

• 论著 •

阿尔伯塔卒中项目早期 CT 评分和溶栓后出血评分以及相关因素对急性脑梗死溶栓后出血转化的预测价值

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【摘要】目的 探讨阿尔伯塔卒中项目早期 CT 评分(ASPECTS)和溶栓后出血评分(HAT 评分)对阿替普酶溶栓后急性脑梗死(ACI)患者出血转化(HT)的预测价值。**方法** 选择天津市静海区医院神经内科 2015 年 1 月至 2017 年 3 月收治的 ACI 患者 121 例, 均采用阿替普酶 0.6 mg/kg 溶栓治疗, 最大剂量 90 mg, 总量的 1/10 在 1 min 内静脉推注, 余量溶于 100 mL 生理盐水中持续静脉滴注(静滴)1 h。溶栓开始前进行 ASPECTS 评分及 HAT 评分, 比较不同 ASPECTS 评分和 HAT 评分患者 HT 发生情况, 用 logistic 回归分析影响 ACI 溶栓后发生 HT 的危险因素; 绘制受试者工作特征曲线(ROC 曲线), 分析 HAT 评分及 ASPECTS 评分诊断发生 HT 的临床价值。**结果** ACI 患者 ASPECTS 评分越高, HT 发生率越低, ASPECTS 评分 0~4、5~7、8~10 分患者的 HT 发生率分别为 57.1% (4/7)、26.7% (8/30)、14.3% (12/84); 同样 ACI 患者 HAT 评分越高, HT 发生率越高, HAT 评分 0、1、2、≥3 分患者的 HT 发生率分别为 7.1% (4/56)、21.0% (8/38)、33.3% (7/21)、83.3% (5/6)。单因素分析显示: 入院时收缩压、既往服用抗血小板药物、入院时头颅 CT 示大脑中动脉高密度征象、发病至溶栓开始时间、HAT 评分、ASPECTS 评分是影响 HT 发生的危险因素 [优势比(OR) 值分别为 0.972、0.279、0.992、0.311、2.628、2.625, 95% 可信区间(95%CI) 分别为 0.935~1.012、0.093~0.836、0.983~1.000、0.105~0.916、1.362~5.071、1.522~4.525, P 值分别为 0.034、0.023、0.042、0.003、0.045]; 多因素 logistic 回归分析显示: 入院时收缩压、既往服用抗血小板药物、入院时头颅 CT 示大脑中动脉高密度征象、发病至溶栓开始时间、HAT 评分、ASPECTS 评分均是影响 HT 发生的独立危险因素 (OR 值分别为 1.766、1.012、1.574、1.030、2.155、2.431, 95%CI 分别为 1.233~2.103、1.009~1.204、1.186~2.091、1.009~1.053、1.237~4.907、1.213~5.815, P 值分别为 0.023、0.004、0.002、0.005、0.007、0.047); HAT 评分及 ASPECTS 评分均可预测静脉溶栓治疗后 HT 发生的风险(均 P<0.05), 且 ASPECTS 的敏感度、特异度、ROC 曲线下面积(AUC)、95%CI 均高于 HAT 评分: (94.4% 比 94.0%、61.4% 比 41.0%、0.77 比 0.70、0.710~0.830 比 0.650~0.800)。**结论** ASPECTS 评分越高, HT 发生率越低, HAT 评分越高, HT 发生率越高; HAT 评分和 ASPECTS 评分均可预测静脉溶栓治疗后 HT 发生的风险, 而 ASPECTS 评分系统的预测价值更高。

【关键词】 脑梗死; 阿尔伯塔卒中项目早期 CT 评分; 溶栓后出血评分; 出血转化

A predictive value of post-thrombolysis hemorrhagic transformation in acute cerebral infarction predicted by Alberta stroke program early CT score, hemorrhage after thrombolysis score and related factors

