European Radiology (2019) 29:4922–4929
https://doi.org/10.1007/s00330-019-06027-9

NEURO

Comparison of CT angiography collaterals for predicting target perfusion profile and clinical outcome in patients with acute ischemic stroke

Shan-shan Lu[1] · Xuan Zhang[1] · Xiao-quan Xu[1] · Yue-zhou Cao[2] · Lin bo Zhao[2] · Qiang-hui Liu[3] · Fei-yun Wu[1] · Sheng Liu[2] · Hai-bin Shi[2]

Received: 12 October 2018 / Revised: 22 December 2018 / Accepted: 18 January 2019 / Published online: 14 February 2019

Abstract

Objectives To compare collateral status on single-phase CT angiography (sCTA) and multiphase CT angiography (mCTA) and their ability to predict a target mismatch on CT perfusion (CTP) and clinical outcome in patients with acute ischemic stroke (AIS).

Methods Seventy-three AIS patients with stroke onset between 5 and 15 h or with unclear onset time and occlusions in the M1/M2 segment of the middle cerebral artery and/or intracranial internal carotid artery underwent head non-contrast CT and CTP. Simulated sCTA and mCTA were reconstructed from CTP data and were compared for collaterals assessment. The ability to predict target mismatch on CTP (an ischemic core < 70 ml, a mismatch ratio ≥ 1.8, and an absolute difference ≥ 15 ml) and 90-day modified Rankin Scale (mRS) score of 0–2 was compared between sCTA and mCTA by using receiver operating curve analysis.

Results sCTA underestimated the collateral status when compared with mCTA ($p < 0.01$). The ability of mCTA to predict target mismatch (AUC = 0.902, 95% confidence interval [CI] 0.809, 0.959) and clinical outcome (AUC = 0.771; 95% CI, 0.655, 0.864) was better than that of sCTA ($p < 0.05$ overall). A mCTA collateral score of > 3 best identified the target mismatch (sensitivity, 78.4%; specificity, 90.9%) and predicted 90-day mRS score of 0–2 (sensitivity, 84.8%; specificity, 69.4%).

Conclusions The collaterals were better estimated by mCTA compared with sCTA. A mCTA collateral score of > 3 optimized the prediction of a target mismatch on CTP and a good clinical outcome in patients with AIS.

Key Points

- *Collateral circulation is a key determinant of ischemic core and penumbra. Better collaterals are associated with smaller ischemic core volumes and larger mismatch ratios on CT perfusion.*
- *The collaterals can be better estimated by multiphase CTA compared with single-phase CTA.*
- *A collateral score of > 3 on multiphase CTA best identifies patients with target mismatch on CT perfusion and predicts 90-day mRS score of 0–2.*

Keywords Collateral circulation · Perfusion imaging · CT angiography · Stroke

Abbreviations

AIF	Arterial input function
AIS	Acute ischemic stroke
AUC	Area under the ROC curve
CBF	Cerebral blood flow
CTA	CT angiography
CTP	CT perfusion
ICA	Internal carotid artery
IMS	Interventional Management of Stroke
MCA	Middle cerebral artery (MCA)
mCTA	Multiphase CT angiography
NCCT	Non-contrast CT

✉ Hai-bin Shi
shihb@njmu.edu.cn

[1] Department of Radiology, The First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu Province, China

[2] Department of Interventional Radiology, The First Affiliated Hospital of Nanjing Medical University, No.300 Guangzhou Road, Gulou district, Nanjing, Jiangsu Province, China

[3] Department of Emergency, The First Affiliated Hospital of Nanjing Medical University, Nanjing, Jiangsu Province, China

NIHSS	National Institute of Health Stroke Scale
RCTs	Randomized controlled trials
ROC	Receiver operating characteristic
sCTA	Single-phase CT angiography
T_{max}	Time to maximum
VIF	Venous input function
VPCT	Volume perfusion CT

Introduction

Recent success in five large randomized controlled trials (RCTs) of endovascular therapies demonstrated high recanalization rates and improved functional outcomes for patients with acute ischemic stroke (AIS) [1–5]. Each of these trials used a slightly different imaging technique with a common goal to identify patients with a small ischemic core at baseline and either adequate collaterals or salvageable brain.

CT perfusion (CTP) provides a quantitative assessment of ischemic core and tissue at risk. Trials such as Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment (SWIFT PRIME) and Extending the Time for Thrombolysis in Emergency Neurological Deficits-Intra-Arterial (EXTEND-IA) demonstrate the feasibility of CTP to select eligible patients [2, 5]. However, criticisms of CTP include its limited brain coverage, motion artifacts, potential variation in post-processing methods, refinement of ischemic core and penumbra, and the time taken to acquire, process, and interpret the imaging [6–8].

