

血尿素氮/白蛋白比值与大动脉粥样硬化性卒中严重程度和短期转归的相关性

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摘要

目的: 探讨血尿素氮/白蛋白比值(Blood urea nitrogen to albumin ratio, BAR)与大动脉粥样硬化性卒中(large artery atherosclerosis, LAA)严重程度和短期转归的相关性。方法: 回顾性纳入2017年9月至2022年8月在青岛大学附属医院住院的LAA型卒中患者。根据入院时美国国立卫生研究院卒中量表评分进一步分为轻度卒中组(≤ 8 分)和中重度卒中组(> 8 分), 根据出院时改良Rankin量表评分进一步分为转归良好组(≤ 2 分)和转归不良组(> 2 分)。采用多变量logistic回归分析确定BAR与LAA严重程度和短期转归的相关性。通过受试者工作特征(receiver operating characteristic, ROC)曲线评估BAR对LAA患者转归不良的预测价值。结果: 研究共纳入2014例患者, 其中, 男性1331例(66.1%), 女性683例(33.9%), 年龄(64.72 ± 11.72)岁。其中轻度卒中1047例(52.0%), 中重度卒中967例(48.0%), 出院时转归良好1030例(51.1%), 转归不良984例(48.9%)。在LAA患者中, 中重度卒中组和短期转归不良组BAR分别显著高于轻度卒中组与短期转归良好组。多变量logistic回归分析显示, BAR是LAA严重程度(OR 1.374, 95% CI 1.308~1.442; $P < 0.001$)和短期转归不良(OR 1.374, 95% CI 1.308~1.442; $P < 0.001$)的独立危险因素, ROC曲线分析显示, BAR预测LAA患者短期转归不良的曲线下面积为0.744 (95% CI 0.722~0.765; $P < 0.001$), 约登指数为0.366, 最佳截断值为7.150, 敏感性和特异性分别为81.7%和54.9%。结论: BAR与LAA型卒中患者的严重程度和短期转归不良有关, 并且对LAA型卒中患者短期转归具有良好的预测价值。

关键词

急性缺血性卒中, 动脉粥样硬化, 血尿素氮, 血清白蛋白

Blood Urea Nitrogen to Albumin Ratio Is Associated with Large Atherosclerosis Stroke, Its Severity and Short-Term Outcome

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Abstract

Objective: To investigate the relationship between Blood urea nitrogen to albumin ratio (BAR) and large artery atherosclerosis (large artery atherosclerosis, LAA) and its correlation with severity and short-term outcomes. **Methods:** LAA stroke patients hospitalized in the Affiliated Hospital of Qingdao University from September 2017 to August 2022 were retrospectively included. According to the score of National Institutes of Health Stroke Scale at admission, they were further divided into mild stroke group (≤ 8 points) and moderate to severe stroke group (> 8 points), and according to the score of modified Rankin scale at discharge, they were further divided into good outcome group (≤ 2 points) and poor outcome group (> 2 points). Multivariate logistic regression analysis was used to determine the correlation between BAR and LAA severity and short-term outcome. The predictive value of BAR for adverse outcomes in LAA patients was evaluated by receiver operating characteristic (ROC) curve. **Results:** A total of 2014 patients were included in the study, including 1331 males (66.1%) and 683 females (33.9%), aged (64.72 ± 11.72) years. Among them, there were 1047 cases (52.0%) of mild stroke, 967 cases (48.0%) of moderate and severe stroke, 1030 cases (51.1%) of good outcome at discharge, and 984 cases (48.9%) of poor outcome. In LAA patients, BAR in moderate to severe stroke group and short-term adverse outcome group was significantly higher than that in mild stroke group and short-term good outcome group, respectively. Multivariate logistic regression analysis showed that BAR was the severity of LAA (OR 1.374, 95% CI 1.308~1.442; $P < 0.001$) and poor short-term outcomes (OR 1.374, 95% CI 1.308~1.442; Independent risk factors ($P < 0.001$), ROC curve analysis showed that the area under the curve for BAR to predict adverse short-term outcomes in LAA patients was 0.744 (95% CI 0.722~0.765; $P < 0.001$), the Jorden index was 0.366, the best cutoff value was 7.150, the sensitivity and specificity were 81.7% and 54.9%, respectively. **Conclusion:** BAR is associated with the severity and short term outcome in LAA patients, and has a good predictive value for short term outcome in patients with LAA.

