Angiographical Jaggy Sign of Remnant M2 Occlusion during Acute Mechanical Thrombectomy

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Background and purpose: During mechanical thrombectomy for acute main trunk occlusion, we sometimes encounter difficult situation; 1 M2 branch of the middle cerebral artery is successfully recanalized, while the other remains occluded. In this study, we focused on the angiographical findings of remnant occlusion. *Methods:* Among 83 patients who underwent mechanical thrombectomy for the acute internal carotid artery or proximal middle cerebral artery (M1) occlusion, 25 patients (30%) intraoperatively exhibited the remnant M2 occlusion, in spite of the recanalization of the other M2. We classified the angiographical findings of the remnant M2 occlusion and examined the clinical features, prognosis, and complications, in relation to additional thrombectomy. *Results:* The remnant M2 occlusion was classified into stump type (40%, 10 cases), round deficit type (28%, 7 cases), and jaggy type (32%, 8 cases). Multivariate analysis suggested that noncardioembolic stroke may lead to jaggy type remnant occlusion with marginal significance ($P = .051$). Additional thrombectomy for the remnant M2 occlusion resulted in failed recanalization in 6% in the nonjaggy (stump or round deficit) type, whereas in 50% in the jaggy type groups ($P = .023$). Symptomatic intracranial hemorrhage occurred in 6% in the nonjaggy and 38% in the jaggy groups ($P = .081$), and poor outcome at discharge in 29% and in 50%, respectively. *Conclusions:* Angiographical jaggy sign in the remnant M2 occlusion suggests the pre-existing or procedure-related pathology, such as atherosclerosis, vasospasm, or arterial dissection. Additional thrombectomy should be carefully determined, as which might lead to adverse events and poor outcomes.

Key Words: Acute ischemic stroke—mechanical thrombectomy—M2 occlusion—symptomatic hemorrhage

Introduction

The effectiveness of mechanical thrombectomy with or without an intravenous tissue plasminogen activator (IV-tPA) for acute occlusion of the internal carotid artery (ICA) and proximal middle cerebral artery (M1) has been shown in several randomized, controlled trials and meta-analyses,[1-6] so mechanical thrombectomy for main trunk occlusion in anterior circulation is currently regarded as standard treatment. In addition, although such procedure for more distal M2 occlusion has not been well established so far, new-generation devices might be associated with a high recanalization rate and a favorable outcome.[7,8]

In recent years, acute mechanical thrombectomy has been increasingly performed worldwide in accordance with the introduction of modern technologies. During mechanical thrombectomy, however, we often encounter a difficult situation; one M2 branch of the middle cerebral artery (MCA) is successfully recanalized, while the other remains occluded. In particular, remnant M2 superior trunk occlusion that includes the central artery would lead to severe

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hemiparesis and subsequent disability. However, since the M2 branch of small-diameter has a relatively thin arterial wall, it is difficult to determine whether additional thrombectomy, which might possibly cause hemorrhagic complication, is beneficial or not. In this study, we classified the type of the remnant branch based on intraoperative angiographical findings in such situation and examined the clinical features, prognosis, and complications, in relation to additional mechanical thrombectomy.

Methods

Patients

This retrospective study was approved by Gunma University Review Board for Medical Research Involving Human Subjects. One hundred and ten patients, who underwent acute mechanical thrombectomy from April 2014 to April 2017, were initially enrolled. Twenty-seven patients with M2 or more distal obstruction on initial diagnosis, posterior circulation obstruction, and concomitant cervical carotid lesion were excluded, and the operative charts of the remaining 83 patients with acute ICA or M1 occlusion were reviewed. Among them, 25 patients (30%) intraoperatively exhibited remnant M2 occlusion or severe stenosis, although the other M2 was well-recanalized. In this study, we retrospectively analyzed clinical data of these patients in detail.

