Magn Reson Med Sci 2019; 18; 62–69
doi:10.2463/mrms.mp.2018-0001
Published Online: May 31, 2018

MAJOR PAPER

A Grading Scale for Pial Collaterals in Middle Cerebral Artery Total Occlusion Based on Time-of-flight MR Angiography Source Images

Huai Wu Yuan[1*], Ren Jie Ji[1], An Li Wang[2], Ya Jie Lin[1], Han Feng Chen[1], Zi Qi Xu[1], Guo Ping Peng[1], and Ben Yan Luo[1,3]

Purpose: To verify whether a new grading based on time-of-flight magnetic resonance angiography source images (TOF-MRAsi) can reflect the abundance of pial collaterals, in patients with total occlusion of M1 segment of middle cerebral artery in the chronic stage.

Methods: In this single-center retrospective study, consecutive patients with total occlusion of M1 segment of middle cerebral artery, with both magnetic resonances angiography and digital subtraction angiography image were included. Time-of-flight magnetic resonance angiography source images were evaluated in a blinded fashion for pial collaterals (PCs) that were graded on a four-point scale. Good and poor PCs were defined as TOF-MRAsis grade <2 and ≥2, respectively. Receiver operating characteristic curve analysis was done to calculate the area under curve, sensitivity, and specificity.

Results: A total of 26 patients were included. The inter-reader agreement for time TOF-MRAsi and digital subtraction angiography images were 0.930 and 0.843, respectively. Compared with digital subtraction angiography grading, the area under curve of pial collateral grading based on TOF-MRAsi was 0.830 (0.636–1.000; $P = 0.006$). The sensitivity and specificity were 0.700 and 0.933, respectively. The modified Rankin Scale at follow-up was lower in patients with good PCs than in those with poor PCs (0[0, 1] vs. 1[1, 3], $P = 0.055$), although statistical significance was not reached.

Conclusion: The grading scale based on TOF-MRAsi could be a new empirical approach for pial collateral evaluation. The clinical use of the proposed approach for identifying patients with total occlusion of middle cerebral artery with a high risk of poor outcome requires evaluation in further studies.

Keywords: *collateral circulation, comparative study, digital subtraction angiography, magnetic resonance angiography, middle cerebral artery occlusion*

Introduction

Pial collaterals (PCs) are important factors affecting the long-term prognosis of patients with M1 segment middle cerebral artery (MCA) total occlusion (MCATO).[1] For patients with MCATO in the chronic stage, new drugs targeting PC are expected to be proven promising in future trials, by improving the poor prognosis of patients through enhancing the abundance of PC. Therefore, methods for PC evaluation that are suitable for repeated use in future clinical trials are desired in follow-ups of imaging outcomes. Digital subtraction angiography (DSA), which is the current gold standard for PC evaluation, divides PC into five grades according to the amplitude and speed of the blood flow from the anterior cerebral artery to the MCA.[2] Another method is to divide PC into four grades based on the source images or maximal intensity projection images of computed tomography angiography (CTA).[3] DSA or CTA were unable to be widely used in PC evaluation because of the invasive nature. Thus, there is a need for a new PC evaluation method without the above drawbacks.

Time-of-flight magnetic resonance angiography (TOF-MRA) has been widely used in intracranial artery visualization. The principle of TOF-MRA without intravenous

[1]Department of Neurology, The First Affiliated Hospital, College of Medicine, Zhejiang University, 79 Qingchun Road, Hangzhou 310003, China
[2]Department of Neurology, Pujiang People's Hospital, Yiwu, China
[3]Collaborative Innovation Center for Brain Science, Zhejiang University, Hangzhou, China

*Corresponding author, Phone: +86-136-1653-9483, Fax: +86-571-8723-6106, E-mail: 1313007@zju.edu.cn

Received: October 24, 2017 | Accepted: April 4, 2018

infusion of contrast agent is based on the saturation effect, inflow enhancement effect, and flow-induced phase effect. TOF-MRA uses signal comparison between blood flow and static vascular walls to directly display blood vessels.[4] Theoretically, blood flow in brain tissue supplied by an occluded MCA could only be derived from retrograde blood flow through PC, and the vascular signal intensity of TOF-MRA source images (TOF-MRAsi) in the territory of the occluded MCA can indirectly reflect the PC quantity. As we know, only Jin et al.[5] reported that TOF-MRAsi might reflect the irregular vascular networks on the skull base in patients with Moyamoya disease. No article has reported the relation between PC graded by TOF-MRAsi and by DSA.

