

基于 DSA 图像的颈内动脉相关灌注区成像 临床应用初探

胡震 金巍 尹豆 邓钰蕾 刘军 李彬寅

【摘要】 研究背景 DSA 是脑血管病不可替代的诊断方法,其对颅内大血管病变较敏感,而对远端灌注信息不全面。为定量评估供血动脉灌注区,本研究首次提出一种依赖去卷积算法和交叉相关(CC)算法的颈内动脉灌注区成像方法。**方法** 纳入 2020 年 6 月至 2021 年 5 月在上海交通大学医学院附属瑞金医院卢湾分院行 DSA 检查的 4 例脑血管病患者和 2 例健康受试者,提取颈内动脉输入函数(AIF),采用去卷积算法计算每个像素点达容时间(Tmax),再采用 CC 算法获得全脑各像素点与颈内动脉灌注相关的 CC 图。2 例健康受试者随机选择 AIF 兴趣区,计算 CC 图均方根误差(RMSE),行信度分析;4 例脑血管病患者绘制 CC 图,行效度分析。**结果** 信度分析显示,1 例健康受试者左和右颈内动脉汤氏位和侧位 CC 图和 Tmax 图的 RMSE 值分别为 0.008 ± 0.011 、 0.022 ± 0.002 、 0.015 ± 0.007 、 0.004 ± 0.008 和 (0.108 ± 0.181) s, (0.181 ± 0.214) s、 (0.301 ± 0.230) s、 (0.035 ± 0.092) s;另 1 例为 0.015 ± 0.023 、 0.007 ± 0.011 、 0.007 ± 0.011 、 0.005 ± 0.012 和 (0.172 ± 0.275) s、 (0.092 ± 0.174) s、 (0.087 ± 0.156) s、 (0.079 ± 0.153) s;且 Tmax 图的平均 RMSE 值低于 DSA 的时间分辨率,表明颈内动脉兴趣区取值框 AIF 取值范围的 CC 图可靠性较高。效度分析显示,1 例急性缺血性卒中静脉溶栓桥接机械取栓患者,CC 图和 Tmax 图充分显示成功取栓后颈内动脉相关灌注改变;1 例亚急性缺血性卒中血管内治疗患者,术后常规 DSA 显示闭塞动脉再通,但 CC 图显示颈内动脉相关灌注无明显变化;1 例大脑中动脉狭窄但无缺血事件患者,尽管常规 DSA 显示大脑中动脉重度狭窄,但 CC 图提示颈内动脉相关灌注良好,无需血管内治疗;1 例急性缺血性卒中但无大脑中动脉狭窄患者,尽管 DSA 未见大脑中动脉狭窄,但 CC 图仅见稀疏的颈内动脉相关灌注。**结论** 基于常规 DSA 图像的 CC 图和 Tmax 图在颈内动脉兴趣区取值框 AIF 取值范围内具有良好的信度。CC 图可提供供血动脉灌注区定量信息,有助于准确诊断和制定适宜的治疗决策。

【关键词】 颈内动脉; 脑血管循环; 血管造影术,数字减影

Preliminary study on internal carotid artery perfusion imaging and clinical application based on digital subtraction angiography

HU Zhen¹, JIN Wei², YIN Dou², DENG Yu-lei², LIU Jun², LI Bin-yin²

¹Department of Neurology, Ruijin Hospital Luwan Branch, Shanghai Jiaotong University School of Medicine, Shanghai 200025, China

²Department of Neurology, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai 200025, China

HU Zhen and JIN Wei contributed equally to the article

Corresponding author: LI Bin-yin (Email: libinyin@126.com)

【Abstract】 **Background** DSA is an irreplaceable diagnostic method for cerebral vascular disease. It is sensitive to intracranial macrovascular disease, but not to distal blood perfusion. In order to quantitatively assess the perfusion area of the feeding artery, this study is the first to propose an imaging method of the internal carotid artery (ICA) perfusion area relying on deconvolution algorithm and cross-

doi:10.3969/j.issn.1672-6731.2022.08.010

基金项目:上海市科委启明星计划(项目编号:21QA1405800)

作者单位:200025 上海交通大学医学院附属瑞金医院卢湾分院神经内科(胡震);200025 上海交通大学医学院附属瑞金医院神经内科(金巍,尹豆,邓钰蕾,李彬寅,刘军)

胡震与金巍对本文有同等贡献

通讯作者:李彬寅,Email:libinyin@126.com

correlation (CC) algorithm. **Methods** Four patients with cerebral vascular disease and 2 healthy subjects who underwent DSA examination in Luwan Branch of Ruijin Hospital Affiliated to Shanghai Jiaotong University School of Medicine from June 2020 to May 2021 were enrolled. The arterial input function (AIF) of the ICA was extracted, and a deconvolution algorithm was used to calculate the time to peak (Tmax) for each pixel. Then the CC algorithm was used to obtain the CC map related to the perfusion of the ICA at each pixel point of the whole brain. Area of interest (ROI) of AIF were randomly selected for 2 healthy subjects, calculated the root mean square error (RMSE) of the CC map for reliability analysis. The CC map was drawn for 4 patients with cerebral vascular disease for validity analysis. **Results** Reliability analysis showed that the RMSE values of Towne's and lateral views of the CC map and Tmax map of the left and right ICA in a healthy subject were 0.008 ± 0.011 , 0.022 ± 0.002 , 0.015 ± 0.007 , 0.004 ± 0.008 , and (0.108 ± 0.181) s, (0.181 ± 0.214) s, (0.301 ± 0.230) s, (0.035 ± 0.092) s; another healthy subject were 0.015 ± 0.023 , 0.007 ± 0.011 , 0.007 ± 0.011 , 0.005 ± 0.012 , and (0.172 ± 0.275) s, (0.092 ± 0.174) s, (0.087 ± 0.156) s, (0.079 ± 0.153) s. The averaged RMSE value of Tmax map was lower than the temporal resolution of DSA, indicating that the reliability of the CC map of the AIF value box in different ROIs of the ICA was high. Validity analysis showed that the CC map and Tmax map of the patient with acute ischemic stroke treated by intravenous thrombolysis bridging to mechanical thrombectomy can fully display the perfusion changes of the ICA after successful thrombectomy. Postoperative DSA in the patient with subacute ischemic stroke after endovascular therapy showed recanalization of the occluded artery, while the CC map showed no significant change in the perfusion of the ICA. The DSA of the patient with middle cerebral artery (MCA) stenosis without related ischemic events showed severe MCA stenosis, but the CC map showed that the ICA was well perfused, and no endovascular treatment was required. The DSA of the patient with acute ischemic stroke without MCA stenosis showed no MCA stenosis, but only sparse ICA-related perfusion was seen on the CC map. **Conclusions** The CC map and Tmax map based on DSA images have good reliability in different ROIs of AIF. The CC map can provide quantitative information on the perfusion area of the feeding arteries, which is helpful for accurate diagnosis and appropriate treatment decisions.

【Key words】 Carotid artery, internal; Cerebrovascular circulation; Angiography, digital subtraction

This study was supported by Shanghai Rising-Star Program (No. 21QA1405800).

