

·论著·

## 缺血性脑卒中取栓后出血转化及长期预后的 影响因子分析

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**摘要 目的:**分析急性缺血性脑卒中(AIS)患者取栓术再通后发生出血转化(HT)和长期预后不良的影响因素。**方法:**收集接受取栓治疗的前循环AIS患者102例的临床资料,根据术后24 h~1周内是否发生HT和随访1年时改良Rankin评分量表(mRS)评分,将患者分为HT组、NHT组和预后良好组、预后不良组。回顾性分析各组临床资料,探究发生HT和长期预后不良的影响因素。**结果:**102例患者,纳入HT组58例、NHT组44例,纳入预后不良组56例、预后良好组46例。单因素分析可知,HT和NHT组、预后良好和预后不良组的Alberta卒中项目早期CT评分(ASPECTS)评分差异有统计学意义( $P=0.000, 0.022$ )；年龄( $P=0.108$ )、冠心病( $P=0.061$ )、低密度脂蛋白( $P=0.078$ )和术前静脉溶栓( $P=0.058$ )可能对术后HT产生影响；取栓次数( $P=0.118$ )、到院至穿刺时间( $P=0.098$ )和发病至穿刺时间( $P=0.023$ )可能对长期预后产生影响；其他资料差异无统计学差异( $P>0.05$ )。将上述影响因素代入多元Logistic回归模型,分析结果显示,取栓前ASPECTS评分是术后发生HT( $P=0.001, OR=0.561, 95\%CI 0.393\sim0.700$ )的影响因素；取栓前ASPECTS评分( $P=0.022, OR=0.719, 95\%CI 0.542\sim0.953$ )和发病至穿刺时间( $P=0.042, OR=1.003, 95\%CI 0.997\sim1.005$ )是患者长期预后不良的影响因素。受试者工作特征曲线(ROC)曲线分析显示,取栓前ASPECTS评分对发生HT( $AUC=0.736, 95\%CI 0.637\sim0.875, P=0.000$ )和长期预后不良( $AUC=0.630, 95\%CI=0.522\sim0.734, P=0.025$ )均有一定的预测能力。**结论:**取栓前ASPECTS评分是取栓再通后发生HT和预后不良的独立危险因素,ASPECTS评分越低,取栓再通后HT发生风险越高,长期预后越差。

**关键词** 急性缺血性脑卒中；血栓切除术；出血转化；预后；ASPECTS评分

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**Analysis of Factors Affecting Hemorrhagic Transformation and Long-term Prognosis of Acute Ischemic Stroke Patients after Thrombectomy** HU Yue, LIN Chang-Chun, LIANG Huai-Bin, LIU Jian-Ren. Department of Neurology, the Ninth People's Hospital, Shanghai Jiaotong University School of Medicine, Shanghai 200011, China

**Abstract Objective:** To analyze the factors affecting hemorrhagic transformation (HT) and long-term prognosis of acute ischemic stroke patients after thrombectomy. **Methods:** 102 patients with anterior circulation thrombectomy and recanalization were enrolled. According to the head CT prompting HT within 24 hours to 1 week after thrombectomy, patients were divided into HT group and NHT group. According to the scores of 1-year modified Rankin Scale (mRS), patients were divided into good prognosis group and poor prognosis group. The clinical data was retrospectively analyzed to find the factors affecting HT and long-term prognosis. **Results:** Of the 102 patients, 58 cases were included in the HT group, 44 cases in the NHT group and 56 cases in the poor prognosis group, 46 cases in the good prognosis group. Univariate analysis showed that the early Alberta Stroke Program Early CT Score (ASPECTS) in the HT and NHT groups, and in the good prognosis and poor prognosis groups were significantly different ( $P=0.000, 0.022$ ). Age ( $P=0.108$ ), coronary heart disease ( $P=0.061$ ), low-density lipoprotein (LDL) ( $P=0.078$ ) and preoperative intravenous thrombolysis ( $P=0.058$ ) may have an impact on postoperative HT. The times of thrombectomy ( $P=0.118$ ), the time from hospital arrival to puncture ( $P=0.098$ ) and the time from onset to puncture ( $P=0.023$ ) may have an impact on the long-term prognosis. Logistic regression analysis showed that the ASPECTS score before thrombus removal is the influencing factor for postoperative HT ( $P=0.001, OR=0.561, 95\%CI 0.393\sim0.700$ ); the number of thrombectomy ( $P=0.118$ ), the time from hospital arrival to puncture ( $P=0.098$ ) and the time from onset to puncture ( $P=0.023$ ) may have an impact on the long-term prognosis. The receiver operating characteristic curve (ROC) curve analysis showed that the ASPECTS score before thrombus removal has an effect on the occurrence of HT ( $AUC=0.736, 95\%CI 0.637\sim0.875, P=0.000$ ) and poor long-term prognosis ( $AUC=0.630, 95\%CI=0.522\sim0.734, P=0.025$ ). **Conclusion:** The ASPECTS score before thrombectomy is an independent risk factor for HT and poor prognosis after thrombectomy. The lower the ASPECTS score, the higher the risk of HT after thrombectomy and the worse the long-term prognosis.