Collateral circulation is an important determinant of the rate of ischemic penumbra recruitment and infarct growth [9–11]. Given that perfusion imaging is tightly correlated with collateral status, the assessment of collateral circulation may therefore decide who will benefit from early recanalization. Data from Interventional Management of Stroke (IMS) III showed that collateral status on baseline CT angiography (CTA) was a robust determinant of clinical outcome and could be used to select patients for endovascular therapy [10]. Previous studies have investigated the association between CTA collaterals and CT perfusion parameters [12, 13]. However, their results were mainly based on conventional single-phase CTA (sCTA). sCTA is a single snap imaging; therefore, it may misclassify patients with good collaterals as poor if performed early in the arterial phase. Multiphase CTA (mCTA) is a new technique that generates time-resolved cerebral angiography of pial arterial filling. This technique is quick to perform, less vulnerable to patient motion, and yields images that are easy to interpret [14]. The Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times (ESCAPE) trial used collateral assessment by mCTA in a majority of patients [3]. However, the relationship between collateral status on mCTA and CT perfusion parameters remains to be elucidated.

With the advent of CT perfusion techniques such as the "volume perfusion CT" (VPCT), it has become possible to reconstruct whole-brain dynamic CTAs from CTP data, producing simulated CTA which can offer image quality comparable to traditional CTA [15]. The objective of our study was (1) to compare the collateral status determined by simulated sCTA and mCTA and (2) to explore their ability to predict a target mismatch quantified by CTP and the clinical outcomes in patients with AIS.

Materials and methods

Study population

From October 2017 to June 2018, consecutive patients presenting to our emergency department with symptoms of AIS within 5 to 15 h or with unclear time of symptom onset were retrospectively identified from our single-institution stroke center. This retrospective study was reviewed and approved by the local institutional Review Board and the written informed consent was waived by the same ethics committee. The inclusion criteria for the study were as follows: (a) patients older than 18 years; (b) National Institute of Health Stroke Scale (NIHSS) scores > 6; (c) occlusions in the M1/M2 segment of the middle cerebral artery (MCA) and/or intracranial internal carotid artery (ICA); and (d) CTP imaging was performed and the image quality was good without significant motion artifacts. The exclusion criteria were as follows: (a) intracranial hemorrhage identified on non-contrast computerized tomography (NCCT); (b) previous moderate to large stroke in the ipsilesional hemisphere identified on baseline NCCT; (c) an inability to undergo CTP because of a history of renal failure, contrast medium allergy, or other reasons; and (d) patients with occlusion in the anterior cerebral artery or posterior circulation. The clinical outcome in this study was analyzed by 90-day modified Rankin Scale (mRS) score of 0–2.

Image acquisition

All patients underwent our institutional stroke imaging protocol for AIS on a 128-slice multidetector CT scanner (optima CT 660, GE healthcare). In our stroke center, CTP was performed in AIS patients with stroke onset time ≥ 5 h and those stroke onsets with unclear time. Patients with stroke onset time < 5 h will undergo only non-contrast CT and CT angiography as additional CTP is not recommended for selecting eligible patients when mechanical thrombectomy can be initiated within 6 h. Whole-brain helical NCCT (120 kVp, 100–350 auto-mAs) was performed with 5-mm section thickness.

Volume perfusion CT data were acquired using a periodic spiral approach (4-dimensional adaptive spiral mode, 100 kVp, 200 mAs, rotation time 0.4 s, maximum pitch 0.984) consisting of 30 consecutive spiral scans of the brain (80 mm in *z*-axis, 2-s delay, 1.7-s temporal resolution) for a total examination time of 53 s after injection of 50-ml contrast medium (iopromide, Ultravist 370, Bayer Schering Pharma) at a flow rate of 5 ml/s followed by a 30-ml saline chaser at the same rate. VPCT data were reconstructed with a slice thickness of 5 mm every 3 mm for perfusion analysis, and with a slice thickness of 0.625 mm every 1 mm for CTA analysis.

CTP analysis

All CTPs were post-processed using commercially available software (Carestream Vue PACS v12.1, Carestream Health) and standard singular value deconvolution (sSVD) algorithms. A semi-automated processing protocol including motion correction, smoothing, arterial input function (AIF), and venous input function (VIF) selection was performed and checked for errors. Parametric maps were automatically generated and overlaid on the source CTP images. Irreversibly infarcted tissues (ischemic core) were defined as the region with relative cerebral blood flow (CBF) < 30% contralateral normal brain tissues. Hypoperfusion volume was defined as tissue with a T_{max} value > 6 s [16–18]. Automatic volumes of ischemic core and hypoperfusion were generated by using these thresholds. The mismatch ratio was calculated as hypoperfusion volume/volume of ischemic core.