The aim of this study was to verify whether a novel grading scale based on TOF-MRAsi can reliably detect PC compared with the gold standard method.

Methods

Patient selection and evaluation

Consecutive MCATO patients with both DSA and TOF-MRA images from November 2011 to October 2016, from the neurology department of the First Affiliated Hospital of College of Medicine of Zhejiang University, were included. Exclusion criteria are as follows: 1) Patients with a period between TOF-MRA and DSA of >30 days. 2) Patients with M1 segment MCA subtotal occlusion and obvious neovascularization at the occlusion section. In accordance with the standard protocol of our institutions for patients with ischemic stroke, demographic data and information on stroke risk factors and medical history, the results of diagnostic tests, such as magnetic resonance diffusion-weighted imaging (DWI), National Institute of Health Stroke Scale (NIHSS) at admission, composite endpoint event (included ischemic stroke, transient ischemic attack, hemorrhagic stroke, myocardial infarction, angina pectoris, death) at follow-up, and modified Rankin Scale (mRS) scores at follow-up were collected regularly. DWI infarct volumes were calculated by multiplying slice thickness plus inter-slice gap by total areas of lesions.[6] In this study, the discharge date was from 2011/11/20 to 2016/08/29, and the follow-up date was from 2017/01/19 to 2017/03/12. The favorable functional outcome was defined as an mRS at follow-up of <2, and poor functional outcome was defined as an mRS at follow-up of ≥2. Doctors were encouraged to decide the therapy regimen based on the American Heart Association/American Stroke Association guidelines.[7–9] The study protocol conformed to the ethical guidelines of the 1964 Declaration of Helsinki and was approved by the institutional ethics committee of the First Affiliated Hospital of College of Medicine of Zhejiang University.

TOF-MRA grading

Time-of-flight magnetic resonance angiography was conducted by radiation specialists by using a 3T magnetic resonance machine (Achieva; Philips Medical Systems, Best, the Netherlands). About 150 slices with five slabs covering almost the whole brain were acquired in an imaging time of 5 min 40 s. The following parameters were executed: TR/TE 27/6.9 ms, flip angle 20°, FOV 24 × 16 cm^2, matrix 320 × 256, 30 slices in each slab, slab overlap 4.8 mm, slice thickness 0.6 mm, and inter-slice spacing 0 mm. Based on previous literature,[10] MRAsi vascular signal was defined dot or linear or serpentine-appearing hyperintensity relative to gray matter in the subarachnoid space or brain parenchyma that corresponded with a typical arterial course. MCA M1 segment occlusion might occlude the lenticulostriate arteries that supply the basal ganglia and internal capsule.[2] These vessels are not collateralized from the cortex. As a result, excellent transcortical collaterals might allow cortex to be salvaged, but permanent hemiplegia might still result from infarction of the internal capsule. Therefore, in this study, the vascular signal intensity of TOF-MRAsi in the territory of the occluded MCA was assessed on the level of the lateral ventricle body. According to the axial source images on the level of the lateral ventricle body, the PC status was divided into four grades: grade 0, no vascular signal intensity in the territory of the occluded MCA; grade 1, vascular signal intensity in the territory of the occluded MCA < 50% of that of the contralateral corresponding regions; grade 2, vascular signal intensity in the territory of the occluded MCA ≥ 50% of that of the contralateral corresponding regions; grade 3, vascular signal intensity in the territory of the occluded MCA equal to or more than that of the contralateral corresponding regions (Fig. 1). Two readers (Ren Jie Ji and Han Feng Chen) blinded to all clinical information and the results of the other radiological data evaluated the TOF-MRAsi. A consensus was reached in cases of discrepant interpretations. Poor PC based on TOF-MRAsi was defined as grade 0 or 1, and good PC was defined as grade 2 or 3.

DSA grading

Huai Wu Yuan and Zi Qi Xu used Philips Allura Xper FD20/20 biplane DSA for all DSA operations. The catheter head was placed in the proximal portion of the common carotid artery, and 5 mL Visipaque (GE Healthcare, Cork, Ireland) was injected at a rate of 7 mL/s under a pressure of 250 Pa. Following the American Society of Interventional and Therapeutic Neuroradiology PC grading system based on consensus,[2] PC status was divided into five grades according to the blood flow from the anterior cerebral artery to the MCA, as follows: grade 0, no collateral flow to ischemic areas; grade 1, slow collateral flow to ischemic peripheral regions accompanied by persistent perfusion defects; grade 2, rapid collateral flow to ischemic peripheral