Procedures

All patients underwent endovascular surgery under local anesthesia. A 9-French (Fr), long sheath was inserted into the femoral artery. A 9-Fr balloon guiding catheter with a 4-Fr and 6-Fr catheter was placed coaxially in the affected ICA. In the case of ICA occlusion, the occlusion balloon was inflated at the origin of the ICA, and manual suction was initially performed. Mechanical thrombectomy was attempted, unless the occlusion was recanalized. Aspiration-type catheter Penumbra (Medicos Hirata, Osaka, Japan) and stent-type catheters Solitaire (Medtronic, Tokyo, Japan) and Trevo (Stryker, Tokyo, Japan) were used as thrombectomy equipment. The operator selected the thrombectomy device freely. In the case of using the stent-type catheter, the Marksmann (Medtronic, Tokyo, Japan) was used to reach the occlusion distally. The occlusion site and length of occlusion were confirmed by performing angiography from the Marksmann and guiding catheter simultaneously. The Solitaire or Trevo was guided to the Marksmann distally and then deployed at the site of thrombotic occlusion. In many cases, immediate flow restoration was observed. After waiting for about 5 minutes, the ICA was occluded by the balloon guiding catheter, and the stent retriever was withdrawn slowly. Manual suction was also performed from the guiding catheter simultaneously. In the case of using the aspiration-type catheter, the 5 MAX or MAX ACE was guided coaxially with the 3 MAX or Marksmann to the proximal site of the occlusion; aspiration was performed when the tip of the catheter caught the thrombus. The Penumbra MAX aspiration pump or manual forced suction[9,10] was used as the aspiration procedure. Percutaneous transarterial balloon angioplasty was added to the procedure for the failed recanalization, based on the operator's judgment. Intra-arterial tissue plasminogen activator and urokinase were not added in any case. In the case of the remnant M2 occlusion, a stent-type catheter smaller

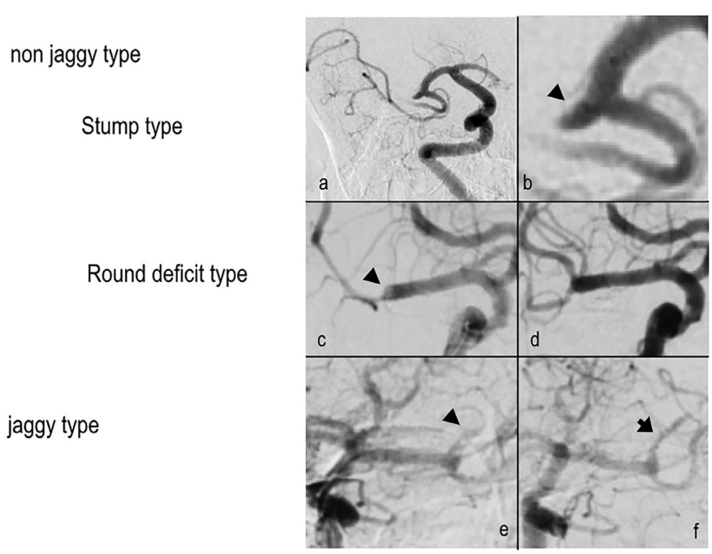

Figure 1. *Angiographic classification of the remnant M2 occlusions. (a): Stump type. (b): Magnification of A. Remnant occlusion is depicted as a stump (black arrow head). (c): Round deficit type. A circular to semicircular contrast defect is recognized in the M1/2 bifurcation (black arrow head). (d): Full recanalization of the remnant M2 occlusion after additional thrombectomy. The M2 superior branch originates from the area with a contrast defect in c. (e): Jaggy type. Although only the proximal part of the M2 superior branch is depicted, a small circular contrast defect with irregular arterial wall is observed (black arrow head). (f): After additional thrombectomy, the M2 superior branch is depicted more distally, but the vessel diameter is thinner with persistent wall irregularity (black arrow).*

than previous one was used to recanalize the occluded branch.

Artis and Artis Zee (Siemens, Tokyo, Japan) were used to perform cerebral angiography. The procedure was performed by a board-certified neuroendovascular surgeon.

Angiographical Classifications

In all cases, the remnant M2 occlusion was observed following the procedure for ICA or M1 occlusion. We usually used the anteroposterior view of the intraoperative digital subtraction angiograms, in which the M1, M1/2 bifurcation, and M2 were well-delineated. We classified the findings of remnant M2 occlusions into 3 types: the stump type, round deficit type, and jaggy type. The stump type was defined as the stump-shaped M2 branch of its origin (Fig 1a and b). The round deficit type was defined as one totally invisible M2 branch and partial defects (from circular to semicircular) of contrast media around the M1 bifurcation (Fig 1c and d). The jaggy type was defined as obstructed branches of a worm-eaten shape, with a wall irregularity and a poorly depicted peripheral artery (Fig 1e and f). In statistical analyses, the stump type and round deficit type were treated as 1 group of non-jaggy type.

