NLR

的受试者操作特征曲线(receiver operating characteristic curve, ROC)并测定 ROC 曲线下面积(area under curve, AUC)。以约登指数(敏感性+特异性-1)确定 NLR 预测儿童青少年抑郁障碍患者自杀意念的最佳临界值,根据该临界值对患者进行分组(高 NLR 组和低 NLR 组)。使用二元 Logistic 回归分析(变量筛选法采用基于最大似然估计的向前逐步回归法)探索首次发作的儿童青少年抑郁障碍患者自杀意念的危险因素。检验水准 $\alpha=0.05$ 。

## 2 结 果

### 2.1 两组人口学和临床特征比较

本研究共纳入 536 例首次发作的儿童青少年抑郁障碍患者,年龄 8~18 岁[(14.91±1.80)岁]。无自杀意念者 429 例(80.04%),有自杀意念者 107 例(19.96%)。NLR 为 0.25~12.86(1.61±0.94)。与无自杀意念组相比,有自杀意念组中性粒细胞计数更高( $Z=-4.073, P<0.01$ ),NLR 水平更高( $Z=-3.532, P<0.01$ ),HAMD-17 评分更高( $F=19.400, P<0.01$ ),差异均有统计学意义。见表 1。

表 1 两组人口学资料和临床特征比较

Table 1 Comparison of demographic data and clinical characteristics between the two groups

变 量	总样本(n=536)	无自杀意念组(n=429)	有自杀意念组(n=107)	$F/\chi^2/Z$	P
年龄(岁)	14.72±1.81	14.64±1.81	15.01±1.80	3.506 <sup>a</sup>	0.062
性别[n(%)]				3.194	0.074
女性	378(70.52)	295(68.76)	83(77.57)		
男性	158(29.48)	134(31.24)	24(22.43)		
病程(月)	6.30±4.48	6.39±4.52	5.91±4.31	0.969 <sup>a</sup>	0.325
中性粒细胞( $10^9/L$ )	3.29±1.29	3.15±1.14	3.85±1.68	-4.073 <sup>b</sup>	<0.010
淋巴细胞( $10^9/L$ )	2.23±0.68	2.23±0.67	2.22±0.71	0.410 <sup>a</sup>	0.839
NLR	1.61±0.94	1.52±0.71	1.96±1.50	-3.532 <sup>b</sup>	<0.010
HAMD-17 评分(分)	22.03±8.69	21.21±8.46	25.28±8.86	19.400 <sup>a</sup>	<0.010

注:NLR,中性粒细胞与淋巴细胞比值;HAMD-17,汉密尔顿抑郁量表 17 项版;<sup>a</sup>方差分析;<sup>b</sup>Mann-Whitney U 检验

### 2.2 ROC 曲线下面积及 NLR 的最佳临界值

ROC 曲线下面积为 0.610(95% CI: 0.550~0.671,  $P<0.01$ )。根据最大约登指数,预测儿童青少年抑郁障碍患者的自杀意念时,NLR 的最佳临界值为 1.52,灵敏度为 59.80%,特异度为 58.50%,约登指数为 0.183。见图 1。

根据最佳临界值对患者进行分组,高 NLR(NLR $\geq$ 1.52)组 244 例(45.52%),低 NLR(NLR<1.52)组 292 例(54.48%)。

### 2.3 自杀意念影响因素的二元 Logistic 回归分析

以自杀意念频率的转换量为因变量(是为 1,否为 0),以性别(男性为 1,女性为 2)、年龄(岁)、病程(月)、HAMD-17 评分、NLR 水平为自变量(高 NLR 为 1,低 NLR 为 0),进行二元 Logistic 回归分析。高 NLR 者发生自杀意念的风险是低 NLR 者的 1.940 倍( $OR=1.940, 95\% CI: 1.251\sim 3.009, P=0.003$ )。见表 2。该模型判断儿童青少年抑郁障碍患者自杀意念的准确率达到 80.2%。



