

· 临床研究 ·

四维CT血管造影评估的急性缺血性脑卒中患者脑侧支循环与预后的相关性

陶景山,臧晓进*,戴益盛,刘斌

(江苏省滨海县人民医院影像科,江苏 滨海 224500)

【摘要】目的 应用动态四维CT血管造影(4D-CTA)评价急性缺血性脑卒中(AIS)患者脑侧支循环状态并分析患者脑侧支循环状态与其预后的相关性。**方法** 收集2020年1月至9月江苏省滨海县人民医院最终纳入研究的47例AIS患者的基线资料及影像学变量资料。所有患者均于发病4.5 h内接受4D-CTA检查,应用多时相CTA(mCTA)脑侧支循环评分与区域软脑膜侧支循环(rLMC)评分对AIS患者脑侧支循环状态进行评估,并采用90 d改良Rankin量表(mRS)评估其神经功能预后。根据mRS评分结果将患者分为侧支循环不良组(19例)与侧支循环良好组(28例)。采用SPSS 25.0软件分析数据,根据数据类型,分别采用 χ^2 检验、t检验或秩和检验进行组间比较。采用Spearman相关分析各指标间的相关性。应用logistic回归分析影响AIS患者神经功能预后不良的指标,并进一步绘制受试者工作特征(ROC)曲线探讨不同指标的预测价值。**结果** 与侧支循环良好组相比,侧支循环不良组美国国立卫生研究院卒中量表(NIHSS)评分更高,半影体积($T_{max} > 6$ s)及梗死核心体积($rCBF < 30\%$)更大,错配比更小,mCTA评分、rLMC评分及90 d mRS评分更低($P < 0.05$)。mCTA评分与基线NIHSS评分、半影体积($T_{max} > 6$ s)、梗死核心体积($rCBF < 30\%$)、错配比呈负相关;与rLMC评分、90 d mRS评分呈正相关。rLMC评分与基线NIHSS评分、半影体积($T_{max} > 6$ s)、梗死核心体积($rCBF < 30\%$)、错配比、90 d mRS评分均呈负相关;与mCTA评分呈正相关。多因素logistic回归分析显示,mCTA评分、基线NIHSS评分均是预测AIS患者神经功能预后不良的指标。ROC结果显示,mCTA评分+基线NIHSS评分联合预测AIS患者神经功能预后不良的价值较单一指标更佳,ROC曲线下面积(AUC)为0.918,灵敏度为89.6%,特异度为92.4%。**结论** mCTA评分+基线NIHSS评分预测AIS患者的神经功能预后具有更好的价值,当mCTA脑侧支循环评分≤3分、基线NIHSS评分>5分时,预示AIS患者神经功能预后不良。

【关键词】 缺血性脑卒中;侧支循环状态;CT血管造影

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Association of cerebral collateral circulation evaluated by four-dimensional computed tomography angiography with prognosis in patients with acute ischemic stroke

TAO Jing-Shan, ZANG Xiao-Jin*, DAI Yi-Sheng, LIU Bin

(Department of Imaging, People's Hospital of Binhai County, Binhai 224500, Jiangsu Province, China)

【Abstract】 Objective To evaluate the collateral circulation status with four-dimensional computed tomography angiography (4D-CTA) after acute ischemic stroke (AIS) and analyze its correlation with prognosis. **Methods** Baseline data and imaging data of 47 AIS patients who admitted in our hospital from January to September 2020 and finally included in this study were collected and analyzed. All of them received 4D-CTA within 4.5 h after onset. The level of cerebral collateral circulation was assessed by multi-phase CT angiography (mCTA) scores and regional leptomeningeal collateral (rLMC) scores. The 90-day modified Rankin score (mRS) was used to evaluate the neurological prognosis, and the patients were divided into poor collateral circulation group ($n=19$) and good collateral circulation group ($n=28$) according to mRS. SPSS statistics 25.0 was used to analyze the data, and Chi-square test, student's t test or rank sum test was used for inter-comparison depending on data types. Spearman correlation analysis was employed for the correlations among indicators. Logistic regression analysis was performed to analyze the factors affecting poor neurological prognosis in AIS patients. Receiver operating characteristic (ROC) curve was drawn to assess the predictive values of these indicators. **Results** Compared with the good collateral circulation group, the poor collateral circulation group had significantly higher National Institutes of Health Stroke Scale (NIHSS) score, larger penumbra volume ($T_{max} > 6$ s) and infarct core volume ($rCBF < 30\%$),