**Key words** acute ischemic stroke; thrombectomy; hemorrhagic transformation; prognosis; ASPECTS

急性缺血性脑卒中(acute ischemic stroke, AIS)是我国成年人残疾的首要原因,其发病率呈逐年上升趋势<sup>[1-3]</sup>。AIS急性期一线治疗为血管再通,主要包括静脉溶栓和机械取栓,机械取栓较静脉溶栓具有时间窗广、再通率高的优点,可更好改善脑组织血流灌注<sup>[4,5]</sup>。出血转化(hemorrhagic transformation, HT)是指脑卒中后首次影像学检查未发现出血,再次影像学检查发现颅内出血的现象,是取栓术后并发症之一。其发生的原因包括术中血管壁损伤、再灌注治疗、抗栓治疗等<sup>[6]</sup>,同时也和患者血压、梗死严重程度等相关<sup>[7]</sup>。HT分为出血性梗死和脑实质血肿<sup>[8]</sup>,和患者术后功能恶化相关<sup>[9,10]</sup>。

Alberta卒中项目早期CT评分(Alberta Stroke Program Early CT Score, ASPECTS)于2000年由Barber等<sup>[11]</sup>学者提出,可用于评估AIS早期缺血改变。ASPECTS评分在静脉溶栓中广泛应用,ASPECTS评分≤7分是静脉溶栓后HT及不良预后的独立危险因素<sup>[12-15]</sup>,其预测价值较佳<sup>[16,17]</sup>。ASPECTS评分与6~24 h取栓患者3个月预后和神经功能改善相关<sup>[18]</sup>。

在既往研究中,ASPECTS评分在机械取栓结局的影响均以3个月改良Rankin评分量表(Modified Rankin Scale, mRS)作为评估标准,缺乏长期随访。本研究首次以患者1年长期预后为研究指标,通过回顾性分析,探究ASPECTS评分和取栓再通后HT及长期预后的相关性和预测作用,指导临床诊疗决策。

## 1 资料与方法

### 1.1 一般资料

选择2014年1月至2019年12月上海交通大学医学院附属第九人民医院收治的前循环AIS取栓再通患者102例。纳入标准:确诊为AIS;行前循环机械取栓术治疗;取栓后血管再通,即脑血流灌注分级≥IIb级;取栓后24 h~1周内行头颅CT检查;此次发病前mRS评分≤1分。排除标准:有血液疾病、恶性肿瘤等高出血风险;取栓前头颅CT平扫提示出血或肿瘤等其他疾病;临床资料不完善;术后1年失访。

本研究已获得上海第九人民医院伦理委员会审批(伦审2018-17-T17),患者或患者家属均签署知情同意书和授权委托书。

### 1.2 方法

1.2.1 基线和临床资料收集 通过取栓数据库和电子病历系统完成采集,包括:人口学资料:性别、年龄;既往史:高血压史、糖尿病史、既往脑卒中史、房颤史、冠心病史;个人史:吸烟史、饮酒史、抗凝药服用史、抗血

小板(platelet, PLT)药服用史。血管危险因素:急诊舒张压、急诊收缩压、低密度脂蛋白(low-density lipoprotein, LDL)、D-D二聚体(D-dimer, D-D)、同型半胱氨酸(homocysteine, Hcy);病因亚型:急性卒中治疗低分子肝素试验(trial of org 10172 in acute stroke treatment, TOAST)分型,包括大动脉粥样硬化型、小动脉硬化型、心源性栓塞型、其他原因和不明原因型;手术相关指标:术前美国国立卫生研究院卒中量表(National Institutes of Health Stroke Scale, NIHSS)、术前ASPECTS评分、取栓次数、术前静脉溶栓治疗、入院至穿刺时间、发病至穿刺时间。

