Parametric Digital Subtraction Angiography Imaging for the Objective Grading of Collateral Flow in Acute Middle Cerebral Artery Occlusion

Wan-ling Wen, Yi-bin Fang, Peng-fei Yang, Yong-wei Zhang, Yi-na Wu, Hui Shen, Jia-jia Ge, Yi Xu, Bo Hong, Qing-hai Huang, Jian-min Liu

■ PURPOSE: **To report the feasibility of parametric color-coded digital subtraction angiography (DSA) in complementing the traditional, subjective way of leptomeningeal collateral assessment in acute middle cerebral artery (MCA) occlusions.**

■ METHODS: **Thirty-three consecutive patients with acute MCA occlusion who received endovascular treatment were recruited for investigation. Eighteen of 33 consecutive patients were included. The target downstream territory (TDT) of MCA and reference point at terminal internal carotid artery of each patient was contoured by 5 raters independently on the basis of anteroposterior 2-dimensional DSA. Two parameters of relative maximum density of TDT (*rDensitymax*) and peak time interval (ΔPT) between reference and TDT were extracted by the use of parametric DSA analysis software. Interrater reliability was tested with intraclass correlation coefficients. Parameters with sufficient interrater reliability entered validity evaluation. Then, the correlation test with the American Society of Interventional and Therapeutic Neuroradiology collateral grading system and efficacy in predicting favorable clinical outcome was evaluated.**

■ RESULTS: **The intraclass correlation coefficient of *rDensitymax* and ΔPT were 0.983, 95% confidence interval 0.968−0.993 and 0.831, 95% confidence interval 0.705−0.923, respectively. The parameter *rDensitymax* showed a strong correlation with the American Society of Interventional and Therapeutic Neuroradiology collateral grading system score (r of Spearman correlation test = 0.869, $P < 0.001$) and mRS at 3 months (partial correlation coefficient = 0.616, $P = 0.009$), whereas ΔPT_average did not. A cut-off point of 0.224 in *rDensitymax* predicted a favorable clinical outcome with high sensitivity and specificity.**

■ CONCLUSIONS: **The relative maximum contrast density of MCA territory on 2-dimensional DSA measured by parametric imaging technique appears to be a simple and reliable metric for the assessment of leptomeningeal collaterals in cases of acute MCA occlusion.**

INTRODUCTION

Leptomeningeal collateral, also known as pial collateral, is one of the most important collateral filling pathways for patients with acute ischemic stroke. For patients with inadequate antegrade blood flow, pial collaterals are major determinants of tissue fate[1] and reported to be correlated with smaller infarction volume compared with the poor ones.[2,3] It also indicates a greater possibility of reperfusion and better clinical outcome in patients with acute middle cerebral artery (MCA) occlusion who received endovascular therapy.[4,5]

Key words
- Acute ischemic stroke
- Assessment
- Collateral
- Digital subtraction angiography
- Parametric

Abbreviations and Acronyms
2D: 2-dimensional
ACA: Anterior cerebral artery
ACG: American Society of Interventional and Therapeutic Neuroradiology collateral grading system
AUC: Area under the curve
DSA: Digital subtraction angiography
ICA: Internal carotid artery
ICC: Intraclass correlation coefficient
MCA: Middle cerebral artery
mRS: Modified Rankin Scale
ΔPT: Peak time interval between reference and target downstream territory
$rDensity_{max}$: Maximum intensity of target territory corrected by the reference
ROC: Receiver operating characteristic
ROI: Region of interest
TDT: Target downstream territory

Department of Neurosurgery, Changhai Hospital, Shanghai, China

To whom correspondence should be addressed: Qing-hai Huang, M.D.; Jian-min Liu, M.D. [E-mail: ocinhqh@163.com; chstroke@126.com]

Wan-ling Wen and Yi-bin Fang contributed equally to the work.

Citation: World Neurosurg. (2016) 88:119-125.
http://dx.doi.org/10.1016/j.wneu.2015.12.084

Journal homepage: www.WORLDNEUROSURGERY.org

Available online: www.sciencedirect.com

There has been no direct, quantitative way to assess cerebral collateral. They usually are assessed indirectly by different modalities of images, namely digital subtraction angiography (DSA), computed tomography angiography, dynamic computed tomography angiography, and arterial spin-labeling, to name a few.[6] DSA stands out for its high spatial and time resolution and often is taken as the reference in many studies that focus on collateral assessment.[7-9] The most widely used collateral grading system based on DSA is the American Society of Interventional and Therapeutic Neuroradiology collateral grading system (ACG). The ACG evaluates both the extent of perfusion and the speed of retrograde filling and has been recommended by the Cerebral Angiographic Revascularization Grading panels[10] for collateral assessment.