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通信作者:臧晓进, E-mail: 2573639751@qq.com

smaller mismatch ratio, lower mCTA score, rLMC score and 90-day mRS score ($P<0.05$). mCTA score was negatively correlated with baseline NIHSS score, penumbra volume ($T_{max}>6$ s), infarct core volume ($rCBF<30\%$), and mismatch ratio, and positively correlated with rLMC score and 90-day mRS score. rLMC score had negative correlations with baseline NIHSS score, penumbra volume ($T_{max}>6$ s), infarct core volume ($rCBF<30\%$), mismatch ratio, and 90-day mRS score, and positive correlation with mCTA score. The results of multivariate logistic regression analysis showed that mCTA score and baseline NIHSS score were both predictors of poor neurological prognosis in AIS patients. ROC curve indicated that combination of mCTA score+baseline NIHSS score showed better predictive values for poor neurological prognosis in AIS patients than a single index, with an area under the ROC curve (AUC) of 0.918, a sensitivity of 89.6%, and a specificity of 92.4%. **Conclusion** mCTA score+baseline NIHSS score has a better value for predicting the poor neurological prognosis in AIS patients. When the mCTA cerebral collateral circulation score less than 3 and the baseline NIHSS score greater than 5, it indicates that neurological prognosis is poor in the patients.

[Key words] ischemic stroke; collateral circulation status; CT angiography

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Corresponding author: ZANG Xiao-Jin, E-mail: 2573639751@qq.com

软脑膜侧支在维持急性缺血性脑卒中(acute ischemic stroke, AIS)患者动脉闭塞远端大脑区域内的血供方面起着至关重要的作用^[1],侧支循环的有效建立对后期神经功能的恢复亦具有重要作用^[2]。因此,侧支循环状态可能与AIS患者的预后相关。近年来,临床主要应用CT血管成像来研究侧支循环状态^[3],但传统的CT血管成像(computed tomography angiography, CTA)不能获得多个时点的信息,而动态四维CT血管造影(four-dimensional computed tomography angiography, 4D-CTA)技术是将CTA的无创与数字减影血管造影(digital subtraction angiography, DSA)的动态多时点采集相结合,通过一段时间内多次、连续、不同时间点的CT采集扫描可以评估颈内血管内的血流情况^[4]。目前探讨基于4D-CTA的多时相CTA(multiphase CTA, mCTA)脑侧支循环评分(以下简称为mCTA评分)预测AIS患者神经功能预后的研究较少。基于此,本研究旨在探讨mCTA评分与AIS患者神经功能预后的相关性。

1 对象与方法

1.1 研究对象

回顾性分析2020年1月至9月江苏省滨海县人民医院收治的4.5 h内接受静脉溶栓治疗的51例AIS患者的临床资料,排除4例脱落病例(2例合并脑出血,1例既往有脑卒中史,1例有头颅移动伪影),最终纳入47例AIS患者。其中男31例,女16例,年龄33~79(62.45±8.77)岁。纳入标准:符合《中国急性缺血性脑卒中诊治指南2018》^[5]中关于AIS的诊断标准;年龄18~81岁;发病至溶栓时间<4.5 h;基线美国国立卫生研究院卒中量表

(national institutes of health stroke scale, NIHSS)评分≥12分;均于静脉溶栓后行4D-CTA检查;签署知情同意书。排除标准:AIS合并出血性脑卒中、脑出血;因图像质量问题而不能测量梗死核心体积者;既往有脑卒中史;肾功能不全或对本研究中对比剂过敏。