Data Collection and Analyses

Clinical data, including sex, age, the modified Rankin Scale (mRS) score on admission, occlusion site, affected side, National Institutes of Health Stroke Scale (NIHSS) score on admission, diffusion-weighted image-Alberta Stroke Program Early CT Score, use of IV-tPA, and stroke subtypes were collected. Regarding the thrombectomy devices, Solitaire and Trevo were assigned to the stent type without distinction. Intraoperative findings were compared between the nonjaggy type group and jaggy type group regarding thrombolysis in cerebral infarction (TICI), reperfusion time, remnant M2 (superior or inferior) occlusion, and device type. The relationships between the jaggy type remnant M2 occlusion and clinical data were examined using univariate and multivariate analyses. Failed recanalization, symptomatic intracranial hemorrhage, and poor mRS score at discharge were compared between the non-jaggy type and jaggy type groups. Failed recanalization was defined as persistent M2 occlusion even after an additional procedure. Symptomatic intracranial hemorrhage was defined as a parenchymal hematoma 1 or 2, according to the standard of Safe Implementation of Thrombolysis in Stroke-Monitoring Study of intracerebral hematoma with mass effect.[11] Poor prognoses at discharge were defined as a mRS score of 5-6.

Statistical Analysis

The chi-square test or Fisher's exact test was used as appropriate to analyze the categorical data. The Student t test was used to compare the average reperfusion time between the aspiration-type and the stent-type groups. A 2-sided P value of .05 or less was considered statistically significant. Univariate analysis with Fisher exact test was used initially to identify potential factors. Multivariate logistic regression analysis was used to calculate the odds ratio (OR) and 95 % confidence intervals (CI) after controlling simultaneously for potential confounders from a P value of greater than .2 in the univariate analysis. Statistical analyses were performed with the commercially available software SPSS (version 24.0; IBM Corp., Armonk, New York).

Results

Patient Characteristics

Patient characteristics are summarized in Table 1. The study population included 17 men (68%) and 8 women (32%) with an average age of 73.7 years (range, 42-88 years). The occlusion site was the ICA in 8 cases (32%) and MCA in 17 (68%). Twelve (48%) occlusions occurred on the right side; no laterality was recognized. The median NIHSS score on admission was 19, and that of the diffusion-weighted image-Alberta Stroke Program Early CT Score was 7. Prior to mechanical thrombectomy, IV-tPA was administered in 13 (52%) patients. The stroke subtypes were cardioembolism in 19 (76%) and noncardioembolism in 6 (24%) cases; half (3/6) of the latter were considered to be atherothrombotic stroke.

Table 1. *Patients characteristics*

No. of cases	25
Age (mean ± SD)	73.7 ± 10.4 (42 88)
Sex	
Man	17 (68%)
Woman	8 (32%)
Baseline mRS	
0-2	23 (92%)
3-6	2 (8%)
Occlusion site	
ICA	8 (32%)
MCA	17 (68%)
Affected side	
Right	12 (48%)
Left	13 (52%)
NIHSS (median and IQR)	19 (15-22)
DWI-ASPECTS (median and IQR)	7 (5-9)
IV-tPA	13 (52%)
Stroke subtype	
Cardioembolism	19 (76%)
Noncardioembolism	6 (24%)

Abbreviations: DWI-ASPECTS, diffusion weighted image Albarta Stroke Program Early CT Score; ICA, internal carotid artery; IQR, interquartile range; MCA, middle cerebral artery; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.

Summary of Thrombectomy

Nonjaggy and jaggy type were recognized 17 and 8 cases, respectively. TICI 2b-3 recanalization could be accomplished in 76% of cases in the nonjaggy type group and 38% in the jaggy type group, and there was no significant difference between the groups ($P = .087$) (Table 2). Puncture to reperfusion time and the onset to reperfusion time were not different between the 2 groups respectively ($P = .207$, .658). Remnant M2 occlusion was more frequently identified in the superior branch than in the inferior branch (80%, 20/25). The types of remnant M2 occlusion were the stump type in 40%, round deficit type in 28%, and jaggy type in 32%; the nonjaggy type (the stump type and round deficit type) reached 68%. Device type (aspiration type or stent type) had no relationship between the 2 groups ($P = .66$). Cardioembolism was considered the stroke etiology in 88% of cases in the nonjaggy type group, whereas in 50% in the jaggy type group ($P = .059$).