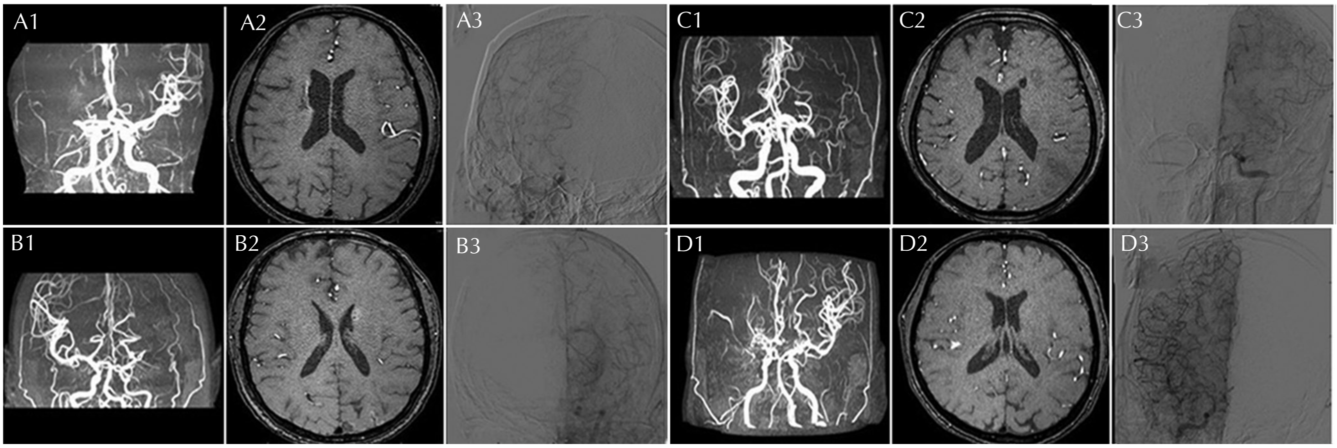

Fig. 1 Typical examples of PC grading based on TOF-MRAsi. (**A1**–**A3**) M1 segment occlusion of right MCA, with grade 0 based on TOF-MRAsi (**A2**). (**B1**–**B3)** M1 segment occlusion of left MCA, with grade 1 based on TOF-MRAsi (**B2**). (**C1**–**C3**) M1 segment occlusion of left MCA, with grade 2 based on TOF-MRAsi (**C2**). (**D1**–**D3)** M1 segment occlusion of right MCA, with grade 3 based on TOF-MRAsi (**D2**). PC, pial collaterals; TOF-MRAsi, time-of-flight magnetic resonance angiography source images; DSA, digital subtraction angiography; MCA, middle cerebral artery.

regions accompanied by persistent perfusion defects; grade 3, slow but complete blood flow to the ischemic regions observed in the venous phase; grade 4, complete and rapid collateral blood flow to the vascular bed in the entire ischemic territory by retrograde perfusion. Two readers (Huai Wu Yuan and Zi Qi Xu) blinded to TOF-MRAsi evaluated the DSA images. A consensus was reached in cases of discrepant interpretations. Poor PC based on DSA was defined as grade 0 or 1, and good PC based on DSA was defined as grade 2 to grade 4, based on previous literature.[11]

Statistical methods

All data were recorded in duplicates and checked by Ya Jie Lin and Ge An Wang. Continuous variables were expressed as mean (standard deviation [SD]) or median (quartiles), and compared using Student's *t*-test or the Mann–Whitney *U*-test as appropriate. Categorical variables were compared using χ^2-test or Fisher's test as appropriate. With DSA as the gold standard, receiver operating characteristic curve analysis was used to calculate the area under the curve (AUC), sensitivity, and specificity of the TOF-MRAsi grading scale. Spearman correlation coefficient was used to assess the correlation of angiographic grading scales with TOF-MRAsi grading scales for PC. A two-tailed value of $P < 0.05$ was considered significant. All statistical analyses were completed using IBM SPSS Statistics, version 17.0 (IBM Corporation, Armonk, NY, USA).

Results

From November 2011 to October 2016, there were 206 consecutive patients with MCATO at our center. Forty-six patients had no TOF-MRA and no DSA images, 86 patients had TOF-MRA but no DSA images, 39 patients had DSA but no TOF-MRA images, and 35 patients had both TOF-MRA and DSA images. Among these 35 patients, there were 9 patients with a period between TOF-MRA and DSA of >30 days and were excluded. Finally, 26 patients were included in the statistical analysis.