1.2 检查方法

先行非增强CT(non-contrast computed tomography, NCCT)扫描(排除出血),再行全脑CTA、CT灌注成像(CT perfusion, CTP)扫描,最后24 h的随访影像检查采用CT平扫。具体方法:先行NCCT扫描,范围从颅底到颅顶,参数:350 mAs, 120 kV, 矩阵512×512,层厚5 mm,旋转时间1 s。然后行全脑CTA、CTP一次扫描,在90 mAs、80 kV下进行“摇篮床”模式动态扫描,使用高压注射器于肘前静脉以4 mL/s的速度注射40 ml浓度为370 mgI/ml的碘普罗胺对比剂,随后同速度注射生理盐水30 ml进行冲洗,延迟4 s后行动态容积扫描,参数:准直32 mm×1.2 mm,矩阵512×512,层厚5 mm,旋转时间0.5,共持续45 s。

1.3 图像处理

(1) CTP数据后处理:应用Syngo.via商业工作站中CT神经灌注软件对所有患者的基线图像进行重建分析,依据基线CTP的CT容积脑灌注成像(volume perfusion CT, VPCT)重建4D-CTA,从而获得冠状位、矢状位、轴位图像,厚度为20 mm;然后手动进行四维降噪,自动选择要输入重建的动脉,采用去卷积算法分别测量 $T_{max}>6$ s的病灶体积、局部脑血流量(regional cerebral blood flow, rCBF)<30%的病灶体积;同时采用mCTA、区域软脑膜侧支循环(regional leptomeningeal collateral, rLMC)评分对4D-CTA上的动脉高峰期图像进行评分。(2) CPA数

据后处理:使用4D-CTA,重建四维大脑后动脉(posterior cerebral artery, PCA)脑血管成像,确定AIS患者病灶及梗死的部位,并在层厚为25 mm条件下重建最大密度投影以评估侧支循环状态。(3)CT平扫数据后处理:测量梗死核心体积。

1.4 评分标准

预后神经功能评分:采用90 d改良Rankin量表(modified Rankin scale, mRS)评分^[6]评估AIS患者神经功能的预后。评分标准:0分为完全无症状;1分为虽有症状但无显著的神经功能障碍;2分为轻度残疾;3分为中度残疾;4分为中重度残疾;5分为重度残疾;6分为死亡。mRS评分越高提示AIS患者神经功能预后越差,其中0~2分提示预后良好,3~6分提示预后不良。

mCTA评分^[7]:0分为任何时候相无一血管显影;1分为任何时候相只有少部分血管显影;2分为延迟2个相位时范围减小、程度下降,或延迟1个相位时无血管显影;3分为延迟2个相位时范围与程度均正常,或延迟1个相位时有少部分血管显影;4分为延迟1个相位时范围与程度均正常;5分为无延迟相位且范围与程度均正常。mCTA评分越高提示AIS患者脑侧支循环越好。

rLMC评分^[8]:包括大脑中动脉(6个区域)、基底节区(1个区域)、大脑前动脉(1个区域)及外侧裂区(1个区域)。前三者评分分别为0、1、2分(0分:无动脉显影;1分:患侧动脉显影较健侧少;

2分:患侧动脉显影较健侧多或相等)。外侧裂区为0、2、4分(0分:无动脉显影;2分:患侧动脉显影较健侧少;4分:患侧动脉显影较健侧多或相等)。总分20分,rLMC评分越高提示AIS患者脑侧支循环越好。

1.5 统计学处理

采用SPSS 25.0统计软件进行数据分析。符合正态分布的计量资料以均数±标准差($\bar{x}\pm s$)表示,组间比较采用t检验;不符合正态分布的计量资料使用中位数(四分位数间距)[$M(Q_1, Q_3)$]表示,组间比较采用秩和检验。计数资料以例数(百分率)表示,组间比较采用 χ^2 检验。采用Spearman相关分析各指标间的相关性。应用单因素、多因素logistic回归分析影响AIS患者神经功能预后的指标,并进一步绘制ROC曲线探讨mCTA评分的预测价值。 $P<0.05$ 为差异有统计学意义。