Keywords

Acute Ischemic Stroke, Atherosclerosis, Blood Urea Nitrogen, Serum Albumin

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1. 引言

脑卒中是世界范围内死亡和残疾的主要原因[1], 急性缺血性卒中占全部卒中 80%左右[2], 在我国, 脑卒中是导致人口死亡的首要原因[3]。按照 TOAST 病因学分型, 缺血性卒中可分为大动脉粥样硬化性卒中(large artery atherosclerosis, LAA)、心源性栓塞(cardioembolism, CE)、小血管闭塞(small vessel occlusion, SVO)、其他明确病因卒中(stroke of other determined etiology, SOE)和病因不明型卒中(stroke of undemonstrated etiology, SUE) [4]。

血尿素氮(BUN)是反映肾功能的重要指标, 是肝脏产生并由肾脏排出的蛋白质代谢产物, 可用于临床

评估肾功能[5]。一项前瞻性研究表明,较高的 BUN 水平可预测 9420 例急性冠脉综合征患者的死亡率,与 eGFR、血清肌酐或估计的肌酐清除率无关[6]。这一证据表明, BUN 相较于其他肾功能指标,可能增加额外的心血管风险,是心血管疾病结局的更好预测因子[5]。人血清白蛋白是循环系统中丰富的可溶性蛋白质成分,具有抗血小板聚集、抗凝血、维持血浆渗透压、转运多种物质等多种生物学功能[7] [8] [9] [10]。血尿素氮/白蛋白比值(BAR)是近年来新发现的一种诊断指标,与心脑血管疾病相关。研究表明, BAR 可作为急性心肌梗死、心脏术后、心力衰竭患者的预后生物标志物[5] [6] [11]-[16]。目前, BAR 与 LAA 型卒中的严重程度及预后的关系仍不清楚。在本研究中,我们旨在探讨血尿素氮/白蛋白比值(BAR)在预测 LAA 型卒中患者方面严重程度和短期转归的相关性以及对其短期转归的预测价值,以其为临床决策提供依据。

2. 对象和方法

2.1. 研究对象

回顾性纳入 2017 年 9 月至 2022 年 8 月在青岛大学附属医院住院的急性缺血性卒中患者。纳入标准 [17] [18] [19]: (1) 经头颅 MRI 或 CT 影像学检查证实缺血性脑卒中; (2) 符合《中国急性缺血性脑卒中的诊治指南(2018)》诊断标准; (3) TOAST 分型为大动脉粥样硬化性脑卒中; (4) 患者年龄 ≥ 18 岁且 < 90 岁,首次发病,时间 ≤ 72 小时; (5) 患者或家属签署知情同意书。排除标准 [18] [20]: (1) TOAST 分型为心源性栓塞型、小血管闭塞型、其他原因或不明原因型脑卒中; (2) 行溶栓或血管内血栓切除术者; (3) 伴颅脑损伤、脑炎、脑肿瘤等非脑血管性脑部疾病; (4) 严重心、肝、肾等器质性疾病; (5) 血液、免疫系统疾病及感染疾病者; (6) 临床资料不完整。

2.2. 资料收集

利用基于医院的卒中专病库智能提取患者基线资料,包括人口统计学(年龄、性别)、血管危险因素(高血压、高脂血症、糖尿病、吸烟、饮酒)、基线血压(收缩压、舒张压)、入院次日清晨空腹静脉血实验室检查结果(总胆固醇、甘油三酯、低密度脂蛋白胆固醇、高密度脂蛋白胆固醇、尿素氮、白蛋白)以及根据尿素氮和白蛋白计算的 BAR)、基线美国国立卫生研究院卒中量表(National Institutes of Health Stroke Scale, NIHSS)评分及其分类、发病前改良 Rankin 量表(modified Rankin Scale, mRS)评分。

入院当天由 2 名神经内科医生根据 NIHSS 量表评估患者神经功能缺损严重程度, ≤ 8 分为轻度卒中, > 8 分为中重度卒中[21]。患者出院时由 2 名对基线资料不知情的神经内科医生根据 mRS 评估患者短期转归, ≤ 2 分为转归良好, > 2 分为转归不良。

