Lenticulostriate arteries appearance before thrombectomy predicts good outcome in acute middle cerebral artery occlusion

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Abstract

Purpose Endovascular therapy is widely used in acute large vessel occlusion. This study investigated whether imaging of lateral lenticulostriate arteries (LSAs) before thrombectomy would potentially be helpful for predicting prognosis of patients with acute M1 segment of middle cerebral artery occlusion (MCAO).

Methods 59 consecutive patients with acute M1 segment of MCAO treated with mechanical thrombectomy at two comprehensive stroke center were analyzed. Patients were categorized into LSA+ (appearing of lateral LSAs) and LSA- (sparing of lateral LSAs) group according to preprocedural digital subtraction angiography (DSA). Baseline data and clinical outcomes were compared. A good clinical outcome was defined as a modified Rankin Scale score of 0 to 2 at 3 months. The association between clinical and imaging parameters and functional outcome was evaluated with logistic regression analysis.

Results LSA+ was shown in 36 patients (61%). LSA+ group had a significantly higher proportion of good outcome (72.2% vs. 8.7%, OR 27.3, 95% CI 5.38-138.4, $P < 0.001$), lower risk of symptomatic intracranial haemorrhages (sICH) (8.3% vs. 47.8%, OR 0.10, 95% CI 0.02-0.42, $P = 0.001$) and lower mortality in hospital (5.6% vs. 34.8%, OR 0.11, 95% CI 0.02-0.58, $P < 0.004$) compared with LSA- group. Patients in LSA+ group had lower baseline NIHSS score ($P < 0.01$) and NIHSS score at 14 days ($P < 0.01$) and smaller infarct core volume ($P = 0.016$) on computed tomography perfusion imaging (CTP) compared to the LSA- group. Multivariate logistic regression analysis showed that a small infarct core volume (OR 6.74, 95% CI 1.148-39.569, $P = 0.035$) and LSA+ (OR 22.114, 95% CI 3.339-146.470, $P = 0.001$) were associated with a good clinical outcome.

Conclusions Our data suggest that appearance of lateral LSAs before mechanical thrombectomy would be potentially helpful for predicting favorable prognosis of patients with acute M1 segment of MCAO.

Background

Randomized trials have demonstrated that second-generation endovascular thrombectomy had an obvious clinical benefit over medical therapy alone among patients with emergent large artery occlusion (LAO)¹⁻⁵. However, poor clinical outcomes, despite successful revascularization, are still common⁶. Thus, patient selection and prognosis prediction are still key issues for thrombectomy. In addition to the time to treatment, infarct core volume, penumbra and collateral circulation, more concise imaging parameters are worth exploring⁷⁻⁹. It is known that collateral circulation and time to treatment both affect the transformation from penumbra to infarct core^{7,8}. However, the area supplied by lateral lenticulostriate arteries (LSAs) lacking of collateral vessels may play a unique role in acute middle cerebral artery occlusion (MCAO) independent of time and collateral flow. Thus, the objective of this study was to investigate whether the lateral LSAs observed before thrombectomy could predict good clinical outcomes.

Methods

Patients

From August 2016 to August 2018, we retrospectively collected all the patients presented with acute stroke due to acute M1 segment of middle cerebral artery occlusion were treated with stent-retriever thrombectomy as the first-line endovascular therapy at two comprehensive regional stroke centers, Shanghai East Hospital and Huashan Hospital. 3-month follow-up were acquired blinded through telephone. All patients underwent an initial imaging protocol including nonenhanced computed tomographic (CT) scan, CT perfusion (CTP) and computed tomography angiography (CTA) before commencing endovascular thrombectomy procedures. CTP/CTA imaging was acquired on the 320-slice CT scanner (Aquilion One, Toshiba Medical Systems) and a 64-slice detector scanner (Discovery CT750 HD; GE Medical Systems, Waukesha, Wisconsin). The inclusion criteria were as follows: (1) acute ischemic stroke, (2) M1 segment of MCAO detected with digital subtraction angiography (DSA), (3) the time from onset to reperfusion therapy was determined by local guidelines at the time^{10,11}. Patients with poor imaging quality were excluded. This study was approved by the Ethics Committee of the Shanghai East hospital and all subjects provided written informed consent.