2 结 果

根据90 d mRS评分,将47例AIS患者分为侧支循环不良组(19例)与侧支循环良好组(28例)。

2.1 2组患者临床资料比较

与侧支循环良好组比较,侧支循环不良组的基线NIHSS评分更高,半影体积($T_{max}>6$ s)及梗死核心体积($rCBF<30\%$)更大,错配比更小,mCTA评分、rLMC评分及90 d mRS评分更低,差异有统计学意义($P<0.05$,表1)。

表1 2组患者临床资料比较

Table 1 Comparison of baseline data between two groups

Item	Poor collateral circulation group($n=19$)	Good collateral circulation group($n=28$)	$\chi^2/t/Z$	P value
Gender(male/female, n)	12/7	19/9	0.111	0.739
Age (years, $\bar{x}\pm s$)	62.30±8.46	62.13±8.89	0.066	0.948
Hypertension[n (%)]	10(52.63)	14(50.00)	0.031	0.859
Diabetes mellitus[n (%)]	3(15.79)	5(17.86)	0.000*	1.000
Hyperlipidemia[n (%)]	6(31.58)	7(25.00)	0.245	0.621
Smoking[n (%)]	7(36.84)	10(35.71)	0.006	0.973
Lesion site(right brain/left brain)	8/11	13/15	0.086	0.770
Infarct location(middle cerebral artery/anterior cerebral artery/internal carotid artery)	13/2/4	18/4/6	0.240*	1.000
Time from onset to CT(min, $\bar{x}\pm s$)	182.21±30.01	172.48±22.05	1.282	0.206
Time from onset to thrombolysis(min, $\bar{x}\pm s$)	227.52±36.13	219.30±31.55	0.827	0.413
Baseline NIHSS(points, $\bar{x}\pm s$)	10.74±2.84	8.17±2.03	3.622	0.001
Penumbra volume($T_{max}>6$ s, cm^3)	2 001(177,253)	133(100,162)	12.028	<0.001
Infarct core volume($rCBF<30\%$, cm^3)	135(93,173)	47(29,80)	10.729	<0.001
Mismatch ratio[$M(Q_1, Q_3)$]	2(1,5)	4(3,10)	4.227	0.029
mCTA[$M(Q_1, Q_3)$]	3(1,4)	4(3,5)	4.029	0.035
rLMC[$M(Q_1, Q_3)$]	10(7,19)	17(11,20)	4.991	0.019
90 d mRS[$M(Q_1, Q_3)$]	1(0,2)	4(3,6)	5.025	0.017

NIHSS: national institutes of health stroke scale; Tmax: time to peak residual function; rCBF: regional cerebral blood flow; mCTA: time-resolved CT angiography; rLMC: regional pial collaterals; mRS: modified Rankin scale. * continuous modified Chi-square test.

2.2 mCTA 评分、rLMC 评分与各指标的相关性

Spearman 分析显示, mCTA 评分与基线 NIHSS 评分、半影体积($T_{max} > 6$ s)、梗死核心体积($rCBF < 30\%$)、错配比呈负相关;与 rLMC 评分、90 d mRS 评分呈正相关。rLMC 评分与基线 NIHSS 评分、半影体积($T_{max} > 6$ s)、梗死核心体积($rCBF < 30\%$)、错配比、90 d mRS 评分均呈负相关;与 mCTA 评分呈正相关(表 2)。

表 2 mCTA 评分、rLMC 评分与各指标的相关性

Table 2 Correlation between mCTA, rLMC and various indicators

Item	mCTA		rLMC	
	r	P value	r	P value
Baseline NIHSS	-0.637	<0.001	-0.337	0.047
Penumbra volume($T_{max} > 6$ s)	-0.596	<0.001	-0.412	0.020
Infarct core volume($rCBF < 30\%$)	-0.564	0.001	-0.399	0.027
Mismatch ratio	-0.585	<0.001	-0.424	0.016
mCTA	-	-	0.489	0.005
rLMC	0.501	0.003	-	-
90 d mRS	0.874	<0.001	-0.387	0.029

NIHSS: national institutes of health stroke scale; T_{max} : time to peak residual function; $rCBF$: regional cerebral blood flow; mCTA: time-resolved CT angiography; rLMC: regional pial collaterals; mRS: modified Rankin scale. -: no datum.