1.2.2 影像学评分资料采集 所有AIS患者均经过脑血管造影术及头颅磁共振证实。于取栓术前及取栓后行头颅CT平扫(西门子双源CT),术前ASPECTS评分由2名神经内科临床工作2年以上的医师盲法评估。取栓再通后24 h~1周行头颅CT判断是否出现HT,并据此分为HT组和NHT组。术后1年预后随访由专业科研护士完成,预后采用mRS评分评估,0~2分纳入预后良好组,3~6分纳入预后不良组。

### 1.3 统计学处理

采用SPSS 25.0软件处理数据。符合正态分布以及方差齐性的计量资料以( $\bar{x} \pm s$ )表示,组间比较采用独立样本均数t检验;不服从正态分布的资料采用中位数(Q<sub>25</sub>, Q<sub>75</sub>)表示,组间比较采用采用Wilcoxon秩和检验;计数资料以频数和构成比表示,组间比较采用 $\chi^2$ 检验或Fisher确切概率检验。将单因素分析中P<0.2的变量带入多元Logistic回归模型进一步分析,采用受试者工作特征曲线(receiver operating characteristic curve, ROC)获取截点值并评估其预测价值。P<0.05为差异有统计学意义。

## 2 结果

### 2.1 治疗方法

入组患者行头颅CT平扫排除脑出血后,按照标准流程行机械取栓术,取栓术均为同一主刀医师。采用SOLITAIRE取栓支架取栓,并按照指南推荐给予治疗、护理和康复训练。

### 2.2 分组及一般资料比较

共纳入患者102例,男61例,女41例;28~93岁。根据是否出现HT,分为HT组58例(56.9%)和NHT组44例(43.1%);根据随访1年的mRS评分,分为预后不良组56例(54.9%)和预后良好组46例(45.1%)。

各组临床资料的单因素分析可知,HT和NHT组、预后良好和预后不良组的ASPECTS评分差异有统计

学意义( $P=0.000, 0.022$ )；年龄( $P=0.108$ )、冠心病( $P=0.061$ )、LDL( $P=0.078$ )和术前静脉溶栓( $P=0.058$ )可能对术后HT产生影响；取栓次数( $P=0.118$ )、到院至穿刺

时间( $P=0.098$ )和发病至穿刺时间( $P=0.023$ )可能对长期预后产生影响；其他资料差异无统计学差异( $P>0.05$ )；见表1、表2。

表1 HT组和NHT组临床资料比较[ $(\bar{x}\pm s)$ 或%或M(Q<sub>25</sub>, Q<sub>75</sub>)]

组别	例数	男性	年龄/岁	高血压	卒中史	糖尿病	冠心病	房颤	吸烟
NHT组	44	56.8	56(66~79)	43.2	15.9	25.0	13.6	18.2	31.8
HT组	58	62.1	73(59~83)	43.1	15.5	25.9	31.0	27.6	31.0
Z/t/χ <sup>2</sup> 值		-0.287	-1.606	0.000	0.003	0.010	3.520	1.340	0.001
P值		0.592	0.108	0.994	0.957	0.921	0.061	0.247	0.933
组别	饮酒	用抗凝药	用抗PLT药	大动脉粥样硬化型	小动脉闭塞型	心源性栓塞型	不明原因型	其他明确病因	
NHT组	11.4	9.1	20.5	40.9	0.0	29.5	29.5	0.0	
HT组	10.3	5.2	13.8	53.4	0.0	19.0	24.1	3.4	
Z/t/χ <sup>2</sup> 值	0.027	0.144	0.799			4.539			
P值	0.870	0.704	0.371			0.209			
组别	LDL/(mmol/L)	HCY/(μmol/L)	D-D/(mg/L)	收缩压/mmHg	舒张压/mmHg				
NHT组	3.1±1.0	12.1(8.3~14.9)	2.5(1.0~6.0)	153(130~170)	82(70~92)				
HT组	3.2±0.7	9.8(7.5~13.3)	2.5(1.2~4.7)	150(130~166)	86(75~100)				
Z/t/χ <sup>2</sup> 值	3.158	1.173	-0.162	0.504	-0.619				
P值	0.078	0.241	0.871	0.614	0.536				
组别	NIHSS/分	ASPECTS/分	术前静脉溶栓	取栓/次	到院至穿刺/min	发病至穿刺/min			
NHT组	13±7	9(7~10)	56.8	1(1~3)	157(100~223)	326(211~559)			
HT组	14±7	7(6~8)	37.9	2(1~30)	165(125~288)	340(239~460)			
Z/t/χ <sup>2</sup> 值	0.050	4.138	3.592	-0.199	-1.177	-0.199			
P值	0.824	0.000	0.058	0.839	0.239	0.842			