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【Abstract】Objective To observe the predictive value of Alberta stroke program early CT score (ASPECTS) and hemorrhage after thrombolysis score (HAT score) for the hemorrhagic transformation (HT) of acute cerebral infarction (ACI) patients after thrombolysis with Alteplase. **Methods** One hundred and twenty-one patients with ACI admitted to the Department of Neurology of Tianjin Jinghai District Hospital from January 2015 to March 2017 were enrolled, they were all treated by using Alteplase 0.6 mg/kg for thrombolysis, maximum dose being 90 mg, and 1/10 of the total dose was intravenously injected in 1 minute, and then the residual part dissolved in 100 mL normal saline was intravenously dripped continuously for 1 hour. The ASPECTS and HAT score were carried out before the start of thrombolysis, and then the HT incidence situations in patients with different ASPECTSs and HAT scores were compared, and logistic regression analysis was used to analyze the risk factors of HT after thrombolysis in patients with ACI; then the receiver operating characteristic (ROC) curve was drawn, and the clinical value of HAT score and ASPECTS in diagnosing HT occurrence was analyzed. **Results** In cases with ACI, it was discovered that the higher the ASPECTS, the lower the incidence of HT, indicating that the incidences of HT in patients with ASPECTSs 0~4, 5~7, 8~10 were 57.1% (4/7), 26.7% (8/30), 14.3% (12/84) respectively; Similarly, in such cases, the higher the HAT scores, the higher the incidence of HT, showing that the incidences of HT of patients with HAT scores 0, 1, 2, ≥ 3 were 7.1% (4/56), 21.0% (8/38), 33.3% (7/21), 83.3% (5/6) respectively. The single factor analysis showed that the risk

factors influencing the HT incidence included the systolic blood pressure on admission, anti-platelet medicine taken in the past history, the sign of high density of middle cerebral artery shown in head CT film on admission, the time of interval between the onset of the disease and the beginning of thrombolysis, HAT score and ASPECTS [odds ratio (*OR*) values were 0.972, 0.279, 0.992, 0.311, 2.628, 2.625, respectively, 95% confidence intervals (95%CI) were 0.9352–1.012, 0.093–0.836, 0.983–1.000, 0.105–0.916, 1.362–5.071, 1.522–4.525, *P* values were 0.034, 0.023, 0.042, 0.034, 0.003, 0.045 respectively]; the multifactorial logistic regression analysis showed that the independent risk factors influencing HT incidence were as follows: the systolic blood pressure on admission, anti-platelet medicines taken in the past history, the sign of high density of the middle cerebral artery shown in the head CT film on admission, the time of interval between the onset of the disease and the beginning of thrombolysis, HAT score and ASPECTS (*OR* values were 1.766, 1.012, 1.574, 1.030, 2.155, 2.431, 95%CI were 1.233–2.103, 1.009–1.204, 1.186–2.091, 1.009–1.053, 1.237–4.907, 1.213–5.815, *P* values were 0.023, 0.004, 0.002, 0.005, 0.007, 0.047); HAT score and ASPECTS could predict the risk of HT incidence after venous thrombolytic therapy, sensitivity, specificity, area under ROC curve (AUC), 95%CI in ASPECTS were higher than those of HAT score (94.4% vs. 94.0%, 61.4 vs. 41.0%, 0.77 vs. 0.70, 0.710–0.830 vs. 0.650–0.800). **Conclusions** It is shown in this study that the higher the ASPECTS, the lower the incidence of HT, and the higher the HAT score, the higher the incidence of HT; both HAT score and ASPECTS can predict the risk of HT incidence after venous thrombolytic therapy, and the predictive value of ASPECTS system is higher than that of HAT score.

【Key words】 Cerebral infarction; Alberta stroke program early CT score; Hemorrhage after thrombolysis score; Hemorrhagic transformation

急性脑梗死(ACI)是指各种原因所致脑部血液供应不足,导致脑组织缺血、缺氧、坏死,并出现相应神经功能缺损的脑血管病急症。ACI致残率和病死率高,严重威胁着患者生命安全。导致ACI的原因很多,但其主要原因是动脉粥样斑块的形成和血小板聚集^[1]。早期静脉溶栓治疗是挽救脑组织的有效方法,而出血转化(HT)是脑梗死溶栓治疗的严重并发症,早期预测HT的发生对降低患者致残率和病死率,改善预后有重要意义。本研究旨在探讨阿尔伯塔卒中项目早期CT评分(ASPECTS评分)联合溶栓后出血评分(HAT评分)对ACI溶栓后HT发生的预测价值。