Conflicts of interest: none declared

DSA 可以提供脑血流的空间和时间信息,其结果判定需逐帧观察动脉和静脉分布,而非全视图,很大程度上依赖影像科或神经介入科医师的经验。多帧 DSA 图像的最小密度投影 (MinP) 可在一帧图像中呈现全部动脉和静脉以获得全视图。然而,不同组别或治疗前后 MinP 图像的比较易受对比剂注射剂量和注射速度的影响。因此,难以通过目测 DSA 评估脑血流动力学特征。如果能够通过多帧 DSA 图像计算出标准化脑灌注参数,则具有量化的生理意义和可比性。脑灌注参数如脑血流量 (CBF)、达峰时间 (TTP) 和达峰时间 (Tmax) 可提供脑血流动力学的定量时间信息,并广泛用于缺血性卒中的临床评估。有研究在急性缺血性卒中患者中测试基于 DSA 的灌注区成像^[1],该方法将多帧 DSA 图像每个像素点的信号强度按照时间展开为函数,再采用去卷积 (deconvolution) 算法获得每个像素点对比剂的灌注参数,其中去卷积函数来自大动脉对比剂的信号强度时间函数,亦称动脉输入函数 (AIF)。但目前的灌注参数尚无法定量评估每条

供血动脉的灌注程度。虽然其他血管成像技术如 MRA 和 CTA 可形成精确定位动脉的三维图像,但 DSA 具有独特优势,即通过造影导管可选择主供血动脉,如颈内动脉 (ICA) 或椎动脉 (VA),因此,基于 DSA 的灌注区成像可以提供某一特定血管的灌注图像。由于同一脑区通常有多条供血动脉,且不同生理或病理状态下主供血动脉可发生改变,故获得实时的灌注区图像具有重要意义。交叉相关 (CC) 算法测量 2 个时间序列的相似性,目前用于动脉自旋标记 (ASL),可计算颈内动脉血流信号与全脑体素之间的最大相关^[2-3]。本研究首次提出基于 CC 值和 Tmax 值获得颈内动脉灌注区成像的方法,通过传统 DSA 图像获得更多的脑灌注指标,辅助临床医师诊断颅内血管病变并制定血管内治疗方案。

对象与方法

一、研究对象

选择 2020 年 6 月至 2021 年 5 月在上海交通大学医学院附属瑞金医院卢湾分院脑病中心住院治

疗并行 DSA 检查的 4 例脑血管病患者以及 2 例同期行 DSA 检查的健康受试者,排除颅内出血、活动性出血或凝血功能障碍;对比剂过敏;心、肺、肝、肾等重要脏器严重功能障碍或恶性肿瘤;合并药物无法控制的严重高血压,以及血糖 < 2.70 mmol/L 或 > 22.20 mmol/L 者。男性 3 例,女性 3 例;年龄为 47 ~ 80 岁,平均(64.67 ± 11.87)岁;脑血管病患者发病前改良 Rankin 量表(mRS)评分为 0 ~ 1 分,中位评分为 0(0, 1)分。1 例为急性缺血性卒中(发病 ≤ 4.50 h),予静脉溶栓桥接机械取栓治疗;1 例亚急性缺血性卒中(发病 2 周至 2 个月),行球囊扩张术 + 支架植入术;1 例 MRA 和 CTA 提示大脑中动脉(MCA)狭窄但无相关缺血事件;1 例急性缺血性卒中但 MRA、CTA 和 DSA 未见病变侧大脑中动脉狭窄;2 例健康受试者 MRA 或 CTA、DSA 均未见颈内动脉异常。本研究经上海交通大学医学院附属瑞金医院卢湾分院道德伦理委员会审核批准,所有受试者或其家属均对检查项目知情并签署知情同意书。

二、研究方法

1. DSA 检查 由同一位经过培训且有丰富临床经验的神经介入科医师采用盲法对所有受试者进行颈内动脉 DSA 检查,采用美国 GE 公司生产的 Innova IGS 630 血管造影 X 射线机,经股动脉穿刺,将 5F 造影导管(VER 451-514H0,美国 Cordis 公司)头端置于颈内动脉近端,经导管注射对比剂碘美普尔(典迈伦,规格 400 mgI/ml),注射速度 4 ml/s,于 1.50 s 内注射完毕,单次注射总剂量 6 ml。采集汤氏位和侧位图像,图像采集速度 0.40 s/帧,采集频率 2.50 Hz,汤氏位图像大小 1000 × 1000 像素、侧位图像大小 750 × 750 像素(像素为 0.20 mm × 0.20 mm),采集时间 12 s,共 30 帧,覆盖自注射对比剂至上静脉窦显影的全部时间段。图片帧数据序列化采集期间,先采集背景图像,再于对比剂注射后 0.50 s 采集后续图像,自后续图像中减去背景图像即获得最终 DSA 图像。

2. 对比剂跟踪算法计算 Tmax 值 首先校正血管厚度,采用 Python 3.7 软件 skimage 包(<https://scikit-image.org/>)绘制 DSA 图像所有血管的中心线和边缘线,假设血管为圆柱体,测量血管内每个像素点至最近中心线的距离(d)并计算像素点在成像方向的血管厚度(即弦长 s),公式为^[4]: $s = 2 \times \sqrt{r^2 - d^2}$,其中 r 为血管半径。由于血管信号强度与对比剂浓度和血管厚度呈正比,故校正血管厚度

后,将 DSA 图像获得的密度-时间函数换算为对比剂浓度-时间函数。采用对比剂跟踪算法计算对比剂自注射后至目标位置 u 的时间参数^[1,5],则位置 u 处的对比剂浓度-时间函数 Cu(t)为颈内动脉对比剂浓度-时间函数 Ca(t)与残差函数 R(t)的卷积,计算公式为: $Cu(t) = CBF \times [Ca(t) \otimes R(t)]$,其中, CBF 为脑血流量, $R(t) = \sqrt{W}^{-1} U^T Cu(t)$,即 R(t)通过奇异值分解(SVD)方法将 Ca(t)分解为 2 个正交矩阵(U 和 VT)和 1 个对角矩阵(W),W 中低于最佳阈值的元素设置为零(\hat{W})^[6],变量 t 是 DSA 采集过程中的离散时间点。Tmax 值为 R(t)达最大值的时间,由此可以获得 DSA 图像任何位置的对比剂延迟到达时间。

3. 交叉相关图的获得 据 Tmax 值将 DSA 图像每个像素点密度-时间曲线平移,匹配 Cu(t)和 Ca(t)的时间点^[7],计算二者的交叉相关值(CC 值),公式为^[3]: $CC = \frac{\sum_t Cu(t)Ca(t)}{\sqrt{\sum_t Cu^2(t)} \sqrt{\sum_t Ca^2(t)}}$ 。CC 值有助于

评估位置 u 处的供血动脉灌注程度,范围为 -1 ~ 1,CC 值为零表示两个位置的血流灌注完全不相关,CC 值 > 0.70 表示两个位置的血流灌注具有较好匹配度,血流可能为同一供血动脉来源;全脑各像素点 CC 值组成的图像即为 CC 图。

4. 交叉相关图信度分析 对 2 例健康受试者行 CC 图信度分析。由 2 位神经介入科医师在 MinP 图像上手动勾画兴趣区(ROI),即完全包含在颈内动脉管径内的矩形区域。由于计算 CC 值时需要 AIF 值去卷积后的 Tmax 值,AIF 值为颈内动脉兴趣区各时间点的平均值,故颈内动脉兴趣区取值框可影响 CC 图。为探究 CC 图在不同兴趣区取值框下的信度,在颈内动脉汤氏位和侧位 DSA 图像中随机选择 25 个兴趣区,兴趣区的选择应满足以下标准,即 MinP 图像上兴趣区矩形的长垂直于血流方向;宽尽量短以减少颈内动脉 AIF 取值范围内的时间效应;避免在重叠灌注区选择兴趣区;尽可能在 C4 段与造影导管头端之间的颈内动脉灌注区选择兴趣区。以造影导管头端上方区域作为参考(图 1, 2),计算 25 个基于 AIF 值所获得 CC 图的均方根误差(RMSE),RMSE 值越小表明 CC 图受兴趣区取值框的影响越小,数据稳定性越佳。