Predictive Factors for Jaggy Type Remnant M2 Occlusion

Although univariate analysis showed no significant difference between jaggy type remnant M2 occlusion and any patient characteristics data (Table 3), stroke subtypes had relatively high OR with marginal significance (OR 4.25, 95 % CI .97-18.57, $P = .059$). Results of the subsequent multivariate analysis also suggested that noncardioembolic stroke may lead to jaggy type remnant occlusion, albeit the CI was wide (OR 7.5, 95 % CI .91-56.78, $P = .051$).

Adverse Events and Outcomes

The rates of failed recanalization of remnant M2 occlusion were significantly lower (6%) in the nonjaggy type group than in the jaggy type group (50%) ($P = .023$) (Table 4). Symptomatic intracranial hemorrhage occurred in 6% of cases in the nonjaggy type and in 38% of the jaggy type group ($P = .081$). In 2 cases of the jaggy type group, additional thrombectomy for remnant occlusion caused massive intracranial hemorrhage leading to death (Fig 2a-c). In one case of the stump type, a small aneurysm in the origin of the recanalized inferior trunk (M2) mimicked the stump of another obstructed artery (Fig 3a and b). Poor outcome at discharge occurred in 29% of cases in the nonjaggy type group and 50% in the jaggy type group ($P = .039$).

Discussion

When a thrombus remains in 1 M2 branch following successful recanalization of the ICA or M1, it is difficult to determine whether additional thrombectomy should be performed or not. Catheter manipulation within the M2 with a small diameter and thin vessel wall may cause arterial injury. In the past, the mortality rate of mechanical thrombectomy for M2 occlusion has been reported as over 20%.[12,13] With the introduction of novel stent-type devices, however, the effectiveness and safety of mechanical thrombectomy have also been suggested for a single M2 occlusion.[8,14] Most patients in this study presented with moderate to severe symptoms due to acute ICA or M1 occlusion (the median NIHSS score of 19). Therefore, severe neurological consequence would have been inevitable, unless TICI 2b-3 recanalization could be achieved.

In this study, remnant M2 occlusion was much more frequently identified in the superior branch than in the inferior branch. Schwaiger et al examined the recanalization rate of thrombectomy from the ICA to M2 by a stent retriever using the running angle of adjacent arteries. When the arterial branching angle was close to a straight line, the recanalization rate was high,[15] which seems consistent with our results, due to the relatively acute angle of the M1 to M2 superior trunk curve.

In the present study, we categorized and examined angiographical findings of remnant M2 occlusion. Although cerebral angiography clearly indicates the

Table 2. *Operative summary*

	Nonjaggy (n = 17)	Jaggy (n = 8)	Total (n = 25)	*P*
TICI				.087*
0-2a	4 (24%)	5 (62%)	9 (36%)	
2b-3	13 (76%)	3 (38%)	16 (64%)	
Puncture to reperfusion time (mean ± SD)	83 ± 39.5	102 ± 30.1		.207†
Onset to reperfusion time (mean ± SD)	314 ± 112.4	337 ± 105.5		.658†
Remnant M2 occlusion				1.00*
Superior branch	14 (82%)	6 (75%)	20 (80%)	
Inferior branch	3 (18%)	2 (25%)	5 (20%)	
Device type				.66*
Aspiration	7 (41%)	2 (25%)	9 (36%)	
Stent	10 (59%)	6 (75%)	16 (64%)	

TICI, thrombolysis in cerebral infarction.
*Calculating using Fisher's exact test.
†Calculating using Student *t* test.