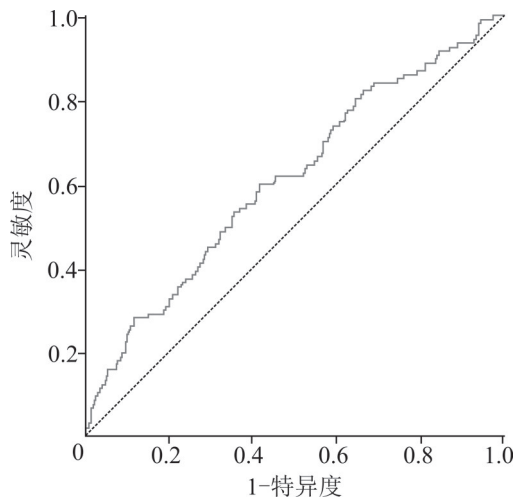


图 1 NLR 预测儿童青少年抑郁障碍患者自杀意念的 ROC 曲线

Figure 1 ROC curve of NLR for predicting suicidal ideation in children and adolescents patients with depressive disorder

表 2 自杀意念影响因素的二元 Logistic 回归分析

Table 2 Binary logistic regression analysis of factors influencing suicidal ideation

变 量	$\beta$	标准差	Wald	P	OR	95% CI
NLR	0.663	0.224	8.758	0.003	1.940	1.251-3.009
HAMD-17	0.049	0.013	15.495	<0.010	1.051	1.025-1.077

注: NLR, 中性粒细胞与淋巴细胞比值; HAMD-17, 汉密尔顿抑郁量表 17 项版

### 3 讨 论

本研究结果显示, 高 NLR 是自杀意念的危险因素, 判断自杀意念的 NLR 的最佳临界值为 1.52, 灵敏度为 59.80%, 特异度为 58.50%。提示 NLR 可能是识别儿童青少年抑郁障碍患者自杀意念的生物标志物, 与既往研究结果一致<sup>[29-31]</sup>。炎症在抑郁和自杀的病理生理机制中以多种途径参与。首先, 炎症产生的细胞因子会对 5-羟色胺和谷氨酸浓度产生影响, 并最终影响基底神经节与皮质之间的奖励和运动回路, 从而导致抑郁情绪和自杀行为<sup>[32-39]</sup>; 其次, 炎症的内感受信号也在抑郁障碍发生中发挥作用, 抑郁障碍患者外周炎症标志物, 特别是白介素-6 (IL-6) 和 C 反应蛋白 (CRP) 水平较高<sup>[40]</sup>, 内感受通路将中枢和外周炎症免疫变化联系起来, 导致自杀等应激反应的发生。

既往研究显示, 针对性地使用减轻炎症反应和免疫调节的疗法可能是抑郁障碍的辅助治疗策略。部分减轻炎症反应的辅助疗法例如减肥、运动和补充 omega-3 脂肪酸等, 已在抗抑郁方面发挥作用<sup>[41-45]</sup>。此外, 识别同时存在自杀意念和免疫失调症状, 是制定个性化自杀预防策略的重要前提<sup>[46]</sup>。

因此, 通过检测 NLR 识别同时自杀意念和免疫失调症状的患者亚群, 可以帮助医生制定更有效的个性化预防策略, 减少自杀行为的发生。

综上所述, NLR 可能是首次发作的儿童青少年抑郁障碍患者自杀意念的危险因素, 在评估该人群自杀风险时, 还应考虑全身炎症指标。本研究局限性: ①仅使用单一问题来评估患者的自杀意念; ②横断面研究, 缺乏炎症指标随治疗变化的相关数据; ③回顾性研究, 未收集入院时患者的服药信息, 且对抽血前服药的时间、药物种类及剂量等可能影响 NLR 的指标未进行详细分析。未来研究可结合其他临床资料和人口学资料, 提高对儿童青少年抑郁障碍患者群体自杀风险评估的准确性, 以制定个性化的预防策略。

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