Operationally defined imaging criteria to select patients with a large anterior circulation occlusion of 6 to 16 h for mechanical thrombectomy were assigned in the Diffusion and Perfusion Imaging Evaluation for Understanding Stroke Evolution (DEFUSE) 3 trial [19]. The imaging criteria included ischemic core volume < 70 ml, a ratio between the volumes of critically hypoperfused tissue and the ischemic core ≥ 1.8, with an absolute difference ≥ 15 ml and an additional exclusion if there was severe hypoperfusion (T_{max} > 10 s) > 100 ml. We used the same criteria to define whether the AIS patients had target mismatch on CTP in this study.

Reconstruction of simulated CTA

A previous report of scanning protocols for mCTA included a peak arterial phase, an equilibrium/peak venous phase, and a late venous phase [14]. The three CTA phases were each 8 s apart. Therefore, for the simulated mCTA in this study, the first phase was reconstructed from the peak arterial phase in the normal distal ICA, based on the AIF curve, with a slice width of 0.625 mm every 1 mm. Considering the temporal resolution of our CTP protocol was 1.7 s, the second phase was reconstructed after a delay of 5 phases after the peak arterial phase. The third phase was reconstructed after another delay of 5 phases after the second phase. Thus, each phase of simulated mCTA was 8.5 s apart, which approximated the original mCTA. The first phase of simulated mCTA data was also used for the following simulated sCTA analysis.

CTA collateral grading

Pial arterial filling on simulated sCTA was scored from 0 to 5 (0, absent; 1, minimal; 2, significantly decreased prominence and extent of pial arteries with regions of no vessels; 3, moderately decreased prominence and extent; 4, mildly decreased prominence and extent; 5, normal or increased prominence and extent) when compared with the opposite normal hemisphere [10]. Collateral score on simulated mCTA was also assigned by using a six-point ordinal scale, scored 0 to 5 based on the distribution of peripheral vessels as well as the delay of phases in pial filling (0, no vessels visible in any phase; 1, a few vessels visible in any phase; 2, a delay of two phases in pial arterial filling and decreased prominence and extent or one-phase delay and some regions with no vessels; 3, a delay of two phases in pial arterial filling or one-phase delay and significantly reduced pial vessels; 4, a delay of one phase in pial arterial filling, but prominence and extent is the same; 5, no delay and normal or increased prominence of pial vessels/normal extent) when compared with the opposite normal hemisphere [14]. All CTA analysis was performed based on 0.625-mm axial source images and 24-mm maximum-intensity projections in the axial plane.

Two neuroradiologists (SS.L and XQ.X, both with 6-year experience), who were blinded to the clinical information and CTP results, independently assessed the collateral scores on sCTA, followed by mCTA 3 days later. For any discrepancy between the two readers, another neuroradiologist (HB.S with 25-year of experience) re-evaluated the images and helped to reach a consensus agreement. Moderate to good collateral status was defined as collateral scores ≥ 3.

Statistical analysis

The inter-reader reproducibility for collateral assessment on sCTA and mCTA was evaluated using Cohen's kappa statistics. Reliabilities < 0.4 was characterized as poor, those 0.4–0.75 were fair to good, and those > 0.75 were considered excellent. A McNemar test was performed to determine whether the collateral status assessed by sCTA and mCTA was significantly different. The differences of ischemic core volume and mismatch ratio based on collateral status were assessed using the Kruskal-Wallis test. The ability of mCTA and sCTA to predict the target mismatch profile on CTP was assessed using receiver operating characteristic (ROC) curves. The area under the ROC curve (AUC), sensitivity, specificity, and positive and negative predictive values for different collateral score thresholds were calculated and reported. The

ability of mCTA, sCTA, and CTP to predict 90-day mRS score of 0–2 was compared by using ROC analyses. All statistical analyses were performed using MedCalc (version 12.3.0) or SPSS (version 16.0). The p value was two-sided, and $p < 0.05$ was used as the level of significance.