Endovascular treatment and DSA assessment

Solitaire stent and manual aspiration thrombectomy were performed as the first-line endovascular treatment. When stent-retriever thrombectomy was not ideal, intra-arterial recombinant tissue plasminogen activator (rtPA) infusion or stenting was performed. Successful revascularization was defined as a modified thrombolysis in cerebral infarction (mTICI) grade of 2b or 3¹².

Two reviewers independently analyzed the pre-interventional DSA. Both readers who had at least three years of training in neuroradiology respectively run blinded to the interventional imaging and all clinical data. The readers determined the presence or absence of lateral LSAs on pre-interventional DSA (see Figure 1 for illustrative cases). The readers repeated his assessment 14 days later blinded to his first assessment in order to evaluate intrarater reliability. In cases of discrepancies, a consensus read was performed with both readers and the third more experienced reader who was not involved in the initial assessment.

Variables and Clinical assessment

Baseline data is included age, sex, cigarette smoking, medical history, disease onset, treatment and initial assessment by multi-model CT. the National Institute of Health Stroke Scale (NIHSS) score (scores range from 0–42, with higher scores indicating increasing severity) were evaluated before thrombectomy, and collateral status based on CTA were evaluated according to previously published criteria¹³. CT perfusion data were postprocessed by a commercial software (MISar; Apollo Medical Imaging Technology, Melbourne, Australia). The infarct core was defined as a cerebral blood flow (CBF) <30% and penumbra based on the difference between the core lesion and the delay time (DT) >3 s lesion, The mismatch ratio

was defined as the proportion of DT >3 s lesion volume (hypoperfusion) with a CBF < 30% lesion volume(core)¹⁴. symptomatic intracranial haemorrhage (sICH) transformation and were defined according to European Cooperative Acute Stroke Study (ECASS)-III criteria¹⁵. The recanalization time was defined as interval between symptom onset and first intracranial DSA series. The primary outcome was defined as good outcome (modified Rankin Scale(mRS) score of 0 to 2) at 90 days. And we also evaluated core infarct volume, NIHSS(a NIHSS score of 42 was assigned in cases of death) and mRS at 14 days, sICH, mortality in hospital and at 90 days, recanalization rates as secondary outcomes.

Statistical analysis

Statistical analysis for categorical variables included Chi-square test, Fisher exact test when cell sizes were small, and odds ratios for selected comparisons. The measurement data were described as mean±standard deviation if normally distributed or the median and analyzed using Student's t test or the Mann-Whitney test. Logistic regression analysis was performed to identify independent predictors for clinical outcome. Variables with a P value of <0.15 in the univariate analysis on clinical outcome were included in a multivariate logistic regression, performed with the forward selection and backward elimination method. A P value of <0.05 was considered significant. All analytic procedures were conducted in SPSS version 21.0.

Results

We initially identified a total of 60 patients meeting the inclusion criteria. One patient were excluded because of poor imaging quality. Among the leaving 59 patients, the mean age was 69.8±11.2years, 40 patients (67.8%) were female, and the median baseline NIHSS was 15. 25 patients (42.4%) received intravenous thrombolysis treatment before thrombectomy and the mean door-to needle time(DNT) was 51min. On pre-intervention DSA, 36 patients (61%) had the appearance of lateral LSAs (LSA+) and 26 patients (39%) were sparing of the LSAs(LSA-).All the 59 enrolled patients completed the follow-up.The study flow chart was summarized in Figure 2. There was initial disagreement on the group assignment of 2 patients, which represents 96.6% interrater agreement. Consensus was then reached on the final group assignments for these discordant designees.

