

【临床研究】

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history of atrial fibrillation ratio, history of coronary heart disease ratio and the levels of NLR, triacylglycerol, LDL-C of patients between the good prognosis group and poor prognosis group ($P>0.05$). The age [odds ratio (OR) = 1.044, 95% confidence interval (CI): 1.009 – 1.082, $P<0.05$], NIHSS score (OR = 6.966, 95% CI: 2.801 – 17.327, $P<0.001$) and NLR (OR = 1.165, 95% CI: 1.018 – 1.333, $P<0.001$) of patients at admission were the independent predictors for poor prognosis of AIS patients without infection symptoms at three months after intravenous thrombolysis. The ROC area under curve of NLR in evaluating the poor prognosis of AIS patients without infection symptoms at three months after intravenous thrombolysis was 0.636, the optimal cut-off value was 3.39, the sensitivity and specificity were 57.5% and 75.6%, respectively.

Conclusion NLR at admission was an independent factor for poor prognosis of AIS patients without infection symptoms at three months after intravenous thrombolysis, and which can be used as a predictor in evaluating poor prognosis of the patients at three months after intravenous thrombolysis.

Key words: acute ischemic stroke; neutrophil-to-lymphocyte ratio; intravenous thrombolysis; prognosis

急性缺血性卒中 (acute ischemic stroke, AIS) 是我国脑卒中最常见的类型, 占全部脑卒中的 69.6% ~ 70.8%^[1-2]。在我国, 住院 AIS 患者中发病后 1 个月内病死率达 2.3% ~ 3.2%^[2-3], 3 个月时病死率达 9.0% ~ 9.6%, 致死/残疾率高达 34.5% ~ 37.1%^[4-5]; AIS 已成为危害我国中老年人身体健康的主要疾病^[6]。中性粒细胞和淋巴细胞是主要免疫细胞, 在 AIS 发生发展中起重要作用。研究表明, 高中性粒细胞/淋巴细胞比值 (neutrophil-to-lymphocyte ratio, NLR) 是心血管疾病、风湿免疫疾病等疾病不良预后的独立危险因素^[7]。既往有较多研究分析了 NLR 对 AIS 非溶栓患者预后的评估作用^[7-8], 但研究中并未排除脑卒中后相关肺炎等严重影响 NLR 的感染性因素, 而脑卒中后相关肺炎可影响中 NLR^[9-11]。AIS 患者静脉溶栓后短期 (3 个月内) 的预后相对容易波动^[12-13], 因此, 及时评估不伴感染症状的 AIS 患者静脉溶栓后 3 个月预后, 对改善 AIS 患者静脉溶栓后的预后十分重要。目前, 关于 NLR 对不伴感染症状的 AIS 患者静脉溶栓后 3 个月预后的预测价值研究国内外报道较少; 因此, 本研究探讨不伴感染症状 AIS 患者入院时 NLR 与静脉溶栓后 3 个月预后的关系, 评估 NLR 对不伴感染症状 AIS 患者静脉溶栓后 3 个月预后的预测价值, 以指导临床制定优化的诊疗方案。

1 资料与方法

1.1 一般资料 选择 2016 年 7 月至 2021 年 12 月郑州人民医院神经内科收治的 200 例不伴感染症状 AIS 静脉溶栓患者为研究对象, 其中男 146 例, 女 54 例; 年龄 25 ~ 91 (59.35 ± 13.02) 岁。病例纳入标准: (1) 符合《中国急性缺血性脑卒中诊治指南 2018》中 AIS 诊断及静脉溶栓的标准^[5], 即急性起病、年龄 ≥ 18 岁、局灶或全面性神经功能缺损、影像学检查排除非血管性病因、脑 CT/磁共振成像排除出血性脑血管病、发病 4.5 h 内, 且患者或患者家属

签字同意静脉溶栓; (2) 入院时不伴感染症状; (3) 无血管内介入治疗指征。排除标准: (1) 巨大动脉瘤、肿瘤晚期患者; (2) 影像学确诊为颅内出血性脑血管病, 头颅 CT 或磁共振成像提示大面积梗死 (梗死面积 > 1/3 大脑中动脉供血区) 患者; (3) 发病 > 4.5 h 患者; (4) 对阿替普酶有过敏或禁忌患者; (5) 伴有严重心、肝、肾、肺功能不全或血液系统疾病患者; (6) 未能控制的严重高血压或血糖异常患者; (7) 有活动性出血、出血倾向、凝血功能异常患者; (8) 血小板计数 < 100 × 10⁹ L⁻¹; (9) 主动脉弓夹层患者; (10) 24 h 内接受过低分子肝素治疗患者; (11) 其他不适合溶栓的情况。本研究获得医院医学伦理委员会审核批准。

1.2 治疗方法 静脉溶栓治疗选用注射用阿替普酶 (德国勃林格殷格翰医药公司, 进口药品注册证号 S20110051), 剂量为 0.9 mg · kg⁻¹ (最大剂量 90 mg), 10% 于 1 min 内静脉推注, 剩余 90% 于 60 min 内静脉泵入。溶栓后, 定期监测患者意识、瞳孔及生命体征变化, 若出现头痛、呕吐及血压升高等症状立即行头颅 CT 检查; 溶栓后 24 h 复查头颅 CT。