Baseline clinical characteristics

There were 18 male patients whose mean (±SD) age was 50.56 ± 11.15 years, and eight female patients whose mean (±SD) age was 48.13 ± 16.64 years. Sixteen (61.5%) and six (23.1%) patients presented with ischemic stroke and transient ischemic attack, respectively, and four (15.0%) patients were asymptomatic. Except asymptomatic patients, the period (median, quartile) from the qualifying event to TOF-MRA was 7.50 (5.75, 18.50) days, and the period (median, quartile) between TOF-MRA and DSA was 6.00 (5.00, 8.25) days (Table 1). A total of six (23.1%) patients were lost to follow-up, and the average follow-up duration of remaining patients was 32 ± 14 months (6.43 months was the minimum and 64.3 months the maximum). Among 20 patients with follow-up, there was one fatal recurrent ischemic stroke.

Accuracy of the PC grading scale based on TOF-MRAsi for DSA grading

The inter-reader agreement for TOF-MRAsi was good ($\kappa = 0.930$). The inter-reader agreement for DSA was also good ($k = 0.843$). The distribution of PC grades based on TOF-MRAsi was as follows: 1 patient with grade 0, 17 patients with grade 1, 7 patients with grade 2, and 1 patient with grade 3. The distribution of PC grades based on DSA was as follows: no patient with grade 0, 15 patients with grade 1, 10 patients with grade 2, 1 patient with grade 3, and no patient with grade 4 (Fig. 2).

Table 1 Patients' characteristics

	Patients (n = 26)
Age, y, mean (SD)	49.81 (12.78)
Male (%)	18 (69.2)
Medical history	
Hypertension (%)	16 (61.5)
Diabetes (%)	7 (26.9)
Hyperlipidemia	0
Ischemic stroke or transient ischemic attack (%)	4 (15.4)
Myocardial infarction or angina	0
Atrial fibrillation	0
Peripheral artery diseases (%)	1 (3.8)
Smoking (%)	9 (34.6)
Familial history (%)	2 (7.7)
Stroke or transient ischemic attack as a qualifying event (%)	22 (84.6)
Time from qualifying event to TOF-MRA, d (median, quartile)	7.50 (5.75, 18.50)
Time between TOF-MRA and DSA, d (median, quartile)	6.00 (5.00, 8.25)
Time between TOF-MRA and MR DWI, d (median, quartile)	3.50 (2.25, 5.75)
DWI infarct volume (cm^3), mean (SE)	1.17 (0.31)
NIHSS at admission (median, quartile)	1 (0, 4.25)
mRS score on follow-up (median, quartile)	1 (0, 2.75)
Composite endpoint event (%)*	1(3.8)
Follow-up time, months, mean (SD) (six patients lost follow-up)	32 ± 14

*Included ischemic stroke, transient ischemic attack, hemorrhagic stroke, myocardial infarction, Angina pectoris, and death. DSA, digital subtraction angiography; DWI, diffusion-weighted image; mRS, modified Ranking Scale; NIHSS, National Institutes of Health Stroke Scale; TOF-MRA, time-of-flight magnetic resonance angiography.

The PC TOF-MRAsi grades were strongly correlated with the PC DSA grades. The relationship of the PC grading scale based on TOF-MRAsi and that based on DSA in the 26 patients was linear, and the linear R^2 was 0.407. The Spearman correlation coefficient was 0.638 (P = 0.001) between the PC TOF-MRAsi grade and the DSA grade. Compared with the gold standard DSA grades, the AUC of TOF-MRA grades was 0.830 (0.636–1.000; P = 0.006). When PC based on TOF-MRA source images was 1.5, the Youden index, sensitivity-(1 − specificity) = 0.700 − 0.067 = 0.633, was up to the maximum. The sensitivity was 0.700 and the specificity was 0.933 (Fig. 3).

Image features and clinical outcomes among different PC TOF-MRAsi grades

Despite DWI infarct volume was lower in patients with good PC than in those with poor PC as determined with TOF-MRAsi (0.92[0.65] cm^3 vs. 1.28[0.35] cm^3, P = 0.272), the significance was not reached. Similar to the above, the mRS score at follow-up was lower in patients with good PC than in those with poor PC as determined with TOF-MRAsi (0[0, 1] vs. 1[1, 3], P = 0.055), but statistical significance was also not reached.