Baseline data: Baseline demographics and details of the intervention were similar between groups except for NIHSS score before thrombectomy (Table 1). No significant differences were observed between the two groups in relation to age, sex, premorbid history of hypertension, diabetes mellitus, atrial fibrillation, dyslipidemia, ischemic stroke, antipalatelet drugs use, anticoagulation drugs use, cardioembolic source, history of smoking, intravenous thrombolysis, onset-treatment time and successful recanalization between the two groups. The NIHSS score of LSA+ group was significantly lower than that of LSA- group. ($P = 0.001$) (Table 1).

Clinical outcome: As the primary outcome, the proportion of patients with a modified Rankin score of 0 to 2 at 90 days was 72.2% in the LSA+ group and 8.7% in the LSA- group(OR 27.3,95% CI 5.38–138.4,

$P < 0.001$, Table 2). When compared to the LSA- group, the LSA+ group had a lower risk of symptomatic intracranial haemorrhages (sICH) (8.3% versus 47.8%, OR 0.10, 95% CI 0.02–0.42, $P = 0.001$) and mortality in hospital (5.6% versus 34.8%, OR 0.11, 95% CI 0.02–0.58, $P < 0.004$). Patients in LSA+ group had lower NIHSS (2 versus 15 $P < 0.01$) and mRS (2 versus 5 $P < 0.01$) at 14 days. There was a significantly smaller core infarct core volume (34ml versus 46ml, $P = 0.016$) on CTP compared to the LSA- group.

Prognosis: In a univariate analysis, the following variables were identified as predictors of a good outcome: young age (age ≤ 80 years), low NIHSS before thrombectomy (NIHSS ≤ 14), small core infarct volume on CTP (core volume ≤ 50 ml) and LSA+ (Tables 3). In a multivariate analysis, a small core infarct volume (OR 6.74, 95% CI 1.148–39.569, $P = 0.035$) and LSA+ (OR 22.114, 95% CI 3.339–146.470, $P = 0.001$) were significant independent predictors of good outcome at 3 months (Table 3).

Discussion

This study showed that except the core infarct volume, the appearance of lateral LSAs on pre-intervention DSA was an independent predictor of good functional outcome at 90 days after thrombectomy in patients with acute M1 segment of MCAO. Only few studies have evaluated the correlation between the appearance of LSAs and basal ganglia infarction after thrombectomy. Kleine et al¹⁶ reported that LSAs occlusion patterns predicted infarction in associated striatal subterritories with a positive predictive value of 96%. Similarly, Friedrich et al¹⁷ reported that the distance to thrombus in acute middle cerebral artery stroke independently predicts basal ganglia infarction after mechanical thrombectomy with high sensitivity and specificity. However, there is no report on the correlation between the appearance of LSAs and the prognosis of thrombectomy. Our study first reported their correlation and provided a simple and new thought for the decision making of thrombectomy.

It is supposed that patients with LSA+ before intervention would have a better clinical outcome for several reasons. (1) Although ischemic penumbra is reversible with early reperfusion, deep brain tissue like basal ganglia and internal capsule which are responsible for the transmission of key neural fiber pathway mainly depends on perforator arteries for blood supply, which have poor collateral circulation¹⁸. Once the LSAs are blocked, irreversible ischemic lesions is formed and even with quick and successful revascularization the functional deficits might not reversible¹⁹. (2) Hemorrhagic transformation is prone to occur after reperfusion treatment in deep brain tissue supplied by LSAs without collateral flow. In this study, the LSA+ group had a lower risk of sICH (8.3% versus 47.8%) compared to the LSA- group.