2.3. 统计学分析

采用 SPSS 26.0 软件进行统计学分析。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;非正态分布的计量资料以中位数和四分位数间距表示,两组间比较采用独立样本 Mann-Whitney U 检验。计数资料以频数和百分率表示,组间比较采用 χ^2 检验或 Fisher 精确概率法。利用二分类多变量 logistic 回归分析确定 BAR 与 LAA 严重程度及短期转归的独立相关性,并计算优势比(odds ratio, OR)和 95% 置信区间(confidence interval, CI)。采用受试者工作特征(receiver operating characteristic, ROC)曲线分析 BAR 对 LAA 短期转归不良的预测价值,并计算其最佳截断值以及敏感性和特异性。P < 0.05 为有统计学意义。

3. 结果

研究期间根据纳入和排除标准,最终 2014 例患者纳入分析。其中,男性 1331 例(66.1%),女性 683

例(33.9%), 年龄(64.72 ± 11.72)岁。其中轻度卒中 1047 例(52.0%), 中重度卒中 967 例(48.0%), 出院时转归良好 1030 例(51.1%), 转归不良 984 例(48.9%)。

3.1. BAR 与 LAA 患者严重程度的相关性

在 LAA 患者中, 中重度卒中组糖尿病构成比、年龄、收缩压、总胆固醇、高密度脂蛋白胆固醇、低密度脂蛋白胆固醇、尿素氮、BAR、住院天数均显著高于轻度卒中组, 而甘油三酯、白蛋白均显著低于轻度卒中组(P 均 <0.05 ; 表 1)。以表 1 轻度卒中组与中重度卒中组比较中 $P < 0.05$ 的变量作为自变量, LAA 严重程度作为应变量, 进行二分类多变量 logistic 回归分析。结果显示, 年龄(OR 1.010, 95% CI 1.001~1.019; $P = 0.026$)、收缩压(OR 1.005, 95% CI 1.000~1.010; $P = 0.030$)、总胆固醇(OR 1.120, 95% CI 1.042~1.205; $P = 0.002$)、住院天数(OR 1.086, 95% CI 1.055~1.118; $P < 0.001$)、BAR(OR 1.374, 95% CI 1.308~1.442; $P < 0.001$)是 LAA 严重程度的独立危险因素。

Table 1. Comparison of demographic and baseline data between mild and moderate to severe stroke in LAA patients
表 1. LAA 患者轻度卒中与中重度卒中人口统计学和基线资料比较

变量	轻度卒中 (n = 1047)	中重度卒中 (n = 967)	t 值、Z 值 或 χ^2 值	P 值
年龄(岁)	62.92 ± 11.71	66.68 ± 11.40	-7.290	<0.001
男性(n, %)	703 (67.1)	628 (64.9)	1.087	0.297
高血压(n, %)	648 (61.9)	600 (62.0)	-0.072	0.942
糖尿病(n, %)	187 (17.9)	208 (21.5)	4.25	0.039
冠心病(n, %)	85 (8.1)	82 (8.5)	-0.294	0.769
高脂血症(n, %)	451 (43.1)	396 (41.0)	-0.925	0.355
吸烟史(n, %)	432 (41.3)	367 (38.0)	-1.516	0.130
饮酒史(n, %)	357 (34.1)	350 (36.2)	-0.985	0.325
舒张压(mmHg)	83.32 ± 12.72	83.09 ± 12.71	0.399	0.690
收缩压(mmHg)	150.91 ± 20.95	153.74 ± 22.60	-2.832	0.004
总胆固醇(mmol/L)	4.02 ± 1.72	4.42 ± 1.61	-5.508	<0.001
甘油三酯(mmol/L)	1.31 (0.98~1.79)	1.23 (0.93~1.72)	-2.452	0.014
高密度脂蛋白胆固醇(mmol/L)	1.19 ± 0.28	1.22 ± 0.27	-2.771	0.006
低密度脂蛋白胆固醇(mmol/L)	2.78 ± 0.85	2.94 ± 0.91	-3.903	<0.001
血尿素氮(mg/L)	286.57 ± 83.27	345.99 ± 104.19	-14.066	<0.001
血清白蛋白(g/L)	39.06 ± 3.24	37.72 ± 3.78	8.494	<0.001
尿素氮/白蛋白比值(mg/g)	7.39 ± 2.26	9.32 ± 3.58	-14.371	<0.001
住院天数(天)	9.07 ± 3.28	10.16 ± 4.57	-6.073	<0.001