5. 交叉相关图效度分析 将 CC 图用于 4 例脑血管病患者的疗效评价。急性缺血性卒中静脉溶栓桥接机械取栓患者于机械取栓前后计算并绘制

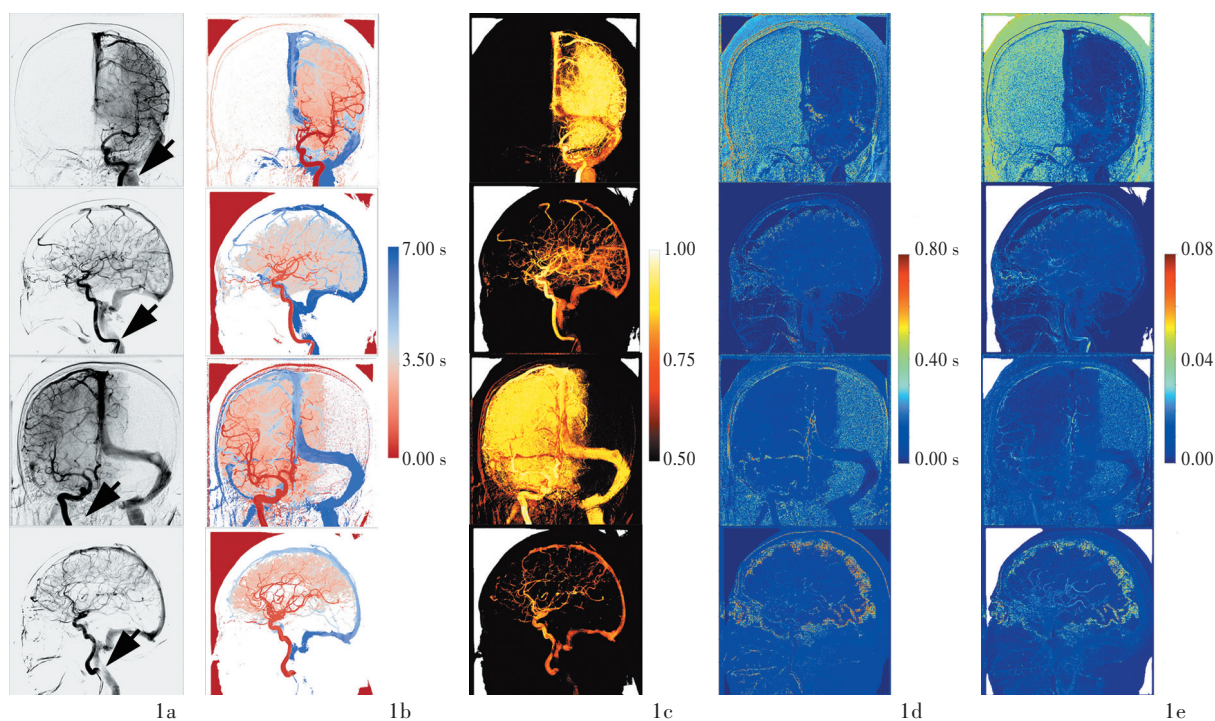


图1 女性健康受试者,79岁,DSA检查所见(自上而下分别为左颈内动脉汤氏位像和侧位像、右颈内动脉汤氏位像和侧位像) 1a MinP图可见颈内动脉C4段与造影导管头端之间的25个兴趣区之一(箭头所示) 1b Tmax图显示各像素点的Tmax值 1c CC图显示左和右颈内动脉灌注区 1d 左颈内动脉汤氏位和侧位Tmax图的RMSE值分别为(0.108±0.181)s和(0.301±0.230)s,右颈内动脉为(0.181±0.214)s和(0.035±0.092)s 1e 左颈内动脉汤氏位和侧位CC图的RMSE值分别为0.008±0.011和0.015±0.007,右颈内动脉为0.022±0.002和0.004±0.008

Figure 1 A 79-year-old female healthy subject, DSA findings (from top to bottom were left ICA Towne's and lateral views, right ICA Towne's and lateral views) MinP map showed one of the 25 ROIs between the ICA C4 segment and the tip of the angiography catheter (arrows indicate, Panel 1a). Tmax map showed the Tmax value of each pixel point (Panel 1b). CC map showed left and right ICA related perfusion regions (Panel 1c). Tmax map showed the RMSE values of left ICA Towne's and lateral views were (0.108±0.181)s and (0.301±0.230)s, and the RMSE values of right ICA were (0.181±0.214)s and (0.035±0.092)s (Panel 1d). CC map showed the RMSE values of left ICA Towne's and lateral views were 0.008±0.011 and 0.015±0.007, and the RMSE values of right ICA were 0.022±0.002 and 0.004±0.008 (Panel 1e).

基于左颈内动脉的全脑CC图,评估取栓后颈内动脉灌注变化;亚急性缺血性卒中血管内治疗患者于支架植入前后计算并绘制基于左颈内动脉的全脑CC图,评估支架植入后颈内动脉灌注变化;大脑中动脉狭窄但无相关缺血事件患者,绘制基于左颈内动脉的全脑CC图,评估发病后非责任颈内动脉灌注变化;无大脑中动脉狭窄的缺血性卒中患者,绘制基于右颈内动脉的全脑CC图,评估发病后责任颈内动脉灌注变化。CC图能够正确反映符合临床和MRI表现的灌注情况,表明CC图具有良好效度。

结 果

一、健康受试者颈内动脉灌注区和CC图信度分析

2例无颈内动脉异常的健康受试者头部MRI显示脑结构正常,无白质病变。1例颈内动脉DSA显

示,左和右颈内动脉汤氏位图像上,各25张具有不同AIF值的CC图的平均RMSE值为 0.008 ± 0.011 和 0.022 ± 0.002 ,各25张Tmax图的平均RMSE值为 (0.108 ± 0.181) s和 (0.181 ± 0.214) s;侧位图像上,CC图的平均RMSE值为 0.015 ± 0.007 和 0.004 ± 0.008 ,Tmax图的平均RMSE值为 (0.301 ± 0.230) s和 (0.035 ± 0.092) s(图1)。另1例颈内动脉DSA显示,左和右颈内动脉汤氏位图像上,各25张具有不同AIF值的CC图的平均RMSE值为 0.015 ± 0.023 和 0.007 ± 0.011 ,各25张Tmax图的平均RMSE值为 (0.172 ± 0.275) s和 (0.092 ± 0.174) s;侧位图像上,CC图的平均RMSE值为 0.007 ± 0.011 和 0.005 ± 0.012 ,Tmax图的平均RMSE值为 (0.087 ± 0.156) s和 (0.079 ± 0.153) s(图2)。由此可见,非造影侧大脑半球和大脑边缘区域背景中RMSE值较大,颈内动脉灌注区RMSE值极小;此外,Tmax图的平均