Table 3. *Prediction factors for jaggy type remnant M2 occlusion*

	Univariate			Multivariate		
	OR	95 % CI	*P*	OR	95 % CI	*P*
Age (≥74 y)	1.18	0.27-8.27	1.000			
Sex (male)	0.89	0.12-4.08	1.000			
Baseline mRS (0-2)	1.13	0.95-1.35	1.000			
Occlusion site (MCA)	1.16	0.68-1.97	1.000			
Affected site (left)	1.82	0.91-3.65	0.200	3.96	0.52-29.87	0.183
NIHSS (≥19)	0.71	0.26-1.93	0.670			
DWI-ASPECTS (≥7)	1.18	0.59-2.38	1.000			
IV-tPA	1.33	0.64-2.78	0.670			
Stroke subtype (noncardioembolism)	4.25	0.97-18.57	0.059	7.5	0.91-56.78	0.051

Abbreviations: DWI-ASPECTS, diffusion weighted image−Albarta Stroke Program Early CT Score; MCA, middle cerebral artery; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.

occlusion site, it is often difficult to speculate the extent of the thrombus and course of the peripheral artery. We think that the anteroposterior view would be suitable to demonstrate the M1 bifurcation and its tributaries, whereas the lateral view provides less information because of overlapping of each vessel. Rotational angiography is useful for further angioarchitecture analyses.

In patients with the stump-type, a relatively small thrombus would have migrated into the M2 branch, and the origin of the remnant M2 occlusion would be clearly visible. Thus, the retriever could be easily guided to the stump and further distal across the thrombus. By contrast, the round deficit findings would indicate that the thrombus was still protruding toward the origin of the recanalized M2 side. Occluded branches are usually present on the opposite side of the contrast defect arc. (Fig 1c and d) The defect of the contrast material would be a landmark for guiding the thrombectomy device. In such cases, additional thrombectomy seems to be highly needed to ameliorate the stenosis of the recanalized M2 and to prevent the distal embolism, as well as to recanalize the remnant occlusion. The thrombus was localized within the M2 branch in the stump type but partially remained or protruded into the M1/2 bifurcation in the round deficit type. Both types lacked any wall irregularity and are considered be embolic stroke in a similar pathological condition. Therefore, we treated them in 1 group, the nonjaggy type, in our statistical analyses.

The main result of this study is that the jaggy type remnant occlusion had a significantly lower recanalization rate than the nonjaggy type. Further, it was related to severe intracranial hemorrhage and poor outcomes. As shown in Figure 1e and f, an arterial wall irregularity observed during procedure did not recover to a normal vessel diameter even after subsequent flow restoration. These findings are highly suggestive of a pathological condition of the arterial wall itself, such as atheromatous plaque, vasospasm, and arterial dissection, rather than a simple embolus. As well-known, the irregularly narrowed or tapered vessel is consistent with an atherosclerotic lesion. Univariate and multivariate analysis suggest that noncardioembolic stroke may be the predictive factor for the jaggy sign. Performing an additional procedure is certainly difficult in the case of a M2 with a small diameter with preexisting atheromatous stenosis, and it often results in the failed recanalization.

Second, mechanical stimulation often causes arterial spasm. The aspiration-type catheter Penumbra has a relatively large diameter of at least 4.7-Fr. Catheter friction and negative aspiration pressure irritate the arterial wall. The stent-type catheters Solitaire and Trevo also cause catheter friction when placed in the thrombus. Since the stent retriever with thrombus withdraws across the proximal arterial lumen, mechanical stimulation may also provoke vasospasm along the M1 to the ICA. Procedure-related arterial spasm might be the cause of the

Table 4. *Treatment results and adverse events*

	Nonjaggy (n = 17)	Jaggy (n = 8)	*P*
Failed recanalization	1 (6%)	4 (50%)	0.023*
Symptomatic intracranial hemorrhage	1 (6%)	3 (38%)	0.081
Poor outcome at discharge (mRS 5-6)	5 (29%)	4 (50%)	0.039*

mRS, modified Rankin Scale.
Calculating using Fisher's exact test.
*Statistical significance.

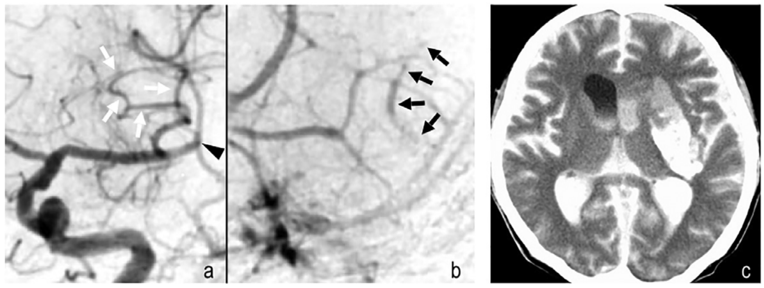

Figure 2. *(a): Intraoperative angiogram in a patient of the jaggy type group with an M1 occlusion. The superior branch is recanalized (white arrow), while the inferior branch is depicted as resembling the beginnings of a jaggy type occlusion (black arrowhead). (b): The venous phase. The contrast agent remains antegrade in the inferior branch, accompanied by the wall irregularity in the periphery (black arrow). (c): Postoperative computed tomography scan demonstrating massive parenchymal, subarachnoid, and intraventricular hemorrhage with extravasation of the contrast material.*