1 资料与方法

1.1 研究对象:选择2015年1月至2017年3月天津市静海区医院神经内科住院治疗的大脑中动脉(MCA)ACI患者121例。

1.1.1 纳入标准:①年龄18~80岁。②在症状出现的3 h内。③有MCA缺血性卒中导致的神经功能缺损症状。④患者家属签署知情同意书。

1.1.2 排除标准:①活动性出血和既往有出血性疾病。②服用抗凝药物,凝血酶原时间(PT)>15 s,或48 h内使用过肝素且实验室检查提示活化部分凝血活酶时间(APTT)延长,血小板计数(PLT)<100×10⁹/L。③收缩压>180 mmHg(1 mmHg=0.133 kPa),或舒张压>110 mmHg。④血糖<2.7 mmol/L。⑤其他不适宜溶栓的情况。

1.1.3 伦理学:本研究符合医学伦理学标准,并经医院伦理委员会批准,取得患者或家属知情同意。

1.2 溶栓方法:给予阿替普酶溶栓,总量按0.6 mg/kg

计算(最大剂量90 mg),总量的1/10在1 min内静脉推注,余量溶于100 mL生理盐水中持续静脉滴注(静滴)1 h。

1.3 资料收集:收集患者的临床基线资料,包括年龄、性别、既往史、早期CT情况、脑梗死面积、发病时间、溶栓开始时间、溶栓治疗前美国国立卫生研究院卒中量表(NIHSS)评分、溶栓前静脉血糖值、溶栓前药物服用情况等。采用单因素和多因素logistic回归分析影响ACI患者溶栓后发生HT的危险因素,绘制受试者工作特征曲线(ROC曲线)分析HAT及ASPECTS评分诊断发生HT的临床价值。

1.3.1 ASPECTS评分方法:将MCA供血区分为10个区域,即尾状核(C)、豆状核(L)、内囊(IC)和区皮质M1、M2、M3、M4、M5、M6以及岛叶(I)。总分为10分,每累及1个区域减1分。

1.3.2 HAT评分方法:①有糖尿病病史或入院时基线血糖>11.1 mmol/L:是评1分,否评0分。②治疗前NIHSS评分<15分评0分,15~19分评1分,≥20分评2分。③初始头颅CT可见低密度区:无评0分,<1/3 MCA供血区评1分,≥1/3 MCA供血区评2分。

1.4 统计学方法:使用SPSS 18.0统计软件处理数据,符合正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示;计数资料以例(率)表示,采用 χ^2 检验或Fisher精确概率法,采用单因素和多因素logistic回归分析影响ACI患者溶栓后发生HT的危险因素,绘制ROC曲线,分析HAT评分及ASPECTS评分诊断发生HT的临床价值。*P*<0.05为差异有统计学意义。

2 结 果

2.1 一般资料:本研究共纳入121例行静脉溶栓治疗的ACI患者,其中男性68例,女性53例;年龄45~78岁,平均(60±6)岁;NIHSS评分为7~22分,平均(12.3±3.4)分,其中未发生HT97例,发生HT24例,HT发生率为19.8%。

2.2 不同ASPECTS评分患者静脉溶栓后HT发生率比较(表1):ASPECTS评分越高,HT发生率越低($\chi^2=8.635,P<0.01$)。

表1 不同ASPECTS评分患者溶栓后HT发生率比较

ASPECTS评分(分)	例数(例)	HT[%(例)]	HT分型[% (例)]		
			非症状性出血	症状性出血	致死性出血
0~4	7	57.1(4)	14.3(1)	28.5(2)	14.3(1)
5~7	30	26.7(8)	16.7(5)	6.7(2)	3.3(1)
8~10	84	14.3(12)	11.9(10)	2.4(2)	0(0)
合计	121	24	16	6	2