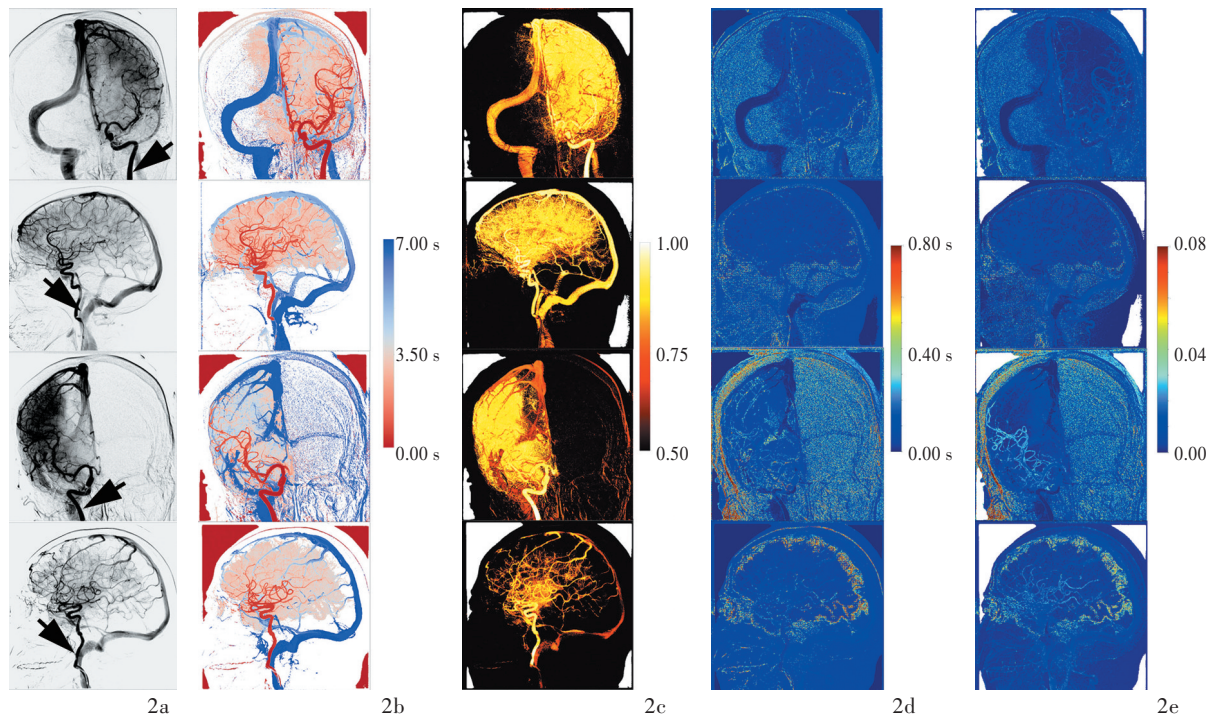


图2 女性健康受试者,57岁,DSA检查所见(自上而下分别为左颈内动脉汤氏位像和侧位像、右颈内动脉汤氏位像和侧位像) 2a MinP图可见颈内动脉C4段与造影导管头端之间的25个兴趣区之一(箭头所示) 2b Tmax图显示各像素点的Tmax值 2c CC图显示左和右颈内动脉灌注区 2d 左颈内动脉汤氏位和侧位Tmax图的RMSE值分别为(0.172±0.275) s和(0.087±0.156) s,右颈内动脉为(0.092±0.174) s和(0.079±0.153) s 2e 左颈内动脉汤氏位和侧位CC图的RMSE值分别为0.0148±0.023和0.007±0.011,右颈内动脉为0.007±0.011和0.005±0.012

Figure 2 A 57-year-old female healthy subject, DSA findings (from top to bottom were left ICA Towne's and lateral views, right ICA Towne's and lateral views) MinP map showed one of the 25 ROIs between the ICA C4 segment and the tip of the angiography catheter (arrows indicate, Panel 2a). Tmax map showed the Tmax value of each pixel point (Panel 2b). CC map showed the left and right ICA related perfusion regions (Panel 2c). Tmax map showed the RMSE values of left ICA Towne's and lateral views were (0.172±0.275) s and (0.087±0.156) s, and the RMSE values of right ICA were (0.092±0.174) s and (0.079±0.153) s (Panel 2d). CC map showed the RMSE values of left ICA Towne's and lateral views were 0.0148±0.023 and 0.007±0.011, and the RMSE values of right ICA were 0.007±0.011 and 0.005±0.012 (Panel 2e).

RMSE值低于本研究DSA的时间分辨率(0.40 s),表明颈内动脉不同兴趣区取值框AIF取值范围对最终的CC图和Tmax图影响轻微。

二、脑血管病患者颈内动脉灌注区和CC图效能分析

1例急性缺血性卒中静脉溶栓桥接机械取栓患者,取栓前DWI显示左侧基底节区急性梗死灶;DSA显示左大脑中动脉M1段闭塞,其远端分支显影较差;CC图显示左大脑中动脉灌注区与左颈内动脉血流的相关性较小,而左大脑前动脉(ACA)灌注区与左颈内动脉血流的相关性较大,表明左大脑中动脉闭塞后左颈内动脉血供重新分布。取栓后复查DSA显示,左侧M1段再通,改良脑梗死溶栓血流分级(mTICI)3级,其远端分支清晰可见。成功取栓后,因脑血流动力学改变,左颈内动脉对大脑前动脉和大脑中动脉灌注区的血流量重新分布,对左大

脑中动脉灌注区的血供增加,尤其是汤氏位图像外侧区,而对左大脑前动脉近端灌注区的血供减少,表明CC图可提供左颈内动脉的血流变化。Tmax图可提供对比剂到达时间信息,取栓后对比剂到达左大脑中动脉灌注区的时间更短,到达左大脑前动脉远端的时间亦更短(图3)。

1例亚急性缺血性卒中血管内治疗患者,入院时DWI显示左侧额叶、颞叶皮质和皮质下白质高信号,提示亚急性梗死灶;DSA显示左大脑中动脉M1段上干闭塞。球囊扩张术+支架植入术后复查DSA显示,左侧M1段上干再通,达mTICI分级2b级,远端血流明显改善;Tmax图显示,左大脑中动脉灌注区Tmax值降低。由于该例患者发病后2周接受血管内治疗,术前CC图显示已有良好的近端侧支循环和灌注;术后CC图显示左颈内动脉对大脑中动脉近端的血供无明显变化(图4)。此外,CC图还有