1.3 观察指标 (1) 一般资料: 通过查阅病历资料收集患者的年龄、性别、吸烟、既往史 (包括高血压、卒中、糖尿病、心房颤动、冠状动脉性心脏病)。(2) NLR: 静脉溶栓前采集患者静脉血 2 mL, 应用 Beckman Coulter UniCel DxH 800 全自动细胞分析仪行血常规检测, 并计算 NLR。(3) 血脂指标: 静脉溶栓前采集患者空腹静脉血 3 mL, 应用罗氏 P800 全自动生物化学分析仪检测总胆固醇、三酰甘油、低密度脂蛋白胆固醇 (low-density lipoprotein cholesterol, LDL-C) 等血脂指标。(4) 美国国立卫生研究院卒中量表 (National Institute of Health stroke scale, NIHSS) 评分^[14]: 于静脉溶栓前行 NIHSS 评分, 总分 42 分, NIHSS 评分越高表示神经功能缺损越严重。(5) 改良 Rankin 量表 (modified Rankin scale, mRS) 评

分^[15]:于患者溶栓后 3 个月时进行 mRS 评分,完全无症状者为 0 分;有症状,但无明显功能障碍,能完成所有日常工作和生活者为 1 分;轻度残疾,不能完成病前所有活动,但不需帮助,能照料自己的日常事务者为 2 分;中度残疾,需部分帮助,但能独立行走者为 3 分;中重度残疾,不能独立行走,日常生活需别人帮助者为 4 分;重度残疾,卧床,二便失禁,日常生活完全依赖他人者为 5 分;mRS 评分 0~2 分者为预后良好。依据 mRS 评分将患者分为预后良好组($n=160$)和预后不良组($n=40$)。

1.4 统计学处理 应用 SPSS 17.0 软件进行统计学分析。计量资料以均数±标准差($\bar{x}\pm s$)表示,2 组间比较采用 Kruskal-Wallis 法 t 检验;计数资料以例数和百分率表示,2 组间比较采用 χ^2 检验;采用多因素 logistic 回归分析各指标与预后的关系,应用受试者操作特征(receiver operating characteristic, ROC)曲线评估 NLR 对预后的预测价值; $P<0.05$ 为差异有统计学意义。

2 结果

2.1 2 组患者的临床资料比较 结果见表 1。预后不良组患者的年龄、入院时 NIHSS 评分、NLR 显著高于预后良好组,差异有统计学意义($P<0.05$);预后良好组与预后不良组患者的性别分布、吸烟比例、有高血压史比例、有卒中史比例、有糖尿病史比例、有心房颤动史比例、有冠状动脉性心脏病史比例及总胆固醇、三酰甘油、LDL-C 水平比较差异无统计学意义($P>0.05$)。

表 1 2 组患者临床资料比较

Tab.1 Comparison of clinical data of patients between the two groups

指标	预后良好组 ($n=160$)	预后不良组 ($n=40$)	t/χ^2	P
年龄/岁	48.22±10.09	73.85±11.85	-2.479	0.014
性别				
男/例(%)	118(73.75)	28(70.00)	0.228	0.633
女/例(%)	42(26.25)	12(30.00)		
吸烟/例(%)	80(50.00)	19(47.50)	0.080	0.777
高血压史/例(%)	96(60.00)	26(65.00)	0.336	0.562
卒中史/例(%)	24(15.00)	9(22.60)	1.306	0.253
糖尿病史/例(%)	27(16.88)	8(20.00)	0.216	0.642
心房颤动史/例(%)	9(5.63)	4(10.00)	1.008	0.519
冠状动脉性心脏病史/例(%)	12(7.50)	4(10.00)	0.602	0.845
总胆固醇/(mmol·L ⁻¹)	4.41±0.98	4.07±1.09	-1.004	0.076
三酰甘油/(mmol·L ⁻¹)	1.47±0.62	1.69±1.05	1.280	0.173
LDL-C/(mmol·L ⁻¹)	2.46±0.65	2.43±0.80	-0.870	0.716
入院时 NIHSS 评分	9.46±2.65	19.68±4.65	-5.927	0.000
NLR	2.72±0.36	3.54±0.89	-2.653	0.032

2.2 不伴感染症状 AIS 患者静脉溶栓后预后的影响因素多因素 logistic 回归分析 校正混杂因素后多因素回归分析显示,入院时年龄[比值比(odds ratio, OR)=1.044,95% 置信区间(confidence interval, CI):1.009~1.082, $P<0.05$]、NIHSS 评分($OR=6.966$,95% $CI:2.801\sim17.327$, $P<0.001$)和 NLR($OR=1.165$,95% $CI:1.018\sim1.333$, $P<0.001$)是不伴感染症状 AIS 患者静脉溶栓后 3 个月不良预后的独立影响因素。