Results

Patient characteristics

Seventy-three patients (male, 57; median age 68.0 years) who met all the inclusion criteria were finally enrolled. These patients had occlusions in the intracranial internal carotid artery (ICA, $n = 9$), M1 segment ($n = 45$), M2 segment ($n = 11$), or ICA combined with M1 ($n = 8$). Baseline NIHSS scores ranged from 7 to 26 (median, 14; interquartile range [IQR], 11–17.5). The stroke onset time ranged from 300 to 900 min (median, 402.5; IQR, 330–489.5). In 25 of 73 (34.2%) patients, the exact stroke onset time was unknown. Intravenous tPA was administered in 9 patients. Endovascular therapy was performed in 41 patients. Good clinical outcome (90-day mRS score of 0–2) was achieved in 33 of 69 (47.8%) patients. The detailed baseline characteristics of all patients are shown in Table 1.

Assessments of collaterals by sCTA and mCTA

The assessment of collateral scores showed good inter-rater agreement on both sCTA and mCTA ($\kappa = 0.718$ and 0.739, respectively). Moderate to good collateral status was identified in 37 patients (50.7%) on sCTA, whereas it was determined in 58 patients (79.5%) on mCTA ($p < 0.001$).

Table 1 Patient characteristics

Variables	Median [IQR] or number (%)
Male	57 (78.1%)
Age, years	68.0 [59.5, 77.0]
Admission NIHSS	14.0 [11.0, 17.5]
Time of onset (min)	402.5 [330, 489.5]
Stroke with unknown onset time	25 (34.2%)
Vessel occlusion, *n* (%)	
Intracranial ICA	9 (12.3%)
MCA-M1	45 (61.6%)
MCA-M2	11 (15.1%)
Intracranial ICA + M1	8 (11.0%)
IV tPA, *n* (%)	9 (12.3%)
Endovascular therapy, *n* (%)	41 (56.2%)

IQR, interquartile range; *NIHSS*, Nation Institutes of Health Stroke Scale; *MCA*, middle cerebral artery; *ICA*, internal carotid artery

CTA collaterals to predict target mismatch and clinical outcome

The distribution of ischemic core volume and mismatch ratio based on different collateral scores assessed on simulated sCTA and mCTA are shown in Table 2. Patients with good collaterals had smaller ischemic cores and larger mismatch ratios compared with those with poor collaterals ($p < 0.05$ overall).

Table 3 presents the diagnostic performance of CTA collateral score in the prediction of target mismatch. The AUC of mCTA when identifying patients with target mismatch was 0.902 (95% CI, 0.809, 0.959), significantly higher than that of sCTA (AUC, 0.815; 95% CI, 0.707 to 0.896) ($p < 0.01$) (Fig. 1). A sCTA collateral score of > 2 had 68.6% sensitivity (95% CI, 54.1, 80.9) and 90.9% specificity (95% CI, 70.8, 98.9). The sensitivity was significantly improved to 78.4% (95% CI, 64.7, 88.7) by a mCTA collateral score of > 3, while the specificity remained the same. A representative case of collateral status assessed by CTA to determine target mismatch is shown in Fig. 2.

The diagnostic performance of CTA collateral score in predicting 90-day mRS score of 0–2 is demonstrated in Fig. 3. The AUC of mCTA collateral score > 3 was 0.771 (95% CI, 0.655 to 0.864; sensitivity, 84.8%; specificity, 69.4%), which was comparable to CTP with target mismatch (AUC = 0.720; 95% CI, 0.599 to 0.821; sensitivity, 93.9%; specificity, 50.0%) ($p = 0.274$), but significantly higher than that of sCTA collateral score > 2 (AUC = 0.667; 95% CI, 0.543 to 0.776; sensitivity 66.7%; specificity, 66.7%) ($p = 0.012$).

Discussion

In the current study, we found that better collaterals were associated with smaller ischemic core volume and larger mismatch ratio on CTP in AIS patients with stroke onset time of 5–15 h or with unclear onset time. The collateral scores assessed by sCTA underestimated pial arterial filling when compared with mCTA. mCTA better identified patients with target mismatch on CTP and predicted 90-day mRS score of 0–2 compared with that of sCTA.

Currently, there is no reference standard for imaging selection in patients with AIS. In many stroke centers, perfusion imaging is used for patient selection. Perfusion imaging was performed in the EXTEND-IA trial and in 81% of patients in the SWIFT PRIME trial [2, 20]. Most recently, the DEFUSE 3 trial showed the benefit of mechanical thrombectomy for AIS patients with large anterior circulation occlusions outside of the 6-h therapeutic window (up to 16 h post-onset) when perfusion imaging revealed a large penumbra and a small ischemic core. However, it is important to note that although perfusion imaging can provide an objective quantitative