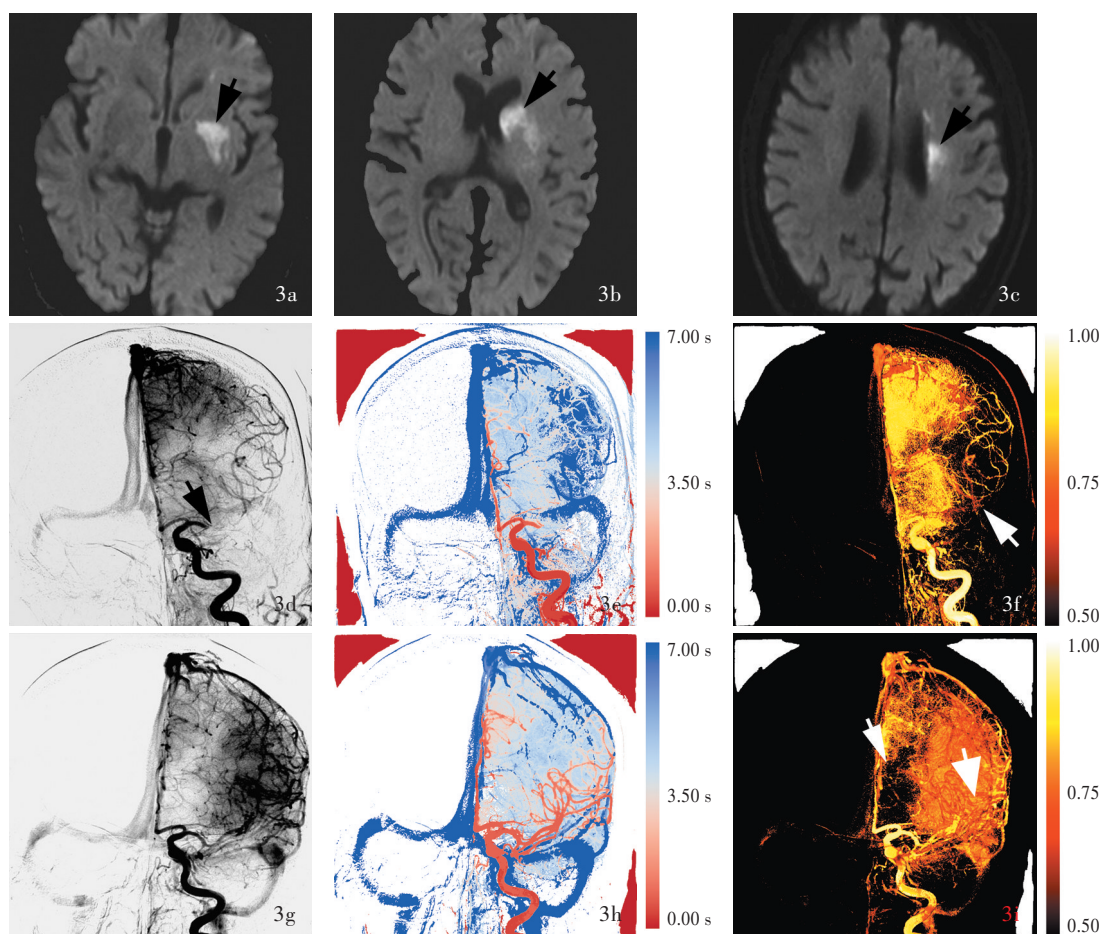


图3 男性患者,80岁,因突发右侧肢体无力伴言语不清30 min急诊入院,临床诊断为急性缺血性卒中,予静脉溶栓桥接机械取栓术。手术前后头部影像学检查所见 3a~3c 术前横断面DWI显示左侧基底节区急性梗死灶(箭头所示) 3d 术前MinP图显示左大脑中动脉闭塞(箭头所示) 3e 术前Tmax图显示左大脑中动脉灌注区Tmax值延迟 3f 术前CC图显示左大脑中动脉灌注区接受左颈内动脉的供血减少(箭头所示) 3g 取栓后MinP图显示左大脑中动脉再通 3h 取栓成功后Tmax图显示对比剂到达左大脑中动脉灌注区的时间较短,到达左大脑前动脉远端的时间亦较短 3i 取栓成功后CC图显示左颈内动脉对左大脑中动脉灌注区的血供增加,特别是外侧区(粗箭头所示),而对左大脑前动脉近端灌注区的血供减少(细箭头所示)

Figure 3 An 80-year-old male patient was admitted due to sudden right limb weakness and alalia for 30 min, diagnosed as acute ischemic stroke, and underwent intravenous thrombolysis bridging to mechanical thrombectomy. Head imaging findings before and after surgery Preoperative axial DWI showed acute infarction in the left basal ganglia (arrows indicate, Panel 3a-3c). Preoperative MinP map showed left MCA occlusion (arrow indicates, Panel 3d). Preoperative Tmax map showed the Tmax value of left MCA blood perfusion area was delayed (Panel 3e). Preoperative CC map showed left MCA blood perfusion area blood flow from the left ICA reduced (arrow indicates, Panel 3f). After successful thrombectomy, MinP map showed the reperfusion of blood flow in the left MCA (Panel 3g). After successful thrombectomy, Tmax map showed the time of the contrast agent to reach the blood perfusion area of the left MCA was shorter, and the time to reach the blood perfusion area of the left ACA was also shorter (Panel 3h). After successful thrombectomy, CC map showed left ICA blood flow with more relevant perfusion in the left MCA region, especially in the outer region (thick arrow indicates), while less perfusion in the proximal region of left ACA (thin arrow indicates, Panel 3i).

助于发现与动脉血流相关性较低的引流静脉(即血流经远端分支进入毛细血管再汇入引流静脉),这在MinP图上是无法显示的。

1例大脑中动脉狭窄但无相关缺血事件患者,入院时FLAIR成像显示左侧大脑半球未见白质高信号,提示无明显缺血性改变;DSA显示左大脑中动脉M1段重度狭窄,皮质分支灌注不良,左大脑前

动脉清晰可见,前交通动脉(ACoA)开放,右大脑前动脉及其远端可见,以及左眼动脉(OA)、左脉络膜前动脉(AChA)和左后交通动脉(PCoA)开放;Tmax图显示前循环Tmax值正常;CC图显示左颈内动脉对左侧大脑半球前循环灌注区的血供充足,该区域无缺血灶(图5),纠正常规DSA因骨质遮挡等原因显示的血管假性狭窄,有助于减少DSA图像的假阳