3.2. BAR 与 LAA 患者短期转归的相关性

在 LAA 患者中, 转归不良组以及年龄、收缩压、总胆固醇、高密度脂蛋白胆固醇、低密度脂蛋白胆固醇、血尿素氮、BAR、住院天数均显著高于转归良好组, 而高脂血症的构成比、甘油三酯、血清白蛋白显著低于转归良好组(P 均 <0.05 ; 表 2)。以表 2 转归良好组与转归不良组比较中 $P < 0.05$ 的变量作为

自变量, 短期转归作为应变量, 进行二分类多变量 logistic 回归分析。结果显示, 年龄(OR 1.013, 95% CI 1.004~1.022; P = 0.006)、收缩压(OR 1.006, 95% CI 1.002~1.011; P = 0.008)、总胆固醇(OR 1.080, 95% CI 1.005~1.162; P = 0.037)、住院天数(OR 1.085, 95% CI 1.054~1.117; P < 0.001)、BAR (OR 1.426, 95% CI 1.356~1.500; P < 0.001)是 LAA 患者短期转归不良的独立预测因素。

Table 2. Comparison of demographic and baseline data between the good outcome group and the poor outcome group of LAA patients

表 2. LAA 患者转归良好组与转归不良组人口统计学和基线资料比较

变量	转归良好 (n = 1030)	转归不良 (n = 984)	t 值、Z 值 或 χ^2 值	P 值
年龄(岁)	62.70 ± 11.63	66.84 ± 11.44	-8.055	<0.001
男性(n, %)	685 (66.5)	646 (65.7)	0.164	0.686
高血压(n, %)	643 (62.4)	605 (61.5)	0.190	0.663
糖尿病(n, %)	186 (18.1)	209 (21.2)	3.231	0.072
冠心病(n, %)	80 (7.8)	87 (8.8)	0.764	0.382
高脂血症(n, %)	456 (44.3)	391 (39.8)	4.093	0.043
吸烟史(n, %)	428 (41.6)	371 (37.7)	3.117	0.077
饮酒史(n, %)	357 (34.7)	350 (35.6)	0.182	0.669
舒张压(mmHg)	83.23 ± 12.69	83.20 ± 13.01	0.058	0.954
收缩压(mmHg)	150.72 ± 21.06	153.89 ± 22.44	-3.270	0.001
总胆固醇(mmol/L)	4.05 ± 1.72	4.38 ± 1.62	-4.363	<0.001
甘油三酯(mmol/L)	1.32 (0.98~1.82)	1.23 (0.93~1.69)	-2.955	0.003
高密度脂蛋白胆固醇(mmol/L)	1.19 ± 0.28	1.22 ± 0.27	-2.497	0.013
低密度脂蛋白胆固醇(mmol/L)	2.79 ± 0.86	2.92 ± 0.89	-3.439	0.001
血尿素氮(mg/L)	283.85 ± 81.59	347.81 ± 103.87	-15.321	<0.001
血清白蛋白(g/L)	39.06 ± 3.22	37.73 ± 3.80	8.473	<0.001
尿素氮/白蛋白比值(mg/g)	7.32 ± 2.23	9.36 ± 3.55	-15.423	<0.001
住院天数(天)	9.08 ± 3.27	10.13 ± 4.57	-5.918	<0.001

3.3. BAR 对 LAA 患者短期转归不良的预测价值

ROC 曲线(图 1)分析显示, BAR 预测 LAA 患者短期转归不良的曲线下面积为 0.744 (95% CI 0.722~0.765; P < 0.001), 约登指数为 0.366, 最佳截断值为 7.150, 敏感性和特异性分别为 81.7%和 54.9%。相比之下, 血清尿素氮和白蛋白对 LAA 患者短期转归不良的预测价值较差, AUC 分别为 0.721 (95% CI 0.699~0.743; P < 0.001)和 0.606 (95% CI 0.582~0.631; P < 0.001)。

4. 讨论

在这项研究中, 我们发现随着 BAR 水平的增高, LAA 型卒中的风险显著升高, BAR 与 LAA 型卒中患者的病情严重程度和预后有关。这项研究表明 BAR 可能作为反映 LAA 型卒中存在的潜在生物学标志物。