Table 2 Associations between CTA collateral score and CT perfusion parameters

CTA collateral score	Number of patients, *n* (%)	Core volume (ml)	Mismatch ratio
Multiphase CTA score		$p < 0.001$	$p < 0.001$
0	0 (0.0)		
1	5 (6.8)	195.3 ± 44.2	0.88 ± 0.48
2	10 (13.7)	110.4 ± 60.4	3.00 ± 1.34
3	16 (21.9)	76.7 ± 46.9	5.82 ± 4.15
4	29 (39.7)	39.6 ± 16.1	7.75 ± 3.27
5	13 (17.8)	41.8 ± 18.0	7.31 ± 4.60
Single-phase CTA		$p < 0.001$	$p = 0.002$
0	4 (5.5)	172.8 ± 78.5	2.67 ± 3.02
1	25 (34.2)	99.0 ± 59.0	4.04 ± 3.12
2	7 (9.6)	60.7 ± 30.5	6.49 ± 3.72
3	15 (20.5)	38.7 ± 10.1	7.28 ± 3.31
4	7 (9.6)	38.4 ± 11.4	8.06 ± 3.53
5	15 (20.5)	37.3 ± 20.7	8.31 ± 4.74

Data are reported as mean ± standard deviation. All *p* values represent the statistical differences of ischemic core volume and mismatch ratio based on variable collateral status. *CTA*, computed tomography angiography

assessment of ischemic core and penumbra, challenges related to lack of a standardized algorithm for post-processing and potential variation in interpretation remain to be solved. In addition, the image quality may be affected to some extent by patient motion [6–8].

Leptomeningeal collaterals provide blood flow to the vascular territory of the occluded artery during AIS. Previous studies have shown that good baseline collaterals are an independent predictor of a small ischemic lesion, higher mismatch, and a good clinical outcome [3, 10, 11, 13, 21]. Data from IMS III have shown that baseline CTA collaterals are a determinant of final clinical outcome and could be used to select patients for endovascular therapy [10]. Dehkharghani et al found that a CTA collateral score of 3 or higher predicted an infarct size of ≤ 50 ml. However, the sensitivity was very low in their study [12]. A key explanation is the fact that collateral scores were assessed based on sCTA, which lacks temporal resolution unlike mCTA, and therefore may misclassify patients with moderate to good collaterals as poor. Menon et al suggested that mCTA was a reliable tool for imaging selection and for the determination of primary clinical outcome in patients with AIS [14]. Kim et al suggested that mCTA was more accurate than sCTA for assessment of collaterals. mCTA combined with non-contrast CT is comparable to CTP for assessment of ischemic core and penumbra [22]. However, the methods used in their study were different from ours as follows: (1) the enrolled AIS patients were within 6-h stroke onset and (2) the CTP criteria (an ischemic core < 70 ml and a mismatch ratio > 1.2, or an ischemic core ≤ 40 ml and a mismatch ratio > 1.8) were different from ours. We selected an ischemic core threshold of 70 ml and a mismatch ratio of 1.8 as criteria of target mismatch, as reported by the recently

Table 3 Diagnostic performance of CTA collateral score in prediction of target mismatch

Threshold	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Multiphase CTA collateral score				
> 1	100.0 (93.0, 100.0)	22.7 (7.8, 45.4)	75.0 (63.0, 84.7)	100.0 (47.8, 100.0)
> 2	98.0 (89.6, 100.0)	63.6 (40.7, 82.8)	86.2 (74.6, 93.9)	93.3 (68.1, 99.8)
> 3	78.4 (64.7, 88.7)	90.9 (70.8, 98.9)	95.2 (83.8, 99.4)	64.5 (45.4, 80.8)
> 4	23.5 (12.8, 37.5)	95.5 (77.2, 99.9)	92.3 (62.4, 99.9)	35.0 (23.1, 48.4)
Single-phase CTA collateral score				
> 0	98.0 (89.6, 100.0)	13.6 (2.9, 34.9)	72.5 (60.4, 82.5)	75.0 (19.4, 99.4)
> 1	78.4 (64.7, 88.7)	81.8 (59.7, 94.8)	90.9 (78.1, 97.5)	62.1 (42.3, 79.3)
> 2	68.6 (54.1, 80.9)	90.9 (70.8, 98.9)	94.6 (81.8, 99.3)	55.6 (38.1, 72.1)
> 3	39.2 (25.8, 53.9)	90.9 (70.8, 98.9)	90.9 (70.8, 98.9)	39.2 (25.8, 53.9)
> 4	25.5 (14.3, 39.6)	90.9 (70.8, 98.9)	86.7 (59.5, 98.3)	34.5 (22.5, 48.1)

Data in parentheses are the 95% confidence interval; *PPV*, positive predictive value; *NPV*, negative predictive value