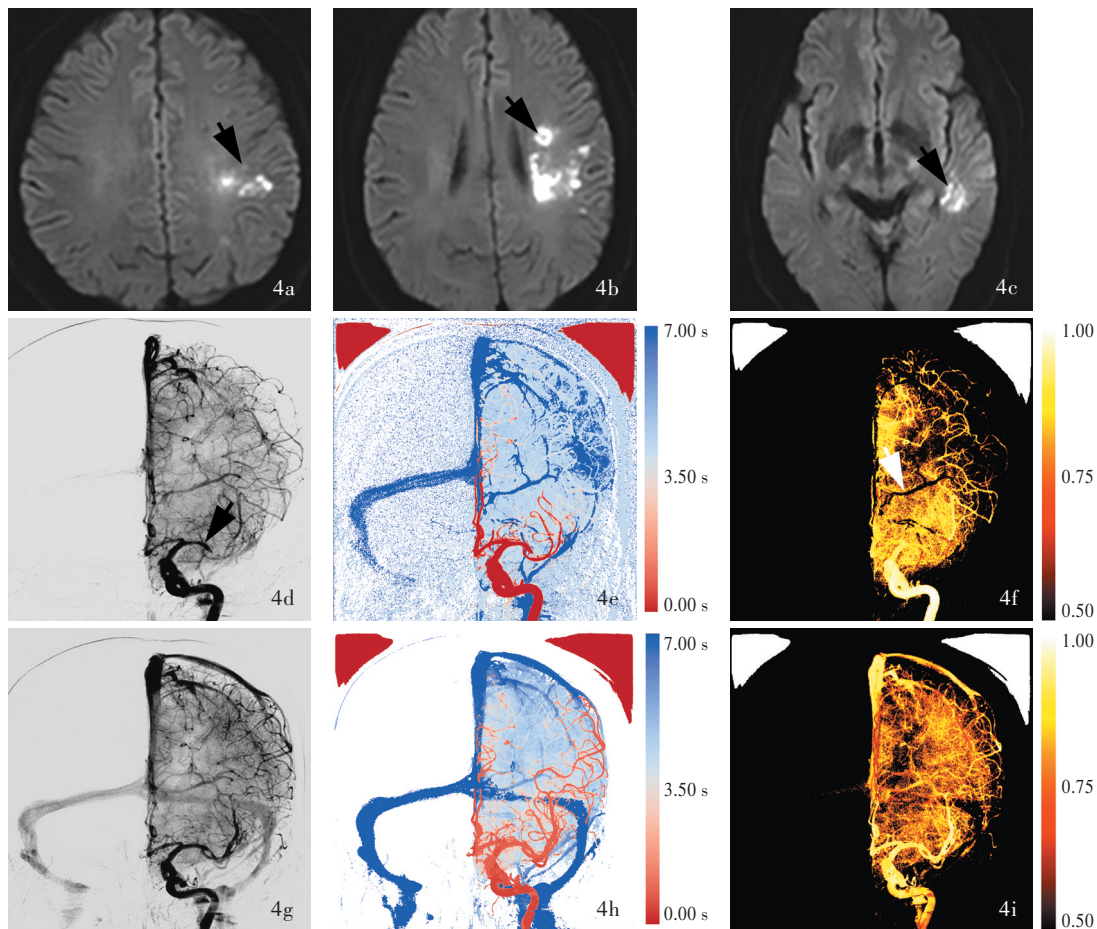


图4 男性患者,59岁,因突发右上肢无力3 d急诊入院,临床诊断为急性缺血性卒中,先予为期2周的抗血小板和调脂治疗,发病2周后行球囊扩张术+支架植入术。手术前后头部影像学检查所见 4a~4c 术前横断面DWI显示左侧额叶、颞叶皮质和皮质下白质高信号(箭头所示) 4d 术前MinP图显示左大脑中动脉M1段上干闭塞(箭头所示) 4e 术前Tmax图显示左大脑中动脉灌注区Tmax值增加 4f 术前CC图显示左大脑中动脉接受左颈内动脉的供血基本覆盖全灌注区,并可见与动脉血流相关性较低(低CC值)的引流静脉(箭头所示) 4g 支架植入后MinP图显示,左大脑中动脉M1段上干再通 4h 支架植入后MinP图显示,左大脑中动脉灌注区Tmax值降低 4i 支架植入后CC图显示,左颈内动脉对大脑中动脉近端的血供与术前无明显变化

Figure 4 A 59-year-old male patient was admitted due to sudden right upper extremity weakness for 3 days, diagnosed as acute ischemic stroke. The patient received standard stroke medication for 2 weeks, including antiplatelet drugs and statins. The patients had balloon angioplasty and stent implantation 2 weeks after onset. Head imaging findings before and after surgery Preoperative axial DWI showed hyperintensity in left frontal lobe, temporal cortex and subcortical white matter (arrows indicate, Panel 4a-4c). Preoperative MinP map showed occlusion in the upper trunk of the left MCA M1 segment (arrow indicates, Panel 4d). Preoperative Tmax map showed the time to peak in the left MCA blood perfusion area was delayed (Panel 4e). Preoperative CC map showed the left MCA received blood flow from the left ICA basically covering the entire perfusion area, and a less correlated draining vein was found (arrow indicates, Panel 4f). After stent implantation, MinP map showed the upper trunk of the left MCA M1 segment reperfusion in the left MCA (Panel 4g). After stent implantation, Tmax map showed decrease in the left MCA area (Panel 4h). After stent implantation, CC map showed similar blood perfusion of left ICA to the proximal region of the MCA before and after stent implantation (Panel 4i).

性结果。

1例急性缺血性卒中但无大脑中动脉狭窄患者,入院时DWI显示急性右侧基底节区和颞叶梗死。治疗后复查DSA显示,右大脑中动脉和大脑前动脉主干未见明显狭窄,其远端清晰可见;Tmax图显示右大脑中动脉和大脑前动脉对比剂到达时间相近;CC图显示右颈内动脉对右大脑中动脉灌注区

和大脑前动脉近端的血供减少,尤其是对右豆纹动脉灌注区的血供明显减少,与梗死区域相吻合(图6)。表明CC图有助于显示右颈内动脉灌注区的血流量程度,提示局部脑组织缺血。