Discussion

This study showed that compared with the gold standard DSA grades for PC detection, semiquantitative grading based on TOF-MRAsi has good sensitivity and specificity, and demonstrated that mRS tended to be lower in patients with good PC grades based on TOF-MRAsi, although the relation between PC TOF-MRAsi grade and DWI infarct volume at admission were not significant because the time from the qualifying event to TOF-MRAsi was about 7 days in patients with ischemic stroke. Previous studies have shown that in patients with MCATO with good PC, there is higher vascular signal intensity at the distal end of the MCATO segment in fluid-attenuated inversion recovery sequences,[12] increased cortical branches in the ipsilateral posterior cerebral artery in three-dimensional MRA images,[13] greater difference in blood flow between lesions and the contralateral posterior cerebral artery in quantitative MRA,[14] and lower degree of cerebral blood flow decrease on dynamic magnetic resonance perfusion (MRP) images.[15] These studies indirectly suggest a correlation between TOF-MRAsi and PC. Other imaging methods, such as CTA, perfusion CT, dynamic susceptibility contrast-enhanced MRP, and arterial spin labeling (ASL) imaging have been used to visualize the collaterals.[16] However, these techniques except ASL still use contrast, and ASL has not been tested in patients with MCATO at chronic stage. Our analysis showed that the use of a novel grading scale for PC based on TOF-MRAsi predicts PC DSA grading with fairly high sensitivity and specificity (70.0% and 93.3%, respectively). The acquired images do not need complex post-processing. TOF-MRAsi enables a simple, non-invasive angiographic characterization with high inter-rater reproducibility for PC grading.

The results have several implications. i) Poor PC contributes to the risk of first or recurrent stroke in patients with MCATO,[17] and the development of collateral signs on MRI can help to identify patients who are more likely to show poor outcomes on long-term follow-up, which will help in selecting patients for additional therapy, such as extracranial–intracranial arterial bypass surgery.[18,19] ii) PC in the chronic stage of MCATO is a promising therapeutic target. Molecules, such as hypoxia-inducible factor 1a and vascular endothelial growth factor were found to be related to the extent of native PC growth in the brain in animal