2.3 影响 AIS 患者神经功能预后不良的单因素 logistic 回归分析

单因素 logistic 回归分析结果显示, 基线 NIHSS 评分、梗死核心体积($rCBF < 30\%$)、mCTA 评分、rLMC 评分是影响 AIS 患者神经功能预后的影响因素($P < 0.05$; 表 3)。

2.4 预测 AIS 患者神经功能预后不良的多因素 logistic 回归分析及 ROC 分析

以侧支循环状态为因变量(1=预后良好, 2=预后不良), 以基线 NIHSS 评分、梗死核心体积($rCBF < 30\%$)、mCTA 评分、rLMC 评分为自变量进行多因素 logistic 回归分析。因脑侧支循环评估的变量有 mCTA 评分、rLMC 评分 2 个变量, 故分成模型 1、2 进行分析, 模型 1 采用 mCTA 评分纳入研究, 结果发现 mCTA 评分是预测 AIS 患者神经功能

预后不良的唯一指标($P < 0.05$);模型 2 采用 rLMC 评分纳入研究, 结果发现基线 NIHSS 评分是预测 AIS 患者神经功能预后不良的唯一指标($P < 0.05$; 表 4)。最后将 mCTA 评分、基线 NIHSS 评分再进行多因素 logistic 回归分析, 结果发现 mCTA 评分、基线 NIHSS 评分均是预测 AIS 患者神经功能预后不良的指标(表 5)。

进一步探讨 mCTA 评分、基线 NIHSS 评分对 AIS 患者神经功能预后不良的价值, 受试者工作特征(receiver operating characteristic, ROC) 曲线分析显示, 当 mCTA 评分≤3 分时可判断 AIS 患者神经功能预后不良, 此时曲线下面积(area under the curve, AUC) 为 0.887, 灵敏度为 82.4%, 特异度为 90.1%;当基线 NIHSS 评分>5 分时可判断 AIS 患者神经功能预后不良, 此时 AUC 为 0.859, 灵敏度为 68.5%, 特异度为 84.7%;mCTA 评分+基线 NIHSS 评分的 AUC 为 0.918, 灵敏度为 89.6%, 特异度为 92.4%。

表 3 影响 AIS 患者神经功能预后不良的单因素 logistic 回归分析

Table 3 Univariate logistic regression analysis on prognosis of neurological function in patients with AIS

Factor	B	OR(95%CI)	P value
Gender	0.040	1.041(0.982–1.225)	0.278
Age	1.330	3.781(2.555–5.596)	0.177
Time from onset to thrombolysis	0.010	1.010(0.848–1.670)	0.710
Hypertension	-0.916	0.399(0.100–1.687)	0.224
Diabetes mellitus	1.318	3.736(1.116–7.032)	0.365
Hyperlipidemia	-1.723	0.179(0.021–1.693)	0.129
Smoking	-0.271	0.763(0.199–3.014)	0.709
Baseline NIHSS	0.456	1.578(1.038–2.387)	0.008
Penumbra volume($T_{max} > 6$ s)	0.023	1.023(0.989–1.358)	0.174
Infarct core volume($rCBF < 30\%$)	0.087	1.091(0.894–1.420)	0.039
Mismatch ratio	-0.068	0.934(0.690–1.103)	0.143
mCTA score	-2.358	0.095(0.035–0.583)	0.005
rLMC score	-0.199	0.820(0.662–1.004)	0.021

AIS: acute ischemic stroke; NIHSS: national institutes of health stroke scale; T_{max} : time to peak residual function; $rCBF$: regional cerebral blood flow; mCTA: time-resolved CT angiography; rLMC: regional pial collaterals.