讨 论

本研究首次提出基于CC值和Tmax值获得颈内

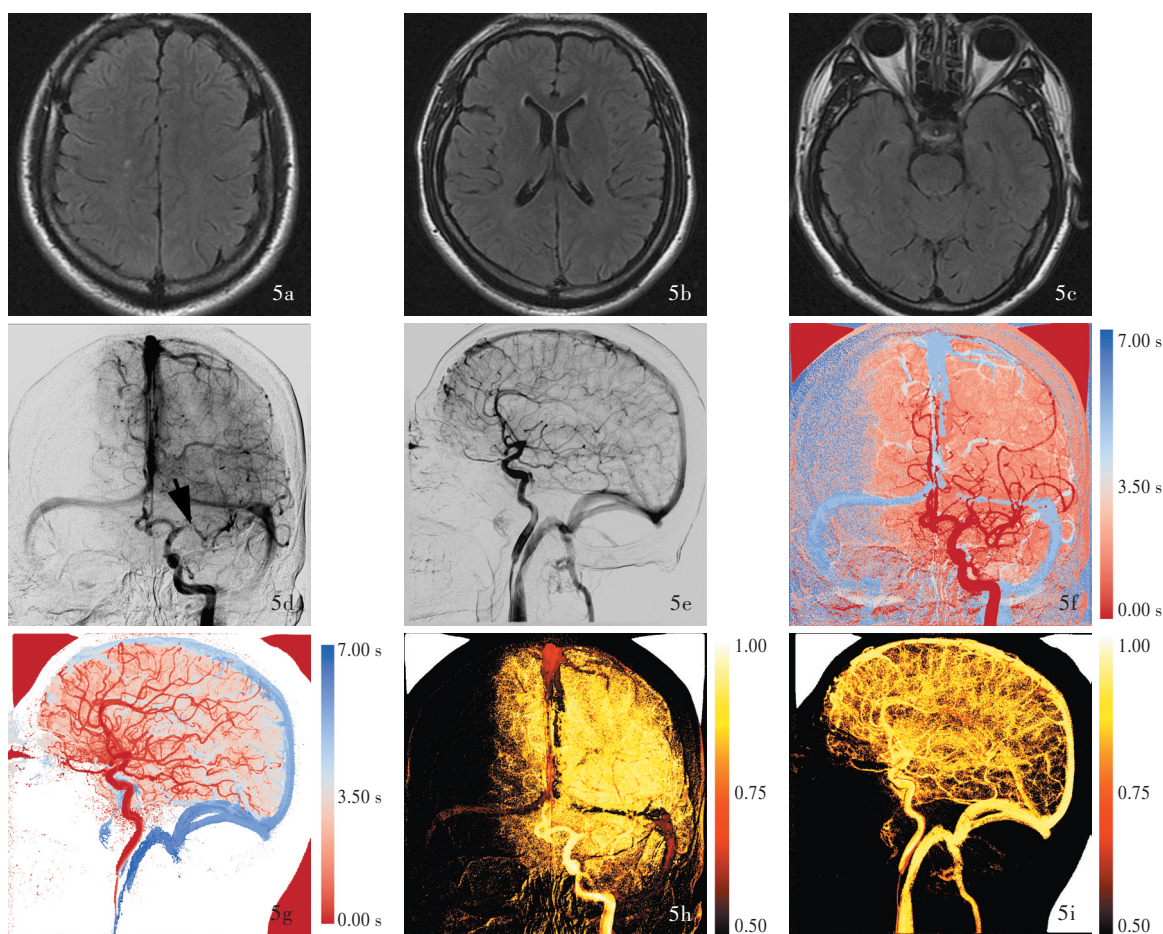


图5 男性患者,47岁,因突发头晕1 d急诊入院,临床诊断为急性脑桥梗死(大脑中动脉灌注区无缺血事件),予为期2周的抗血小板和调脂治疗。入院时头部影像学检查所见 5a~5c 横断面T₂-FLAIR成像显示前循环灌注区未见缺血灶 5d,5e 汤氏位和侧位MinP图显示,左大脑中动脉M1段重度狭窄(箭头所示) 5f,5g 汤氏位和侧位Tmax图显示左大脑中动脉灌注区Tmax值基本正常 5h,5i 汤氏位和侧位CC图显示左颈内动脉对左大脑中动脉的灌注基本覆盖全域

Figure 5 A 47-year-old male patient was admitted due to abrupt dizziness, diagnosed as acute pontine infarction (no ischemia in MCA perfusion area), and underwent antiplatelet drugs and statins for 2 weeks. Head imaging findings at admission Axial T₂-FLAIR showed no ischemic foci in the blood supply area of the anterior circulation (Panel 5a-5c). Towne's (Panel 5d) and lateral (Panel 5e) views of MinP map showed severe stenosis in the left MCA M1 segment (arrow indicates). Towne's (Panel 5f) and lateral (Panel 5g) views of Tmax map showed the peak time of the left MCA blood perfusion area is basically normal. Towne's (Panel 5h) and lateral (Panel 5i) views of CC map showed the left MCA receives blood flow from the left ICA, and basically covers the entire area.

动脉灌注区成像的方法,通过传统 DSA 图像获得更多脑灌注参数,辅助临床医师诊断颅内血管病变并制定血管内治疗方案。

本研究阐述一种基于常规 DSA 图像的颈内动脉灌注区定量成像方法。与 CTA 或 MRA 相比,DSA 具有高时间分辨率、可灵活选择血管的优势。既往主要采用反卷积算法计算对比剂自颈内动脉到达远端的时间^[1],本研究将 Tmax 值输入 CC 公式并进一步绘制 CC 图。CC 图可校正灌注时间信息,用于不同对比剂注射剂量和注射速度的 DSA 图像对比分析,信度分析提示基于颈内动脉兴趣区取值框

AIF 取值范围的 CC 图具有良好的可靠性,可使多帧 DSA 图像的更多信息可视化,而这些信息通常在传统 DSA 图像中无法显示。

正常的神经功能依赖充足的脑灌注。缺血性卒中后脑灌重新分配以维持血供,且脑灌重的重新分布决定缺血性卒中的预后,缺血程度、侧支循环、脑血流动力学等因素相互影响^[8-9]。因此,需要探索一种个体化评估方法辅助脑血管病的诊断与治疗。本组有 1 例急性缺血性卒中中静脉溶栓桥接机械取栓患者,取栓后左大脑中动脉 M1 段再通并恢复其远端灌注,CC 图显示左颈内动脉灌注自左侧额

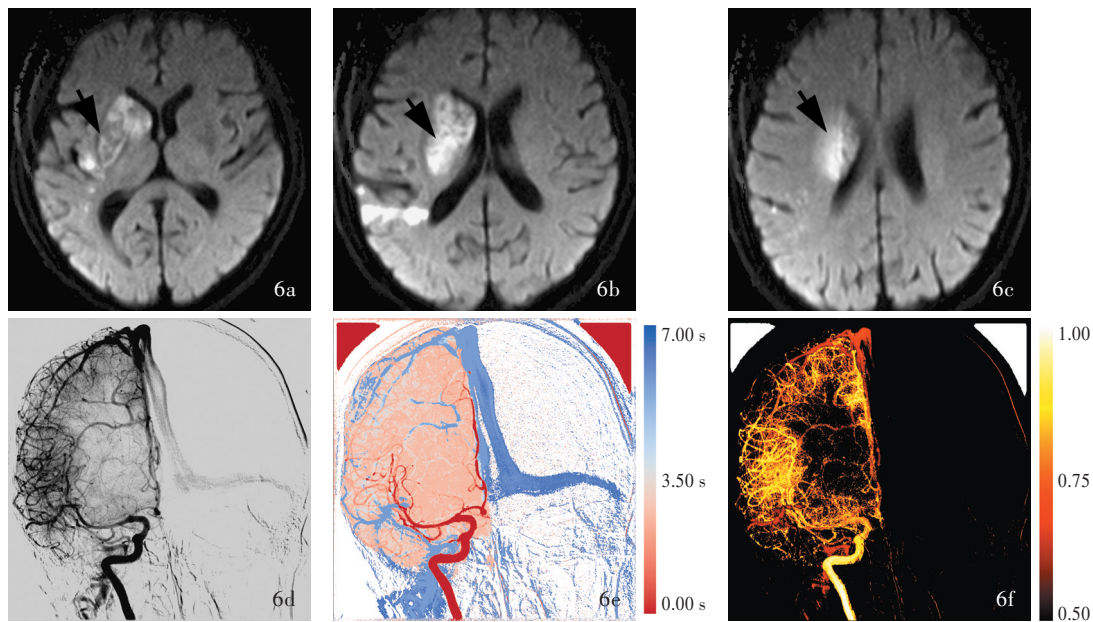


图6 女性患者,66岁,临床诊断为急性右侧基底节区和颞叶梗死,予为期2周的抗血小板和调脂治疗。头部影像学检查所见 6a~6c 入院时横断面DWI显示右侧基底节区和颞叶高信号影(箭头所示) 6d 治疗后汤氏位MinP显示,右大脑中动脉M1段无明显狭窄 6e 治疗后汤氏位Tmax图显示右大脑中动脉灌注区Tmax值基本正常 6f 治疗后汤氏位CC图显示右颈内动脉对右大脑中动脉和大脑前动脉灌注区的血供减少

Figure 6 A 66-year-old female patient with acute right basal ganglia and temporal lobe infarction underwent antiplatelet drugs and statins for 2 weeks. Head imaging findings Axial DWI showed hyperintensity in the right basal ganglia and temporal lobe at admission (arrows indicate, Panel 6a-6c). Towne's view of MinP map showed no obvious stenosis in the right MCA M1 segment after the therapy (Panel 6d). Towne's view of Tmax map showed the peak time of the right MCA blood supply area was basically normal after the therapy (Panel 6e). Towne's view of CC map showed decrease in blood perfusion in the feeding area of right ICA to the right MCA and ACA after the therapy (Panel 6f).