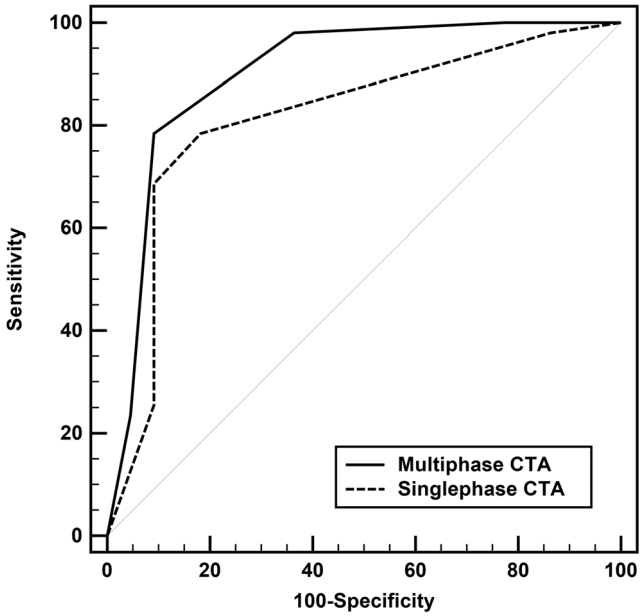

Fig. 1 The diagnostic performance of CT angiography (CTA) collateral scores in the prediction of target mismatch profiles on CT perfusion. The area under the curve of multiphase CTA (mCTA) is 0.902, significantly higher than that of single-phase CTA (0.815) ($p < 0.01$). A mCTA collateral score of > 3 best identifies patients with target mismatch, with a sensitivity of 78.4% and a specificity of 90.9%

published DEFUSE 3 trial [19]. DEFUSE 3 is currently one of the only two RCTs showing a benefit of mechanical thrombectomy between 6 and 16 h from stroke onset [23]. Therefore, considering the stroke onset time in our study, the DEFUSE 3 eligibility should be adhered to in clinical practice. Our findings are consistent with prior reports showing that collaterals can be better estimated by mCTA compared with sCTA; good collaterals on mCTA predict a small ischemic core and a large mismatch, suggesting that collateral assessment and perfusion imaging are measuring the same biological construct of the ischemic pathophysiology. Our study adds to the growing body of evidence that collateral status is tightly related to perfusion in AIS. We also found that the ability of mCTA to predict 90-day mRS score of 0–2 was comparable to CTP, but better than sCTA. This finding is clinically relevant as collateral assessment by mCTA may be an alternative tool for CTP in AIS patients extending the 6-h time window for endovascular therapy.

There are several limitations to our study. First, this is a single-center retrospective study. The sample size was relatively small and may limit the reliability of results. Larger studies are needed to conclusively demonstrate the utility of mCTA in clinical decision-making. Second, the timing for the three phases in our simulated mCTA was not exactly the same as for the original mCTA. However, we considered that the mismatched timing may not significantly affect our results. Moreover, the arterial peak phase could be determined accurately according to the AIF curve. It has previously been shown that angiographic reconstructions from the peak arterial scan of the VPCT data may offer image quality comparable to traditional CTA [15, 24]. Third, collateral assessment using categorical scales can be prone to inter-observer variability.