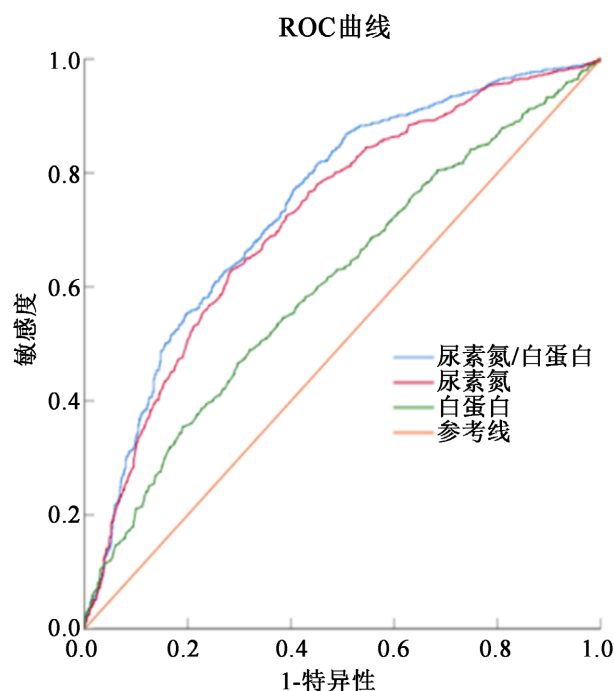


Figure 1. The ROC curve of BAR for predicting adverse outcomes in LAA
图 1. BAR 预测 LAA 患者转归不良 ROC 曲线

血尿素氮(BUN)是人体蛋白质代谢的主要产物, 主要由肾脏排泄[22]。一项在 3355 例急性缺血性卒中患者中进行的前瞻性研究表明, BUN 与急性缺血性卒中患者住院死亡率显著相关[23]; 研究表明, BUN 可作为有效参数预测急危重症患者预后不良, 危重症患者的氧化应激反应剧烈, 导致蛋白分解代谢旺盛, BUN 合成增多[24]。

血清白蛋白(ALB)由肝脏合成, 是机体重要的营养物质, 具有抗血小板聚集、抗凝血、维持血浆渗透压、转运多种物质等多种生物学功能[7] [8] [9], 一项前瞻性研究表明, 低血清白蛋白水平增加缺血性卒中风险, 血清白蛋白浓度与脑卒中风险之间存在独立负相关性[25]。研究表明, ALB 能够维持血浆渗透压, 降低血液黏稠度, 改善动脉反应性, 减轻缺血-再灌注损伤, 从而改善梗死部位的血液循环[26]。

血尿素氮/白蛋白比值(BAR)是近年来新发现的一种生物学指标, 具有无创、易获得、应用范围广等优点, 被应用于多种临床疾病的预测[27]。研究表明, BAR 可作为胃肠道出血、大肠杆菌菌血症等疾病的患者的不良结局和重症监护的有用预测因子[28] [29] [30]。研究表明, BUN 升高和 ALB 降低与心脑血管疾病患者的不良预后密切相关, 包括急性冠脉综合征、急性心肌梗死、心力衰竭和缺血性卒中[5] [6] [11]-[16] [25]。Tianyong Han 等人研究发现, BAR 值与脓毒症严重程度呈正相关, BAR 值越高, 脓毒症患者预后越差[31]。BAR 与 LAA 型卒中关系目前尚不清楚, 本研究表明 BAR 是 LAA 患者的独立危险因素, 与患者病情严重程度及短期转归相关。

急性缺血性脑卒中发生后, 机体为维持脑灌注进行全身血流量重新分布, 流经肾脏的血流量相对减少, 神经激素分泌异常, 导致 BUN 合成增多[32]。ALB 能够反映机体的血浆胶体渗透压情况[25], ALB 水平降低说明血浆胶体渗透压降低, 血液黏稠度升高, 脑血流速度减慢[33], 脑血管灌注量不足, 缺血性脑卒中进一步加重。急性缺血性脑卒中发生后, 全身血液重新分布, 肝脏血流量减少, ALB 合成减少, 且机体蛋白质的分解代谢亢进, ALB 消耗增多, 进而导致 ALB 水平降低[34]。

本研究存在一些局限性。首先, 本研究为回顾性研究, 无法确定 BAR 与 LAA 之间的因果关系。其

次,这是一项观察性研究,可能存在一些无法测量或残留的混杂效应。最后,患者来自单个卒中中心,可能存在选择偏倚。因此,其结果仍需要更大样本量的多中心研究来进一步验证。

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