注：收缩压和舒张压为急诊时测量；NIHSS 和 ASPECTS 为取栓前评分

表2 预后良好组和预后不良组临床资料比较[ $(\bar{x}\pm s)$ 或%或M(Q<sub>25</sub>, Q<sub>75</sub>)]

组别	例数	男性	年龄/岁	高血压	卒中史	糖尿病	冠心病	房颤	吸烟
预后良好组	46	60.9	70(60~82)	47.8	10.9	19.6	21.7	26.1	26.1
预后不良组	56	58.9	68(57~81)	39.3	19.6	30.4	25.0	21.4	35.7
Z/t/χ <sup>2</sup> 值		0.040	0.956	0.751	1.470	1.549	0.427	0.252	1.087
P值		0.842	0.339	0.386	0.225	0.213	0.699	0.616	0.297
组别	饮酒	用抗凝药	用抗PLT药	大动脉粥样硬化型	小动脉闭塞型	心源性栓塞型	不明原因型	其他明确病因	
预后良好组	8.7	6.5	17.4	45.7	0.0	28.3	26.1	0.0	
预后不良组	12.5	7.1	16.1	50.0	0.0	19.6	26.8	3.6	
Z/t/χ <sup>2</sup> 值	0.038	0.015	0.032			3.295			
P值	0.768	0.902	0.859			0.348			
组别	LDL/(mmol/L)	HCY/(μmol/L)	D-D/(mg/L)	收缩压/mmHg	舒张压/mmHg				
预后良好组	3.0±0.8	10.4(8.0~13.0)	2.3(0.9~5.1)	150(131~167)	86(76~100)				
预后不良组	3.2±0.9	10.9(7.5~15.5)	2.6(1.5~5.5)	150(130~170)	81(70~93)				
Z/t/χ <sup>2</sup> 值	0.590	-0.045	-0.658	-0.161	1.074				
P值	0.444	0.964	0.511	0.827	0.283				
组别	NIHSS/分	ASPECTS/分	术前静脉溶栓	取栓/次	到院至穿刺/min	发病至穿刺/min			
预后良好组	13±6	8(7~9)	39.1	1(1~2)	155(117~207)	319(189~393)			
预后不良组	14±7	7(6~9)	51.8	2(1~3)	198(108~351)	354(256~563)			
Z/t/χ <sup>2</sup> 值	1.040	2.287	1.628	-1.563	-1.653	-2.276			
P值	0.310	0.022	0.202	0.118	0.098	0.023			

注：收缩压和舒张压为急诊时测量；NIHSS 和 ASPECTS 为取栓前评分

### 2.3 术后发生HT及患者长期预后影响因素分析

将上述影响因素代入多元Logistic回归模型,分析结果显示,取栓前ASPECTS评分是术后发生HT( $P=0.001$ ,  $OR=0.561$ , 95% CI 0.393~0.700)的影响因素;取栓前ASPECTS评分( $P=0.022$ ,  $OR=0.719$ , 95% CI 0.542~0.953)和发病至穿刺时间( $P=0.042$ ,  $OR=1.003$ , 95% CI 0.997~1.005)是患者长期预后的影响因素;见表3、4。

表3 HT影响因素的多元Logistic回归分析

项目	B	S.E.	Wald $\chi^2$
术前静脉溶栓	-0.586	0.497	1.391
年龄	0.008	0.018	0.205
冠心病史	1.139	0.631	3.259
LDL	0.096	0.303	0.100
ASPECTS评分	-0.579	0.181	10.244
项目	P	OR	95%CI
术前静脉溶栓	0.238	0.556	0.210~1.474
年龄	0.651	1.008	0.973~1.045
冠心病史	0.071	3.123	0.907~10.756
LDL	0.752	1.100	0.608~1.992
ASPECTS评分	0.001	0.561	0.393~0.799