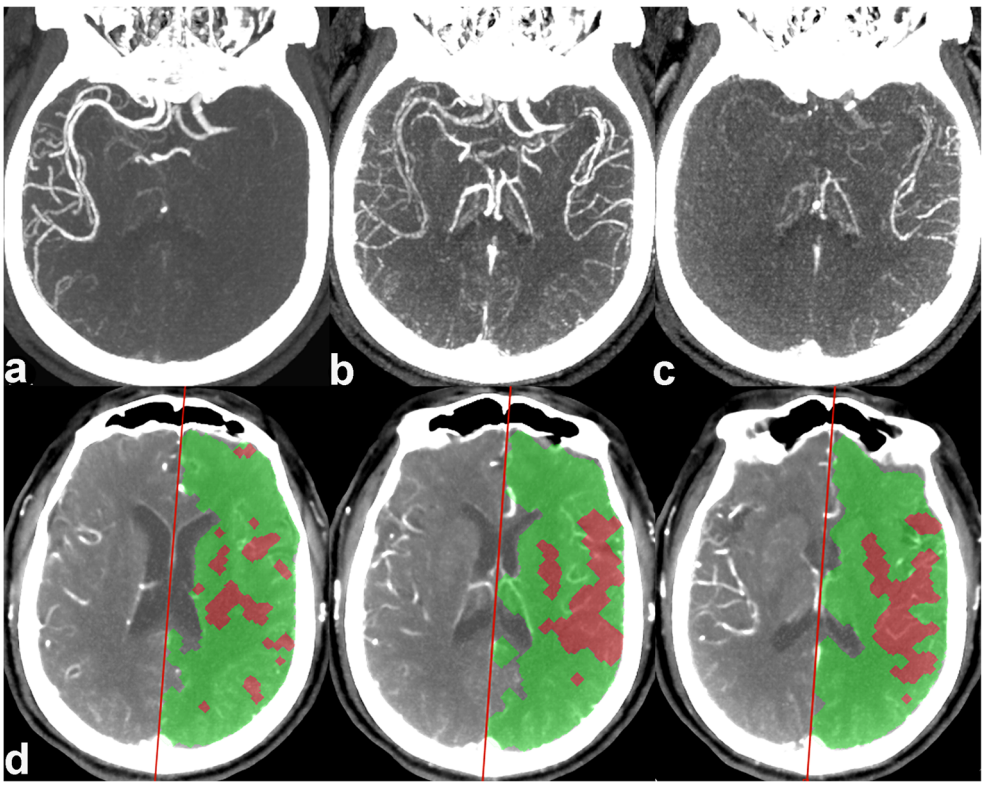

Fig. 2 A 65-year-old man presented with left middle cerebral artery syndrome (National Institutes of Health Stroke Scale, 16) underwent CT perfusion (CTP) after 375 min stroke onset. Simulated single-phase CT angiography (**a**) indicates poor collateral circulation on the left (collateral grade, 1) while simulated multiphase CT angiography (**a**–**c**) indicates good collaterals (collateral grade, 4). CTP (**d**) shows an ischemic core of 61.6 ml and a mismatch ratio of 7.19, indicating that the patient may be eligible for endovascular therapy

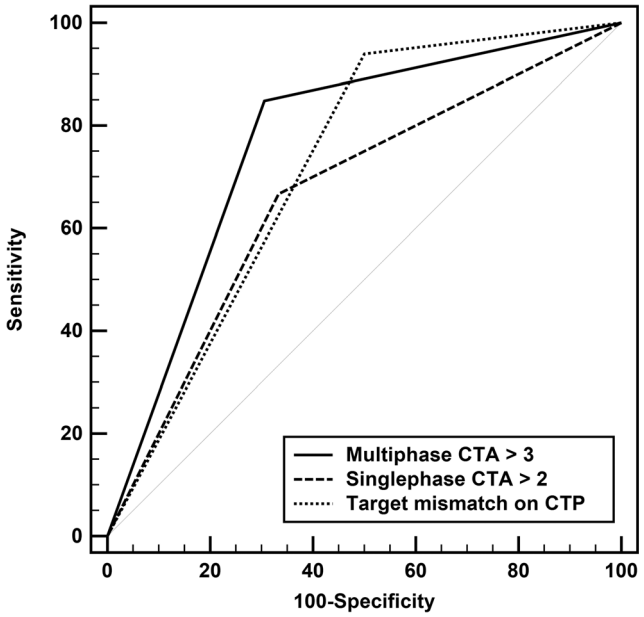

Fig. 3 Comparison of CT angiography (CTA) collateral scores and CT perfusion (CTP) for prediction of 90-day mRS score of 0–2. The area under the curve of a multiphase CTA (mCTA) collateral score > 3 is 0.771, comparable to that of target mismatch on CTP (0.720) ($p = 0.274$), but significantly higher than that of a single-phase CTA (sCTA) collateral score > 2 (0.667) ($p = 0.012$)

Despite the good inter-rater agreement in our study, it is important to improve this classification in the future. Quantitative measurement for collaterals may help to strengthen its role in patient selection for endovascular therapy.

In conclusion, better collaterals were associated with smaller ischemic core volumes and larger mismatch ratios on CTP. Collateral status was better estimated by mCTA compared with sCTA. A mCTA collateral score of > 3 best identified AIS patients with target mismatch on CTP and predicted their clinical outcomes. A specific population of AIS patients with M1/M2 and/or internal carotid artery occlusions may benefit from mCTA to determine their eligibility for endovascular therapy.

Acknowledgements We sincerely thank Mrs. Min-lin Zhou from the National Clinical Research Center of Kidney Diseases, Jinling Hospital, for her reviewing of all the statistics. We also thank Dr. Kai Qiu and Dr. Wei Wang for their kind help in collecting the clinical information.

Funding The authors state that this work has not received any funding.

Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Dr. Hai-bin Shi.

Email address: shihb@njmu.edu.cn.