顶叶重新分布至左侧颞叶,提示缺血区恢复正常血供模式,血管再通治疗有效;该例患者并未行左大脑前动脉的血管内治疗,但其灌注区也发生血供变化,提示一级侧支循环参与脑灌注的分布变化。因此,脑灌注的重新分布不仅取决于责任血管,还取决于整个同侧大脑半球的循环状况,且这种现象可以在CC图上清楚地显示出来。急性缺血性卒中推荐血管内治疗,但对于超时间窗患者的治疗仍存争议。单纯球囊扩张术或者支架植入术治疗缺血性卒中的有效性存有争议^[10-12]。本组有1例亚急性缺血性卒中患者,超出静脉溶栓治疗时间窗,接受为期2周的抗血小板和调脂治疗后,行左大脑中动脉M1段上干球囊扩张术+支架植入术,血管成功再通,但CC图显示支架植入前后左颈内动脉灌注分布相似。尽管上述两例患者的动脉闭塞部位和治疗策略相似,但血管内治疗的不同时机导致不同临床结局。因此,仅从单一动脉狭窄程度并不能获得足够的信息以评估血管内治疗的必要性,还需评估同侧大脑半球灌注情况以供临床制定治疗决策。

常规DSA图像无法直观显示大动脉对小血管及其远端的灌注程度。本研究CC图可显示颈内动脉相关灌注区,并为评估脑血流动力学提供补充信息。本组有1例大脑中动脉狭窄但无相关缺血事件患者,常规DSA图像显示左大脑中动脉M1段重度狭窄,但CC图可见左侧大脑半球灌注正常,提示侧支循环已代偿,无需行血管内治疗。另有1例急性缺血性卒中但无大脑中动脉狭窄患者,虽然常规DSA图像完整显示右大脑中动脉和大脑前动脉,但CC图可见右侧大脑半球深部低灌注,提示右大脑中动脉和大脑前动脉穿支供血不足,进而为血管内治疗提供依据。由此可见,仅根据常规DSA图像进行评估可出现假阳性或阴性结果,CC图可提供颈内动脉灌注的定量信息,有助于更准确地评估血管,从而制定适宜的治疗策略。

与其他基于DSA图像的血流算法相比,本研究首次提出基于CC值和Tmax值获得颈内动脉灌注区成像的方法,突出“颈内动脉灌注相关性”这一概念。既往研究中有学者采用去卷积算法计算脑血

流量^[1]、采用独立成分分析(ICA)获得血流平均通过时间(MTT)^[13]、采用深度学习(DL)模型计算TICI评分^[14],虽然能够获得部分脑血流动力学参数,但无法提供DSA图像各灌注区的来源信息。本研究CC图可以直观显示颈内动脉对全脑的灌注相关性,较脑血流量、血流平均通过时间等参数更有利于展示脑灌注的分布情况。常规DSA的二维图像存在重叠效应,每个像素点叠加动脉、脑组织和静脉的密度-时间函数。然而该技术局限可以通过本研究中的算法得到部分弥补:CC图的每个像素点相关系数代表每个灌注区责任动脉与颈内动脉血流的相关性,通过引流静脉和静脉窦中较低的CC值将其与动脉区分开。

本研究受限于技术限制和临床病例数,信度分析仅在2例前循环正常的健康受试者中验证颈内动脉兴趣区取值框AIF取值范围的CC图的可靠性,信度分析仅纳入4种常见临床表型的4例脑血管病患者,病例数较少,无法进行统计学分析,仅描述其影像学所见,为初步探索,后续尚待在更大样本量、更多样化临床表型中进行统计学分析以验证其可靠性和有效性。

结 论

本研究构建基于常规DSA图像的CC图作为评估脑血流动力学的补充方法,并采用基于AIF的去卷积算法和CC值计算每个像素点相关系数,结果显示,在超选择性颈内动脉造影中CC图具有良好的信度,并可提供颈内动脉相关灌注区的定量信息,从而为脑血流动力学提供新的指标,辅助血管性病变的诊断和制定适宜的血管内治疗方案。

利益冲突 无

参 考 文 献

- [1] Scalzo F, Liebeskind DS. Perfusion angiography in acute ischemic stroke [J]. *Comput Math Methods Med*, 2016: ID2478324.
- [2] Juttukonda MR, Li B, Alaktoum R, Stephens KA, Yochim KM, Yacoub E, Buckner RL, Salat DH. Characterizing cerebral hemodynamics across the adult lifespan with arterial spin labeling MRI data from the Human Connectome Project-Aging [J]. *Neuroimage*, 2021, 230:117807.
- [3] Kaso A. Computation of the normalized cross-correlation by fast Fourier transform[J]. *PLoS One*, 2018, 13:e0203434.
- [4] Clough AV, Krenz GS, Owens M, al-Tinawi A, Dawson CA, Linehan JH. An algorithm for angiographic estimation of blood vessel diameter[J]. *J Appl Physiol* (1985), 1991, 71:2050-2058.
- [5] Ostergaard L, Sorensen AG, Kwong KK, Weisskoff RM, Gyldensted C, Rosen BR. High resolution measurement of cerebral blood flow using intravascular tracer bolus passages. Part II: experimental comparison and preliminary results [J]. *Magn Reson Med*, 1996, 36:726-736.
- [6] Gavish M, Donoho DL. The optimal hard threshold for singular values is $4/\sqrt{3}$ [J]. *IEEE Trans Inf Theory*, 2014, 60:5040-5053.
- [7] Calamante F, Christensen S, Desmond PM, Ostergaard L, Davis SM, Connelly A. The physiological significance of the time-to-maximum (Tmax) parameter in perfusion MRI[J]. *Stroke*, 2010, 41:1169-1174.
- [8] Prabhakaran S, Ruff I, Bernstein RA. Acute stroke intervention: a systematic review[J]. *JAMA*, 2015, 313:1451-1462.
- [9] Leigh R, Knutsson L, Zhou J, van Zijl PC. Imaging the physiological evolution of the ischemic penumbra in acute ischemic stroke[J]. *J Cereb Blood Flow Metab*, 2018, 38:1500-1516.
- [10] Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, Kamel H, Kernan WN, Kittner SJ, Leira EC, Lennon O, Meschia JF, Nguyen TN, Pollak PM, Santangeli P, Sharrief AZ, Smith SC Jr, Turan TN, Williams LS. 2021 guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association [J]. *Stroke*, 2021, 52:e364-467.
- [11] Alexander MJ, Zauner A, Chaloupka JC, Baxter B, Callison RC, Gupta R, Song SS, Yu W; WEAVE Trial Sites and Interventionalists. WEAVE trial: final results in 152 on-label patients[J]. *Stroke*, 2019, 50:889-894.
- [12] Aghaebrahim A, Agnoletto GJ, Aguilar-Salinas P, Granja MF, Monteiro A, Siddiqui AH, Levy EI, Shallwani H, Kim SJ, Haussen DC, Nogueira RG, Lopes D, Saied A, Jovin TG, Jadhav AP, Limaye K, Turk AS, Spiotta AM, Chaudry MI, Turner RD, Brasiliense LBC, Dumont TM, Cherian J, Kan P, Sauvageau E, Hanel RA. Endovascular recanalization of symptomatic intracranial arterial stenosis despite aggressive medical management[J]. *World Neurosurg*, 2019, 123:e693-699.
- [13] Lee HJ, Hong JS, Lin CJ, Kao YH, Chang FC, Luo CB, Chu WF. Automatic flow analysis of digital subtraction angiography using independent component analysis in patients with carotid stenosis[J]. *PLoS One*, 2017, 12:e0185330.
- [14] Nielsen M, Waldmann M, Frölich AM, Flottmann F, Hristova E, Bendszus M, Seker F, Fiehler J, Sentker T, Werner R. Deep learning-based automated thrombolysis in cerebral infarction scoring: a timely proof-of-principle study[J]. *Stroke*, 2021, 52:3497-3504.

(收稿日期:2022-08-05)

(本文编辑:彭一帆)