2.3 不同HAT评分患者静脉溶栓后HT发生率比较(表2):HAT评分越高,HT发生率越高($\chi^2=20.872,P<0.01$)。

表2 不同HAT评分患者溶栓后HT发生率的比较

HAT评分(分)	例数(例)	HT[%(例)]	HT分型[% (例)]		
			非症状性出血	症状性出血	致死性出血
0	56	7.1(4)	7.1(4)	0(0)	0(0)
1	38	21.0(8)	15.8(6)	5.2(2)	0(0)
2	21	33.3(7)	23.8(5)	9.5(2)	0(0)
≥3	6	83.3(5)	16.7(1)	33.3(2)	33.3(2)
合计	121	24	16	6	2

表3 121例ACI患者溶栓后发生HT的单因素分析

指标	β 值	$s_{\bar{x}}$	χ^2 值	OR值	95%CI	P值
有高血压病史	0.659	0.515	1.634	1.932	0.704~5.304	0.201
入院时收缩压	0.028	0.020	1.930	0.972	0.935~1.012	0.034
既往服用抗血小板药物	1.276	0.560	5.199	0.279	0.093~0.836	0.023
入院时血糖水平	1.232	0.542	5.162	0.292	0.101~0.844	0.203
入院时头颅CT示MCA高密度征象	-0.008	0.004	3.789	0.992	0.983~1.000	0.042
发病至溶栓开始时间	1.169	0.552	4.493	0.311	0.105~0.916	0.034
HAT评分	0.950	0.305	8.403	2.628	1.362~5.071	0.003
ASPECTS评分	0.965	0.432	2.055	2.625	1.522~4.525	0.045

注:OR为优势比,95%CI为95%可信区间

表4 121例ACI患者溶栓后发生HT的多因素logistic回归分析

指标	β 值	$s_{\bar{x}}$	χ^2 值	OR值	95%CI	P值
入院时收缩压	0.571	0.136	19.393	1.766	1.233~2.103	0.023
既往服用抗血小板药物	0.087	0.045	4.648	1.012	1.009~1.204	0.004
入院时头颅CT示MCA高密度征象	0.454	0.145	9.876	1.574	1.186~2.091	0.002
发病至溶栓开始时间	0.030	0.011	7.977	1.030	1.009~1.053	0.005
HAT评分	0.911	0.613	7.014	2.155	1.237~4.907	0.007
ASPECTS评分	0.818	0.344	5.029	2.431	1.213~5.815	0.047
常数项	-30.923	10.913	10.454			

2.4 ACI患者溶栓后发生HT的单因素logistic回归分析(表3):以HT(0=无HT,1=HT)作为因变量,以有高血压病史(0=无,1=有)、入院时收缩压、既往服用抗血小板药物(0=未用,1=服用)、入院时血糖水平、发病至溶栓开始时间、入院时头颅CT示MCA高密度征象(0=无,1=有)、HAT评分、ASPECTS评分作为协变量,逐一引入logistic行单因素回归分析,结果显示,入院时收缩压、既往服用抗血小板药物、发病至溶栓开始时间、入院时头颅CT示MCA高密度征象、HAT评分、ASPECTS评分是HT发生的危险因素(均P<0.05)。

2.5 ACI患者溶栓后发生HT的多因素logistic回归分析(表4):将单因素分析中有统计学意义的指标进一步纳入多因素logistic回归分析进行统计,结果显示,入院时收缩压、既往服用抗血小板药物、发病至溶栓开始时间、入院时头颅CT示MCA高密度征象、HAT评分、ASPECTS评分是HT发生的独立危险因素(均P<0.05)。

2.6 HAT评分和ASPECTS评分诊断HT发生的临床价值(表5;图1):HAT及ASPECTS评分均可预测静脉溶栓治疗后HT发生的风险(均P<0.05),而ASPECTS评分系统的预测价值较HAT评分更高。

表5 HAT评分及ASPECTS评分
诊断发生HT的临床价值

指标	敏感度 (%)	特异度 (%)	AUC	95%CI	$s_{\bar{x}}$	约登指数	P值
HAT评分	94.0	41.0	0.70	0.650~0.800	0.013	0.350	0.01
ASPECTS评分	94.4	61.4	0.77	0.710~0.830	0.245	0.558	0.03