The study of independent factors determining the effect of thrombectomy is a hot topic of concern. The existing evidence showed that time to treatment, infarct core volume and collateral circulation may be used as reference factors. In particular, the DAWN trial²⁰ and DEFUSE-3 trial²¹ suggests that the value of perfusion imaging is more prominent. However, multimodal imaging is not widely used. Thus, we are still in lack of concise imaging signs which are intuitive and easy to popularize. Using DSA to evaluate LSAs has several advantages in clinical application and promotion. First, this imaging marker is routine examined before thrombectomy. In addition, compared with preoperative multi-model imaging (CT or

Magnetic resonance),LSAs has advantages of shorter time and easier operation, and provides potentially new decision-making factors for emergency thrombectomy in hospitals without preoperative evaluation of core infarction and ischemic penumbra. This study also confirmed the core infarct volume is an independent prognostic predictors for thrombectomy,which is similar to other studies²²⁻²⁴.

Our study had several limitations, including the retrospective design and limited sample size. In addition, the assessment of LSAs by DSA has limited spatial resolution. Two patients differed in their assessment mainly because of small LSAs not obvious and partial anatomical variations exists in LSAs. Therefore, it is necessary to expand sample size and develop prospective research to further verify results of the study.

Conclusions

This study suggested that the appearance of LSAs on pre-interventional DSA is a strong predictor of good clinical outcome after stent-retriever thrombectomy in patients with acute M1 segment of MCAO. Our study provided a new thought for the patient selection for thrombectomy especially in those stroke centers without multimodal imaging.

Abbreviations

CBF:cerebral blood flow

CI:Confidence interval

CT:computed tomographic

CTA:computed tomography angiography

CTP:computed tomography perfusion imaging

DNT:door-to needle time

DSA:digital subtraction angiography

DT:delay time

LAO:large artery occlusion

LMCA: left middle cerebral artery

LSAs:lateral lenticulostriate arteries

LSA+:appearing of lateral LSAs

LSA-:sparing of lateral LSAs

MCAO:middle cerebral artery occlusion

mRS:modified Rankin Scale

mTICI:modified thrombolysis in cerebral infarction

NIHSS:National Institute of Health Stroke Scale

OR:Odds Ratio

rtPA:recombinant tissue plasminogen activator

slCH:symptomatic intracranial haemorrhages

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Shanghai East hospital and all subjects provided written informed consent.

Consent for publication

Not applicable.

Availability of data and materials

Study related data and materials are accessible on request from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

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Authors' contributions

LFF and CC conceived and designed the study,wrote the first draft of the manuscript and analyzed the data.HL,YXY,GMR and LY carried out data collection.SH,XYP and CWJ were responsible for the DSA assessment. DQ and CX revised the paper.LG designed the study and finalized the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1. Demographics and Aspects of the Intervention Between Patients LSA+ and LSA- Patterns

Characteristic	LSA+(n=36)	LSA-(n=23)	All patients(n=59)	<i>p</i> value
age $\pm$ yr $\pm$ (SD)	69.3 $\pm$ 11.2	70.6 $\pm$ 11.4	69.8 $\pm$ 11.2	0.342
Gender,female(%)	24(66.7)	16(69.6)	40(67.8)	0.816
Premorbid history of: n (%)				
Hypertension	17(47.2)	13(56.5)	30(50.8)	0.486
Diabetes Mellitus	5(13.9)	21.7	10(16.9)	0.433
Dyslipidemia	4(11.1)	3(13.0)	7(11.9)	0.823
Ischemic Stroke	11(30.6)	5(21.7)	16(27.1)	0.458
Cardioembolic Source,n(%)	18(50.0)	12(52.2)	30(50.8)	0.871
Smoking,n(%)	10(27.8)	7(30.4)	17(28.8)	0.826
Antipalatelet,n(%)	10(27.8)	6(26.1)	16(27.1)	0.877
Anticoagulation,n(%)	5(13.9)	4(17.4)	9(15.3)	0.715
Intravenous rtPA,n (%)	13(36.1)	12(52.2)	25(42.4)	0.223
DNT,min	54 $\pm$ 25 $\square$ n=13 $\square$	49 $\pm$ 18 $\square$ n=12 $\square$	51 $\pm$ 21(n=25)	0.217
NIHSS before thrombectomy	14 $\square$ 10-17 $\square$	16 $\square$ 15,20 $\square$	15 $\square$ 14-18 $\square$	0.004**
Onset to CTP time ,min	186(112-295)	134(101-189)	160(108-257)	0.103
Onset to puncture time, min	320(227-448)	255(180-305)	264(214-402)	0.069
Onset to clot first reperfusion time,min	357(280-484)	305(189-347)	316(280-445)	.0148
LMCA occlusion,,n(%)	21(58.3)	18(78.3)	39(66.1)	0.115
local anesthesia,n(%)	28(77.8)	18(78.3)	46(78.0)	0.965
Successful recanalization (mTICI 2b/3), n (%)	33(91.7)	18(78.3)	51(86.4)	0.142
)				
Ischemic core volume,ml	34 $\pm$ 23	46 $\pm$ 41	48 $\pm$ 31	0.016*
Mismatch ratio	3.2(2.6-4.5)	3.5(2.7-4.4)	3.3(2.6-4.4)	0.625