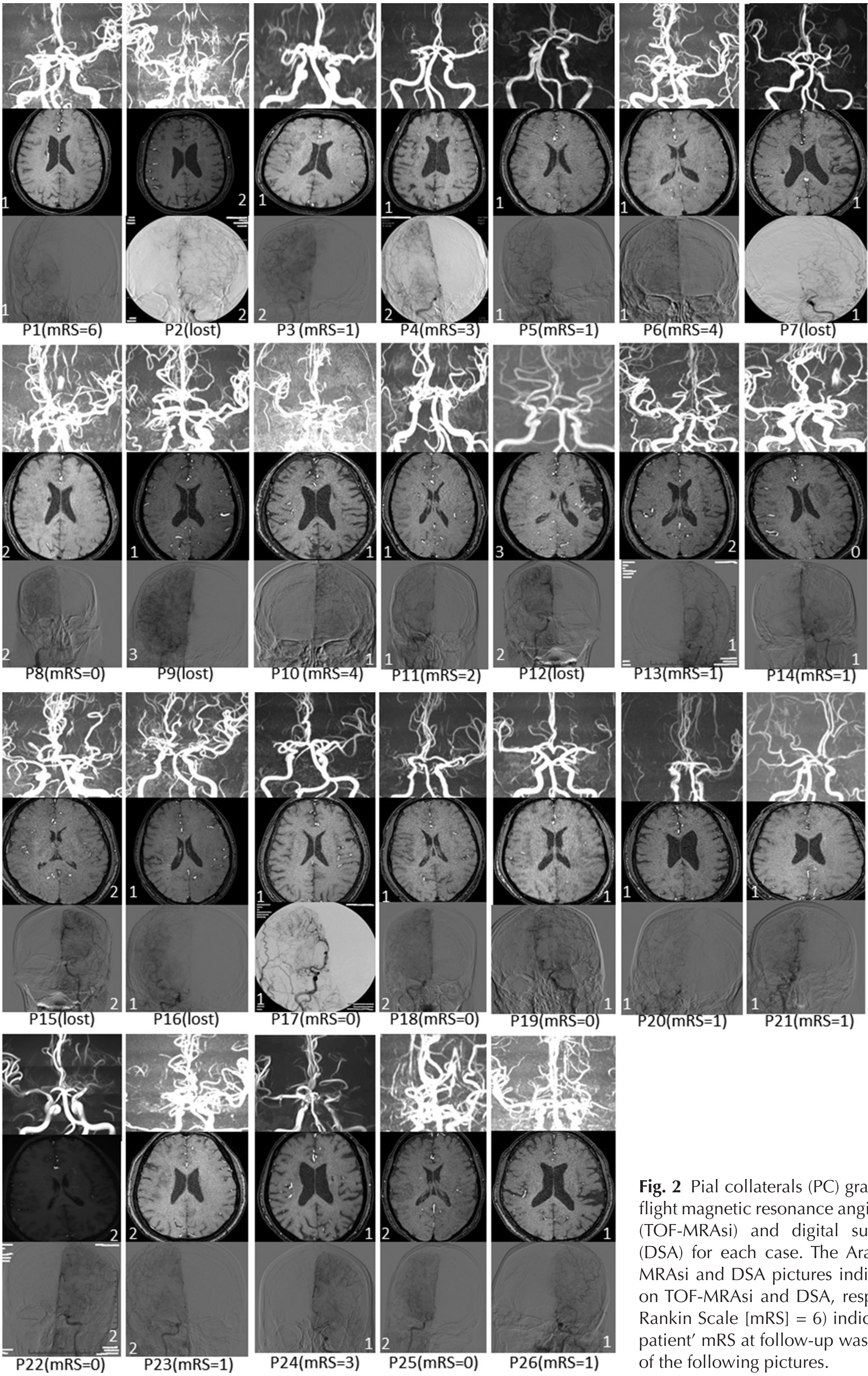

Fig. 2 Pial collaterals (PC) grading based on time-of-flight magnetic resonance angiography source images (TOF-MRAsi) and digital subtraction angiography (DSA) for each case. The Arabic numerals in TOF-MRAsi and DSA pictures indicate PC grading based on TOF-MRAsi and DSA, respectively. P1 (modified Rankin Scale [mRS] = 6) indicates patient 1, and the patient' mRS at follow-up was 6. And so on, for each of the following pictures.

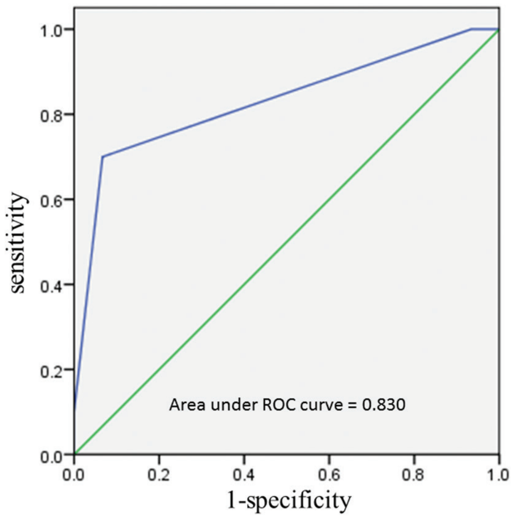

Fig. 3 The receiver operating characteristic (ROC) curves of pial collateral (PC) grading based on time-of-flight magnetic resonance angiography source images (TOF-MRAsi) in predicting gold standard digital subtraction angiography (DSA) grades.

experiments.[20,21] Even albumin treatment has been shown to exert a significant therapeutic effect after ischemia by augmenting collateral perfusion in animal experiments.[22] When new drugs targeting PC in the chronic stage of MCATO are tested in future clinical trials, PC grading based on TOF-MRAsi is expected to be a useful tool for repeated observations of imaging outcomes because of its non-invasiveness and lack of need for contrast.