表 4 影响 AIS 患者神经功能预后的多因素 logistic 回归分析

Table 4 Multivariate logistic regression analysis on prognosis of neurological function in patients with AIS

Factor	Model 1			Model 2		
	B	OR(95%CI)	P value	B	OR(95%CI)	P value
Baseline NIHSS	0.635	1.877(0.932–3.821)	0.093	0.548	1.730(1.091–2.74)	0.029
Infarct core volume($rCBF < 30\%$)	0.080	1.083(0.873–1.344)	0.296	0.041	1.042(0.873–1.243)	0.687
mCTA	-2.740	0.065(0.006–0.678)	0.020			
rLMC				-0.249	0.779(0.593–1.073)	0.129

AIS: acute ischemic stroke; NIHSS: national institutes of health stroke scale; $rCBF$: regional cerebral blood flow; mCTA: multiphase CTA; rLMC: regional leptomeningeal collateral.

**表5 影响AIS患者神经功能预后的多因素
logistic回归分析(综合2个模型)**

Table 5 Multiple logistic regression analysis on prognosis of neurological function in AIS patients (combining 2 models)

Factor	B	OR(95%CI)	P value
mCTA	1.175	3.238(2.104–4.984)	0.009
Baseline NIHSS	0.079	1.082(1.041–1.125)	0.010

AIS: acute ischemic stroke; NIHSS: national institutes of health stroke scale; rCBF: regional cerebral blood flow; mCTA: time-resolved CT angiography; rLMC: regional pial collaterals.

3 讨论

有研究显示,侧支循环状态会影响缺血性脑组织存活的时间,侧支循环的开放意味着可以挽救的缺血脑组织更多,降低了梗死体积扩大、出血转化及死亡的风险,从而改善预后^[9,10]。当发生AIS时,患者神经功能损伤程度取决于侧支循环的建立及其开放速度^[11]。目前我国影像学评估侧支循环建立的方法较多,本研究通过4D-CTA采用mCTA评分(时相划分最为全面)与rLMC评分(区域划分最为精细)评估AIS患者的侧支循环状态,并探讨其与预后的关系。

本研究结果显示,与侧支循环良好组相比,侧支循环不良组的NIHSS评分更高,半影体积($T_{max} > 6$ s)及梗死核心体积($rCBF < 30\%$)更大,错配比更小,mCTA评分、rLMC评分及90 d mRS评分更低($P < 0.05$)。说明侧支循环越差,基线NIHSS越高^[12],梗死核心体积越大,mCTA评分、rLMC评分越低,预后越差。张铭思等^[13]通过研究发现,侧支循环良好与较小梗死灶体积相关。 T_{max} 是反映脑组织缺血最灵敏的指标^[14]。本研究选择将 $T_{max} > 6$ s的伪彩图像测量的病灶体积定义为半影,将 $rCBF < 30\%$ 的伪彩图像测量的病灶体积定义为梗死核心体积,可能与本研究采用内卷积核算法有关系,使 T_{max} 评估缺血程度更加准确。mCTA评分、rLMC与90 d mRS评分相关系数分别为0.874、-0.387,说明mCTA评分评估AIS患者神经功能预后时的脑侧支循环时相评分较rLMC更优,原因是mCTA评分较rLMC评分具有较高的时间分辨率,包括3个时相信息,且每期图像可进行多个区域的脑侧支循环评估。Lin等^[15]报道与传统mCTA和CTP相比,mCTA评分对AIS患者具有更好的预后预测,且诊断准确性较高,与本研究结果相似。logistic回归分析显示,mCTA脑侧支循环评分、基线

NIHSS评分是预测AIS患者神经功能预后的指标。ROC结果显示,判断AIS患者神经功能预后不良的最佳截断值是mCTA评分≤3分,基线NIHSS评分>5分,二者联合检测对于预测AIS患者神经功能预后不良的价值更好,此时AUC为0.918,灵敏度为89.6%,特异度为92.4%,准确率为90.7%。提示,mCTA评分+基线NIHSS评分联合预测AIS患者神经功能预后价值更高。原因可能是最终梗死核心体积是脑侧支循环状态的主要决定因素^[16]。

综上所述,mCTA评分可以独立预测AIS患者的神经功能预后,当mCTA评分≤3分时预示AIS患者神经功能预后不良。本研究也存在一些不足,如样本量少,患者神经缺损程度较轻,日后需进行大样本、多中心的研究,以期为预测AIS神经功能预后提供更有价值的参考。

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