intraoperative jaggy findings in some patients of this study.

Finally, we should bear in mind the possibility of idiopathic or iatrogenic arterial dissection. The possibility of idiopathic dissection in the MCA should be noted, although isolated MCA dissection is relatively rare.[16] Most of reported cases had M1 dissection (75%), and M2 dissection was even more rare (21.7%).[16] Furthermore, the jaggy type lesion may be procedure-related dissection, which could occur in the device passageway or indwelling site. Renu et al examined the vascular wall damage after mechanical thrombectomy by postoperative magnetic resonance imaging, which would be indicated with hemorrhagic transformation and the final infarct volume.[17] Although there is no detailed angiographical analysis about the procedure-related intracranial arterial dissection, the data from cardiac interventional radiology may have some implications. The National Heart Lung and Blood Institute classification is widely used in coronary artery dissection during percutaneous coronary artery intervention. Type F (occlusion after narrowing) in that classification may be considered a similar finding to our jaggy type, which is reported to cause myocardial infarction, with increased mortality rate.[18] Eshtehardi et al also classified iatrogenic coronary dissection,[19] and reported that "zipper" type dissection that extends to distal major branches, which may be related to an unstable hemodynamic condition. The jaggy finding may suggest arterial dissection and/or vascular injury, so additional procedures may cause serious complications. Careful judgment is needed for a jaggy type remnant occlusion.

This study has multiple limitations. First, our study did not provide the histopathological findings of the jaggy type occlusion. Further study focusing on the pathology in mechanical thrombectomy is needed. Second, this study was conducted in the era of the first-generation stent retriever. Currently, mechanical thrombectomy devices are being improved, which affects the treatment results. Third, the small sample size and retrospective nature of our analyses undoubtedly lessens the validity of the results.

Conclusions

One of the M2 branches sometimes remains obstructed after mechanical thrombectomy for acute main trunk occlusion in anterior circulation. In such a situation, the angiographic configuration of the remnant M2 occlusion could provide pivotal information. Careful attention

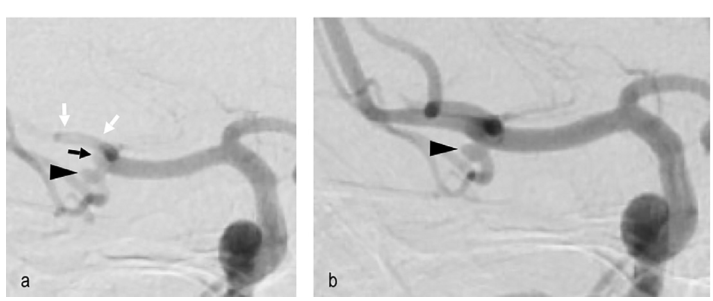

Figure 3. *(a): Intraoperative angiogram in a patient with internal carotid artery occlusion. The M1 terminal shows a trifurcation pattern, and only 1 M2 branch (the inferior trunk) is recanalized, but a stump-like finding is identified in the origin of the inferior trunk (arrow head). One occluded branch (black arrow) is hidden by another occluded M2 branch (white arrow), and only a small stump is visible (black arrow). (b): Full recanalization after additional thrombectomy. A small aneurysm mimics a stump-type remnant occlusion (black arrow head).*

should be paid to the arterial wall irregularity, such as a narrow worm-eaten shape and poor peripheral visualization (jaggy type), because of the possible underlying or procedure-related pathology, such as atherosclerosis, vasospasm, or arterial dissection.

Conflict of Interest

The authors declare that they have no conflict of interest.

Compliance with Ethical Standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

Informed Consent

Informed consent was obtained from all individual participants include in the study.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jstrokecerebrovasdis.2019.03.043.

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