As this study is a retrospective study with a small sample, it has some limitations. i) The qualifying event and timing for MRI was long and heterogeneous; thus, there was no significant association between the PC TOF-MRAsi grade and DWI infarct volume at admission in our study. A prospective study could overcome these shortcomings. ii) Since the degree of collateral status indirectly indicate the cerebrovascular reactivity that would be useful information to determine the therapeutic strategy,[23] a comparative study between PC on TOF-MRAsi and hemodynamic state by performing single-photon emission computed tomography and/or positron emission tomography of the brain will make this method more convincing. iii) There is an insufficient display of small artery by non-contrast 3D-TOF MRA. Compared non-contrast 3D-TOF MRA, post-contrast 3D-TOF MRA can enhance the signal-to-noise ratio and eliminate the flow artifact, so it is possible to improve the accuracy of PC evaluation by post-contrast 3D-TOF MRA source images. Another method, black-blood MRA on a 1.5T MRI system, was reported better than 3D-TOF MRA on display of lenticulostriate arteries in which the diameter is usually about 80–1400 μm.[24] Therefore, it is also possible to improve accuracy of PC evaluation by black-blood MRA source images. On the other hand, higher magnetic field intensity brings higher spatial resolution, so it is better to visualize the PC by 3D-TOF MRA source images on 3T other than 1.5T MRI system. iv) For patients with MCATO in the acute stage, good PC status has been identified as a predictor for better outcome after intravenous thrombolysis or arterial embolectomy and extended treatment time window.[25,26] However, our data were not obtained several hours after stroke; thus, further studies are needed to determine whether the PC grading based on TOF-MRAsi described in this study can also be comparable to DSA in the acute stage of the disease, and whether this can be used as a guide for treatment in the emergency setting. v) The patients did not accept MRA or DSA again during the follow-up, so we did not know the influence of spontaneous recanalization on functional outcome on follow-up.[27] This might weaken the difference of functional outcome between patients with good and poor PC assessed by TOF-MRAsi. However, when considering that the time from the qualifying event to TOF-MRAsi was about 7 days in patients with ischemic stroke, spontaneous recanalization after MRA might be a small probability event. vi) Blood flow in brain tissue supplied by an occluded MCA could only be derived from retrograde blood flow through PC, from the anterior and the posterior cerebral artery. Therefore, it is a flaw of this study that we do not include comparison with collateral flow from the posterior cerebral artery that is usually depicted on vertebral angiography. However, so far there is not a standard method to grade the PC depicted by DSA from posterior cerebral artery to MCA.[2,28] When we try to verify whether PC based on TOF-MRA source images could be comparable to PC based on DSA from posterior cerebral artery to MCA, it is an unsolved problem to define a cutoff point between poor PC and good PC based on DSA for the calculation of the sensitivity and specificity in ROC analysis. vii) Because the PC TOF-MRAsi grading in this study is still a semi-quantitative method, the DSA manifestation of patients with the same PC TOF-MRAsi grade may seem somewhat different. More accurate assessment techniques for PC are needed for clinical evaluations.

Conclusion

This study demonstrates that a novel grading scale for PC based on TOF-MRAsi that accurately predicts the DSA grade. The clinical use of the proposed approach for identifying MCATO patients with a high risk of poor outcome requires evaluation in further study.

Funding

This work was supported by the General Project Plan of Zhejiang Medical Technology (grant no. 2015KYB122), the Medical Science and Technology Project co-founded by Zhejiang Province and the Ministry of Health of China (grant no. 2016152769), the Clinical Research Innovation Plan of China Stroke (2016).

Conflicts of Interest

The authors declare that they have no competing interests.