表4 预后不良影响因素的多元Logistic回归分析

项目	B	S.E.	Wald $\chi^2$
取栓次数	0.191	0.178	1.156
发病至穿刺时间	0.003	0.002	4.119
入院至穿刺时间	0.002	0.002	0.111
ASPECTS评分	-0.330	0.144	5.264
项目	P	OR	95%CI
取栓次数	0.282	1.211	0.854~1.716
发病至穿刺时间	0.042	1.003	1.000~1.006
入院至穿刺时间	0.739	1.001	0.997~1.005
ASPECTS评分	0.022	0.719	0.542~0.953

ROC曲线分析显示,取栓前ASPECTS评分对HT有一定的预测能力(AUC=0.736, 95%CI 0.637~0.875,  $P=0.000$ );其截点为8.5(灵敏度81.0%, 特异度54.5%, 约登指数为0.355);取栓前ASPECTS评分<9分时,患者易发生再通后HT。取栓前ASPECTS评分对长期预后不良也有一定提示作用(AUC=0.630, 95%CI=0.522~0.734,  $P=0.025$ );其截点为6.5(灵敏度89.1%, 特异度39.3%, 约登指数为0.284);取栓前ASPECTS评分<7分时,患者长期不良预后不良的可能性增加,见图1。

### 3 讨论

本研究首次探究取栓前ASPECTS评分与取栓后1年长期预后的关系,发现取栓前ASPECTS评分为

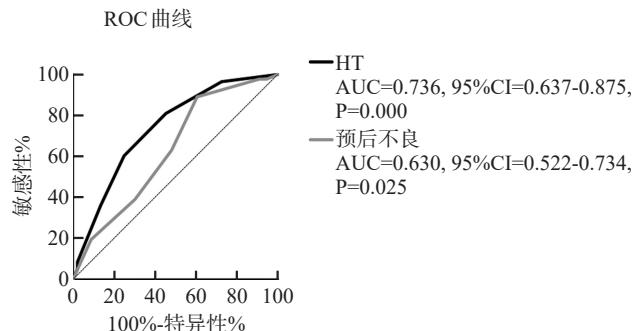


图1 取栓术后发生HT及患者长期预后不良的ROC曲线

AIS患者取栓再通后HT和长期预后不良的独立影响因素,当取栓前ASPECTS评分<9分时,患者发生取栓再通后HT的可能性更大,当ASPECTS评分<7分时,患者长期预后较差。发病至穿刺时间也是长期预后不良的独立危险因素。

头颅CT平扫是我国脑血管病首选检查方法。虽有报道,头颅磁共振弥散加权成像(Diffusion Weighted Imaging, DWI)-ASPECTS评分或头颅CT灌注可较好显示梗死核心和缺血半暗带<sup>[18,19]</sup>,但我国多数基层医院不具备行此检查的设备及人员。头颅CT平扫可在卒中急性期鉴别出血性卒中<sup>[20]</sup>,ASPECTS评分依靠其进行评分,可在取栓前对患者术后出血风险和长期预后进行评估,帮助快速制定诊疗方案<sup>[21]</sup>,减少取栓发病至穿刺时间,改善患者预后。当ASPECTS评分>8分时,排除禁忌后需尽快行机械取栓;当ASPECTS评分为7分或8分时,术后出血风险增加,但仍可从取栓治疗中获益,建议行取栓治疗,并调整用药方案预防术后HT发生;当ASPECTS评分<7分时,提示患者缺血损伤较为严重,术后出血风险大,长期预后不佳,此时取栓治疗决策需慎重。

本研究仍存在一定局限性:①本研究为单中心,样本量较小,未来宜进行多中心验证。②本研究为回顾性研究,宜行前瞻性研究进一步验证。③本研究ASPECTS评分由医师评定,目前已有人工智能系统进行包括ASPECTS评分在内的影像学评分软件<sup>[22-25]</sup>。未来宜借助成熟的人工智能评分软件再次验证。④本研究选取前循环卒中患者,宜对后循环卒中患者进行补充研究。

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