In clinical practice, however, the differentiation between partial and complete perfusion of ischemic area (ACG grade 2 or 3) requires extensive experience, especially when MCA territory is overlapped by the branches of the anterior cerebral artery (ACA). Moreover, "partial" or "complete" might not be precise enough to characterize leptomeningeal collaterals because acute MCA occlusion patients with ACG grade 2 often have heterogeneous clinical outcomes.[5,11,12] In this study, we reported the feasibility of using a parametric color-coded DSA analysis method[13,14] for the quantitative assessment of leptomeningeal collaterals in patients with acute MCA occlusion.

MATERIALS AND METHODS

Patients

The study was approved by our institutional ethical committee. Patients with acute ischemic stroke who received endovascular recanalization treatment in our center during September 1, 2013, to April 20, 2015, were reviewed retrospectively for this study. The inclusion criteria were as follows: 1) unilateral MCA/M1 segment occlusion confirmed by DSA; and 2) image data compatible with the quantitative DSA analysis tool (*syngo* iFlow, Siemens Medical GmbH, Forchheim, Germany). Exclusion criteria were as follows: 1) cases whose leptomeningeal collaterals were not visualized by ipsilateral internal carotid artery (ICA) injection; 2) cases companied by severe proximal arterial stenosis that could dramatically affect the hemodynamics of cerebral blood flow; and 3) severe motion artifacts.

Thirty-three consecutive patients with 33 MCA main stem occlusions met the initial inclusion criteria. Among 33 patients with MCA, 2 were excluded for severe cervical ICA stenosis, 5 were excluded for the dominant pial collateral flow could only be seen from contralateral ICA injection or vertebral artery injection, and 8 were excluded for motion artifacts. A total of 18 acute M1 occlusion patients who received endovascular intervention were recruited eventually. None received noninvasive perfusion examination before endovascular intervention.

DSA Acquisition

Two-dimensional DSA images were acquired on an angiographic system (Artis Zee biplane, Siemens Medical GmbH, Forchheim, Germany) by the use of clinical standard protocol. Injections were performed with a power injector through a guiding catheter at C1 segment of the ICA and initial segment of the dominant vertebral artery, with a 2-second x-ray delay. Injection volume and rate was 7 mL and 5 mL/s for ICA and 6 mL and 4 mL/s for the vertebral artery. Angiograms in standard anteroposterior and lateral views were both obtained. Exposure time was controlled manually to ensure the appearance of internal jugular vein.

ACG Assessment

On the basis of 2-dimensional (2D) DSA images of each patient, 2 senior neurointerventionists who specialize in cerebrovascular diseases with 12 and 20 years of experience, respectively, performed ACG ratings by consensus. The ACG scores ranged from 0 to 4 (Grade 0, no collaterals visible to the ischemic site; Grade 1, slow collaterals to the periphery of the ischemic site, with persistence of some of the defect; Grade 2, rapid collaterals to the periphery of the ischemic site, with persistence of the defect, and only to a portion of the ischemic territory; Grade 3, collaterals with slow but complete angiographic blood flow of the ischemic bed by the late venous phase; Grade 4, complete and rapid collateral blood flow to the vascular bed in the entire ischemic territory by retrograde perfusion).

Quantitative Collateral Measurement

Region of Interest (ROI) Selection. All measurements were performed on a color-coded DSA software (*syngo* iFlow) based on the 2D-DSA acquisition of ipsilateral ICA injection in the anteroposterior view. The *syngo* iFlow converts a time series of 2D-DSA into a single composite DSA image. This single DSA image is color-coded based on the time that the contrast agent reaches its peak value. As shown in **Figures 1, 2** ROIs were drawn on each patient's DSA image. The first ROI, i.e., the reference ROI, was drawn on the ICA terminus, proximal to the MCA and ACA bifurcation. The second ROI, i.e., the target downstream territory (TDT), was drawn along the midline of the affected hemisphere, superior border of the transverse sinus, and surface of the brain.

Parameters of Interest. For each set of manually drawn reference and TDT contours, the time versus intensity graph was produced automatically by the software. The x-axis in the plot shows the time (in seconds) and y-axis shows the sum of pixel intensities within the ROI. The following primary parameters could be directly measured and displayed: 1) ROI_{area}: area of every ROI in mm^2; 2) ROI_{Peak}/Ref_{Peak}: ratio of peak of total contrast of every ROI to the reference; 3) $ROI_{Peak\ Time}$: the time that contrast intensity of selected ROI reached the peak value; and 4) ROI_{AUC}/Ref_{AUC}: ratio of area under the curve (AUC) of each ROI to the reference ROI.

The parameters of interest in this study were relative maximum density ($rDensity_{max}$) of TDT and peak time interval between reference and target downstream territory (ΔPT), The formulas are listed to follow:

$$rDensitymax = \frac{Peak_{TDT}}{Area_{TDT}} \Big/ \frac{Peak_{ref}}{Area_{ref}}$$

$$\Delta PT = Peak\ time_{TDT} - Peak\ time_{ref}$$

The $rDensity_{max}$ of TDT equals the maximum contrast intensity of TDT ($Peak_{TDT}$) within the duration of 2D-DSA acquisition in relative to that of the reference ROI ($Peak_{ref}$), while $Peak_{ref}$ was