2.3 NLR 对不伴感染症状 AIS 患者静脉溶栓后 3 个月不良预后的预测价值分析 结果见图 1。NLR 评估不伴感染症状 AIS 患者静脉溶栓后 3 个月不良预后 ROC 曲线下面积为 0.636,最佳界值为 3.39,敏感度、特异度分别为 57.5%、75.6%。

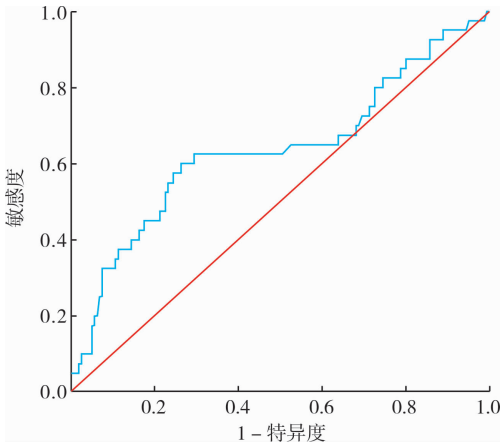


图 1 NLR 评估不伴感染症状 AIS 患者静脉溶栓 3 个月不良预后的 ROC 曲线

Fig.1 ROC curve of NLR in evaluating the poor prognosis of AIS patients without infection symptoms at three months after intravenous thrombolysis

3 讨论

中性粒细胞计数及淋巴细胞计数受个体基础疾病、应激程度、营养状态等因素的影响,个体差异较大;而 NLR 包含了中性粒细胞和淋巴细胞 2 种白细胞亚型的信息,是一种稳定而可靠的炎症指标。NLR 已被证实对心血管疾病、感染、炎症性疾病、脑卒中后脑水肿、癌症的预后具有预测价值,同时由于血常规检查的常规使用和廉价优势,目前较多研究者建议将 NLR 作为一种炎症指标^[16-19]。研究表明,中性粒细胞、淋巴细胞与 AIS 发生发展及临床预后相关^[20-22]。LIU 等^[23] 研究报道,入院时高 NLR 可能是预测轻型 AIS 患者静脉溶栓治疗后短期预后不良的指标。有研究报道,AIS 患者活化的中性粒细

胞可破坏血脑屏障,血液中中性粒细胞越高,脑梗死面积越大,神经功能损伤越严重^[20]。血液中淋巴细胞释放的抗炎因子、修复组织因子等对缺血缺氧的脑组织细胞发挥积极的神经保护作用,但 AIS 患者机体应激反应抑制了机体免疫功能,导致淋巴细胞数目减少及淋巴细胞特性改变,进而抑制免疫功能,加重神经损伤^[21-22]。另有研究报道,存活 AIS 患者 NLR 较死亡患者显著升高, AIS 患者入院时 NLR 与脑梗死面积、NIHSS 评分均呈显著正相关, NLR 可作为 AIS 患者短期病死的独立预测因子^[24-25]。既往研究也认为, AIS 患者入院时 NLR 越高,其静脉溶栓后 3 个月预后越差^[26]。但既往研究没有排除卒中后严重影响 NLR 的感染性因素。因此,本研究以不伴感染症状 AIS 患者为研究对象,分析患者入院时 NLR 与静脉溶栓后 3 个月不良预后的关系,评估其对患者静脉溶栓后 3 个月不良预后的预测价值。

本研究结果显示,不良预后组患者入院时年龄、NIHSS 评分和 NLR 显著高于良好预后组, 2 组患者的性别分布、吸烟比例、高血压史比例、卒中史比例、糖尿病史比例、心房颤动史比例、冠状动脉性心脏病史比例及总胆固醇、三酰甘油、LDL-C 水平比较差异无统计学意义;多因素 logistic 回归分析结果显示,患者入院时年龄、NIHSS 评分、NLR 与不良预后呈正相关,是患者静脉溶栓后 3 个月不良预后的独立影响因素;ROC 曲线分析结果显示, NLR 预测不伴感染症状 AIS 患者静脉溶栓后 3 个月不良预后的 ROC 曲线下面积为 0.636,最佳界值为 3.39,敏感度、特异度分别为 57.5%、75.6%;这与 KIM 等^[27]、ROSSO 等^[28]、CHEN 等^[29]研究结果一致,这些研究结果说明, NLR 可作为不伴感染症状 AIS 患者静脉溶栓后 3 个月不良预后的预测指标。

综上所述,不伴感染症状 AIS 患者入院时 NLR 是静脉溶栓后 3 个月不良预后的独立影响因素,可作为静脉溶栓后 3 个月不良预后的预测指标。本研究以不伴感染症状 AIS 患者为研究对象,排除了严重影响中性粒细胞、淋巴细胞的感染因素,因此研究结果更为精准可靠。但是,本研究为单中心研究、样本量小,后续需开展多中心研究、大样本量研究,并动态监测 NLR 变化,分析 NLR 与不同亚型 AIS 静脉溶栓患者功能预后的相关性,以期 AIS 提供一个简单易行、可操作性及实用性强的临床血清学检测指标。

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