注:AUC为ROC曲线下面积

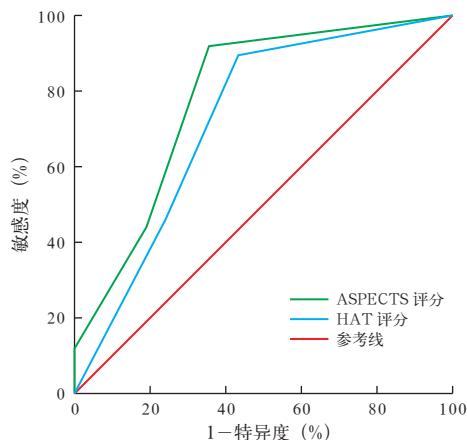


图1 ASPECTS 和 HAT 评分预测 ACI 溶栓后 HT 转化的 ROC 曲线

3 讨论

ASPECTS 评分是评估 MCA 早期缺血性变化的半定量评分系统,可准确、快速获得病灶大小的信息^[2]。Tei 等^[3]研究显示,ASPECTS 评分≥8 分,约 80% 的患者预后良好,而 ASPECTS 评分≤7 分者,仅 28.8% 的患者预后良好,ASPECTS 评分≤3 分者均预后不良。刘艳等^[4]研究表明,ASPECTS 评分<5 分 MCA 梗死患者,发生脑微血管出血的可能性会提高。ASPECTS 评分被广泛用于评估静脉溶栓指征及预测患者预后,评分<7 分者通常预后较差,而且溶栓后更易出血^[5-6]。本研究显示,ASPECTS 8~10 分者 HT 发生率为 14.3%,5~7 分者 HT 发生率为 26.7%,0~4 分者 HT 发生率为 57.1%,ASPECTS 评分越低,HT 发生率越高,与其他研究相似。

HAT 评分是溶栓治疗的分层系统被广泛用于预测阿替普酶溶栓治疗后颅内出血的风险。当 HAT 评分达到 3 分时,张新宇等^[7]研究发现,症状性颅内出血的比例达到了 12.6%;但也有报道,症状性颅内出血的发生率为 1.7%~1.8%^[8];姜超等^[9]研究显示,症状性出血的发生率为 33%,致死性出血的发生率为 17%;而本研究显示,症状性出血和致死性出血发生率均为 33.3%,显著高于其他研究,但可能与入选样本量相对较小有关。因此当 HAT 评分≥3 分时,选择溶栓治疗应该更加慎重。HAT 评分可有效预测静脉溶栓后 HT 的风险,HAT 评分越低,HT 发生率越低,预后越好。

本研究单因素 logistic 回归分析显示,入院时收缩压、既往服用抗血小板药物、入院头颅 CT 示 MCA 高密度征象、发病至溶栓开始时间、HAT 评分、ASPECTS 评分是 HT 发生的危险因素。进一步将单因素 logistic 回归分析中有统计学意义的指标纳入

多因素 logistic 回归分析,结果显示上述因素是 HT 发生的独立危险因素。服用抗血小板药物史不是溶栓治疗的禁忌证,血小板聚集功能检测也不是溶栓前必须检查项目,但本研究提示既往服用抗血小板药物为 HT 发生的独立危险因素,这与相关文献^[10]报道相似。研究表明,入院时收缩压、血糖水平、发病早期 CT 示低密度梗死灶、溶栓时间窗、HAT 评分均为静脉溶栓治疗后发生 HT 的危险因素,可能与这些因素更易损伤血脑屏障、血管基底膜、血管内皮细胞紧密连接完整性等有关^[11]。而本研究血糖水平、既往有高血压病史是其危险因素,但尚未达到统计学意义,可能与入选的样本量相对较少有关。

本研究 HAT 评分预测 HT 发生的敏感度、特异度、ACU 分别为 94.0%、41.0%、0.70, ASPECTS 评分预测 HT 发生的敏感度、特异度、ACU 分别为 94.4%、61.4%、0.77, 表明 HAT 评分及 ASPECTS 评分均可预测静脉溶栓治疗后 HT 发生的风险,而 ASPECTS 评分的预测价值更高。

但本研究也有不足之处,收集的样本量相对较小,希望在以后的临床工作中,收集更多样本量来进行研究,以期进一步指导临床工作,降低溶栓后 HT 的发生率。

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