References

1. Ichijo M, Iwasawa E, Numasawa Y, et al. Significance of development and reversion of collaterals on MRI in early neurologic improvement and long-term functional outcome after intravenous thrombolysis for ischemic stroke. AJNR Am J Neuroradiol 2015; 36:1839–1845.
2. Higashida RT, Furlan AJ, Roberts H, et al. Technology Assessment Committee of the American Society of Interventional and Therapeutic Neuroradiology; Technology Assessment Committee of the Society of Interventional Radiology. Trial design and reporting standards for intra-arterial cerebral thrombolysis for acute ischemic stroke. Stroke 2003; 34: e109–e137.
3. Lima FO, Furie KL, Silva GS, et al. The pattern of leptomeningeal collaterals on CT angiography is a strong predictor of long-term functional outcome in stroke patients with large vessel intracranial occlusion. Stroke 2010; 41:2316–2322.
4. Jindal G, Miller T, Raghavan P, Gandhi D. Imaging evaluation and treatment of vascular lesions at the skull base. Radiol Clin North Am 2017; 55:151–166.
5. Jin Q, Noguchi T, Irie H, et al. Assessment of Moyamoya disease with 3.0-T magnetic resonance angiography and magnetic resonance imaging versus conventional angiography. Neurol Med Chir (Tokyo) 2011; 51:195–200.
6. Oh MS, Yu KH, Lee JH, et al. Aspirin resistance is associated with increased stroke severity and infarct volume. Neurology 2016; 86:1808–1817.
7. Powers WJ, Derdeyn CP, Biller J, et al. American Heart Association Stroke Council. 2015 American Heart Association/American Stroke Association Focused Update of the 2013 Guidelines for the Early Management of Patients with Acute Ischemic Stroke Regarding Endovascular Treatment: A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association. Stroke 2015; 46:3020–3035.
8. Meschia JF, Bushnell C, Boden-Albala B, et al. American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Functional Genomics and Translational Biology; Council on Hypertension. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the american heart association/american stroke association. Stroke 2014; 45:3754–3832.
9. Furie KL, Kasner SE, Adams RJ, et al. American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Clinical Cardiology, and Interdisciplinary Council on Quality of Care and Outcomes Research. Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: a guideline for healthcare professionals from the american heart association/american stroke association. Stroke 2011; 42:227–276.
10. Lee KY, Latour LL, Luby M, Hsia AW, Merino JG, Warach S. Distal hyperintense vessels on FLAIR: an MRI marker for collateral circulation in acute stroke? Neurology 2009; 72:1134–1139.
11. Lau AY, Wong EH, Wong A, Mok VC, Leung TW, Wong KS. Significance of good collateral compensation in symptomatic intracranial atherosclerosis. Cerebrovasc Dis 2012; 33:517–524.
12. Lee SH, Seo KD, Kim JH, Suh SH, Ahn SJ, Lee KY. Correlation between hyperintense vessels on FLAIR imaging and arterial circulation time on cerebral angiography. Magn Reson Med Sci 2016; 15:105–110.
13. Lee CE, Ng HB, Yip CW, Lim CC. Imaging collateral circulation: magnetic resonance angiography and perfusion magnetic resonance imaging at 3 T. Arch Neurol 2005; 62:492–493.
14. Ruland S, Ahmed A, Thomas K, et al. Leptomeningeal collateral volume flow assessed by quantitative magnetic resonance angiography in large-vessel cerebrovascular disease. J Neuroimaging 2009; 19:27–30.
15. Villringer K, Serrano-Sandoval R, Grittner U, et al. Subtracted dynamic MR perfusion source images (sMRP-SI) provide collateral blood flow assessment in MCA occlusions and predict tissue fate. Eur Radiol 2016; 26:1396–1403.
16. Robson PM, Dai W, Shankaranarayanan A, Rofsky NM, Alsop DC. Time-resolved vessel-selective digital subtraction MR angiography of the cerebral vasculature with arterial spin labeling. Radiology 2010; 257: 507–515.
17. Raymond SB, Schaefer PW. Imaging brain collaterals: quantification, scoring, and potential significance. Top Magn Reson Imaging 2017; 26:67–75.
18. EC/IC Bypass Study Group. Failure of extracranial–intracranial arterial bypass to reduce the risk of ischemic stroke. Results of an international randomized trial. N Engl J Med 1985; 313:1191–1200.
19. Powers WJ, Clarke WR, Grubb RL, Videen TO, Adams HP, Derdeyn CP; COSS Investigators. Extracranial–intracranial bypass surgery for stroke prevention in hemodynamic cerebral ischemia: the carotid occlusion surgery study randomized trial. JAMA 2011; 306:1983–1992.
20. Anan M, Abe T, Shimotaka K, et al. Induction of collateral circulation by hypoxia-inducible factor 1alpha decreased cerebral infarction in the rat. Neurol Res 2009; 31: 917–922.
21. Lohr NL. Collateral development: the quest continues. Circ Res 2014; 114:591–593.
22. Defazio RA, Zhao W, Deng X, Obenaus A, Ginsberg MD. Albumin therapy enhances collateral perfusion after laser-induced middle cerebral artery branch occlusion: a laser speckle contrast flow study. J Cereb Blood Flow Metab 2012; 32:2012–2022.
23. Bahr-Hosseini M, Shakur SF, Amin-Hanjani S, Charbel FT, Alaraj A. Angiographic correlates of cerebral hemodynamic changes with diamox challenge assessed by quantitative magnetic resonance angiography. Stroke. 2016; 47:1658–1660.
24. Okuchi S, Okada T, Ihara M, et al. Visualization of lenticulostriate arteries by flow-sensitive black-blood

MR angiography on a 1.5 T MRI system: a comparative study between subjects with and without stroke. AJNR Am J Neuroradiol 2013; 34:780–784.

25. Seeta Ramaiah S, Churilov L, Mitchell P, Dowling R, Yan B. The impact of arterial collateralization on outcome after intra-arterial therapy for acute ischemic stroke. AJNR Am J Neuroradiol 2014; 35:667–672.
26. Ribo M, Flores A, Rubiera M, et al. Extending the time window for endovascular procedures according to collateral pial circulation. Stroke 2011; 42:3465–3469.
27. Kassem-Moussa H, Graffagnino C. Nonocclusion and spontaneous recanalization rates in acute ischemic stroke: a review of cerebral angiography studies. Arch Neurol 2002; 59:1870–1873.
28. McVerry F, Liebeskind DS, Muir KW. Systematic review of methods for assessing leptomeningeal collateral flow. AJNR Am J Neuroradiol 2012; 33:576–582.