Note: rtPA: recombinant tissue plasminogen activator; LMCA: left middle cerebral artery; mismatch ratio: hypoperfusion/infarct core;DNT:door-to needle time;mTICI:modified thrombolysis in cerebral infarction;CTP:computed tomography perfusion imaging.* $p<0.05$;** $p<0.01$.

Table2 Clinical Outcomes of patients Between Patients LSA+ and LSA- Patterns

Characteristic	LSA+(n=36)	LSA-(n=23)	<i>p</i> value	OR[95%CI]
sICH,n(%)	3[8.3]	11[47.8]	0.001	0.10[0.02-0.42]
Death in hospital,n(%)	2[5.6]	8[34.8]	0.004	0.11[0.02-0.58]
NIHSS socre at 14days	2[1,6]	15[12,42]	<0.001	
mRS(0-2) at 14 days,n(%)	23(63.9)	2(8.7)	<0.001	18.6(3.7-92.2)
mRS at 14 days	2[1-3]	5[4-6]	<0.001	
mRS(0-2) at 90 days,n(%)	26[72.2]	2[8.7]	<0.001	27.3[5.38-138.4]
mRS at 90 days	1[0.25-3.75]	5[4-6]	<0.001	

Note: sICH symptomatic intracranial haemorrhages;OR, odds ratio; CI, confidence interval; NIHSS National Institute of Health Stroke Scale; mRS :modified Rankin Scale

Table 3. Univariate and multivariate analysis of Determinants of a good outcome.

Covariate	Unadjusted	95%CI	<i>p</i>	Adjusted	95%CI	<i>p</i>
	OR		value	OR		value
Mismatch ratio $\geq$ 1.8	2.000	0.45-8.90	0.290			
Good collateral circulation	2.017	0.63-6.46	0.234			
Onset to clot first reperfusion time $\leq$ 6h	0.635	0.22-1.84	0.401			
Successful recanalization (mTICI $\geq$ 2b)	1.603	0.35-7.42	0.413			
Age $\leq$ 80 years	3.409	0.82-14.20	0.081	3.275	0.49-21.84	0.220
NIHSS $\leq$ 14 before thrombectomy	5.556	1.74-17.79	0.003	2.377	0.49-11.55	0.283
sICH	0.122	0.02-0.61	0.006	0.550	0.07-4.33	0.570
Core infarct volume $\leq$ 50ml	6.863	1.71-27.58	0.004	6.740	1.15-39.57	0.035
LSA+	27.300	5.38-138.42	<0.001	21.589	3.32-140.47	0.001

Note: OR, odds ratio; CI, confidence interval; NIHSS National Institute of Health Stroke Scale; sICH symptomatic intracranial haemorrhages

Figures

Figure 1

A. LSA-: No perforator artery from LMCA supplying basal ganglia on Towne's position in DSA. B. LSA+: A group of lateral lenticulostriate arteries (white arrow) originating from LMCA supplying basal ganglia on Towne's position in DSA.

Figure 2

The study flow chart