Conflict of interest The authors of this manuscript declare no relationships with any companies whose products or services may be related to the subject matter of the article.

Statistics and biometry Mrs. Min-lin Zhou from national clinical research center of kidney diseases, Jinling Hospital, kindly provided statistical advice for this manuscript.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- Retrospective
- Case-control study
- Performed at one institution

References

1. Berkhemer OA, Fransen PS, Beumer D et al (2015) A randomized trial of intraarterial treatment for acute ischemic stroke. N Engl J Med 372:11–20
2. Campbell BC, Mitchell PJ, Kleinig TJ et al (2015) Endovascular therapy for ischemic stroke with perfusion-imaging selection. N Engl J Med 372:1009–1018
3. Goyal M, Demchuk AM, Menon BK et al (2015) Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med 372:1019–1030
4. Jovin TG, Chamorro A, Cobo E et al (2015) Thrombectomy within 8 hours after symptom onset in ischemic stroke. N Engl J Med 372: 2296–2306
5. Saver JL, Goyal M, Bonafe A et al (2015) Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. N Engl J Med 372:2285–2295
6. Goyal M, Menon BK, Derdeyn CP (2013) Perfusion imaging in acute ischemic stroke: let us improve the science before changing clinical practice. Radiology 266:16–21
7. Kudo K, Sasaki M, Yamada K et al (2010) Differences in CT perfusion maps generated by different commercial software: quantitative analysis by using identical source data of acute stroke patients. Radiology 254:200–209
8. Bivard A, Levi C, Spratt N, Parsons M (2013) Perfusion CT in acute stroke: a comprehensive analysis of infarct and penumbra. Radiology 267:543–550
9. Liebeskind DS (2003) Collateral circulation. Stroke 34:2279–2284
10. Menon BK, Qazi E, Nambiar V et al (2015) Differential effect of baseline computed tomographic angiography collaterals on clinical outcome in patients enrolled in the Interventional Management of Stroke III trial. Stroke 46:1239–1244
11. Berkhemer OA, Jansen IG, Beumer D et al (2016) Collateral status on baseline computed tomographic angiography and intra-arterial treatment effect in patients with proximal anterior circulation stroke. Stroke 47:768–776
12. Dehkharghani S, Bammer R, Straka M et al (2016) Performance of CT ASPECTS and collateral score in risk stratification: can target perfusion profiles be predicted without perfusion imaging? AJNR Am J Neuroradiol 37:1399–1404
13. Vagal A, Menon BK, Foster LD et al (2016) Association between CT angiogram collaterals and CT perfusion in the Interventional Management of Stroke III trial. Stroke 47:535–538
14. Menon BK, d'Esterre CD, Qazi EM et al (2015) Multiphase CT angiography: a new tool for the imaging triage of patients with acute ischemic stroke. Radiology 275:510–520

15. Frolich AM, Psychogios MN, Klotz E, Schramm R, Knauth M, Schramm P (2012) Angiographic reconstructions from whole-brain perfusion CT for the detection of large vessel occlusion in acute stroke. Stroke 43:97–102
16. Campbell BC, Christensen S, Levi CR et al (2011) Cerebral blood flow is the optimal CT perfusion parameter for assessing infarct core. Stroke 42:3435–3440
17. Calamante F, Christensen S, Desmond PM, Ostergaard L, Davis SM, Connelly A (2010) The physiological significance of the time-to-maximum (Tmax) parameter in perfusion MRI. Stroke 41: 1169–1174
18. Olivot JM, Mlynash M, Thijs VN et al (2009) Optimal Tmax threshold for predicting penumbral tissue in acute stroke. Stroke 40:469–475
19. Albers GW, Marks MP, Kemp S et al (2018) Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. N Engl J Med 378:708–718
20. Saver JL, Jahan R, Levy EI et al (2012) Solitaire flow restoration device versus the merci retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. Lancet 380:1241–1249
21. Boers AM, Jansen IG, Berkhemer OA et al (2017) Collateral status and tissue outcome after intra-arterial therapy for patients with acute ischemic stroke. J Cereb Blood Flow Metab 37:3589–3598
22. Kim EY, Shin DH, Noh Y, Goh BH, Lee YB (2016) Comparison of imaging selection criteria for intra-arterial thrombectomy in acute ischemic stroke with advanced CT. Eur Radiol 26:2974–2981
23. Powers WJ, Rabinstein AA, Ackerson T et al (2018) 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 49:e46–e110
24. Yang CY, Chen YF, Lee CW et al (2008) Multiphase CT angiography versus single-phase CT angiography: comparison of image quality and radiation dose. AJNR Am J Neuroradiol 29:1288–1295