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Original Article

Analysis of the Anatomical Factors Affecting Ability to Navigate Penumbra Catheter through Internal Carotid Siphon

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Objective: The efficacy and safety of aspiration thrombectomy using Penumbra catheter with acute large vessel occlusion in the anterior circulation have been reported in previous studies. In some cases, the carotid siphon (CS) is elongated, and with this anatomy, especially where there is bifurcation of the ophthalmic artery (OA), navigation of Penumbra catheters into distal internal carotid artery (ICA) is interrupted, which is known as the 'ledge effect'. We investigate the anatomical characteristics of CS that cause interruption of navigation of the Penumbra catheter.
Methods: Between January 2015 and March 2018, mechanical thrombectomy using Penumbra 60 was performed on 51 patients with middle cerebral artery (MCA) or intracranial ICA occlusion. Patients were divided into two groups: The 'ledge-effect' group those in whom the Penumbra catheter was unable to be navigated into the distal ICA through the CS, and 'no ledge-effect' group those in whom this was possible. The anatomical characteristics of CS, the diameter of ICA, diameter of OA, OA/ICA ratio and radius of the CS were evaluated using angiographical imaging.
Results: The 'ledge-effect' group numbered eight cases (17%). Only the value of the CS radius was significantly smaller in the ledge-effect group ($p = 0.0019$), other parameters were not significantly different between the groups. The cutoff radius value was 3.62 mm.
Conclusion: The most notable anatomical factor affecting possibility of navigation of the Penumbra catheter through the CS was the CS radius. This could be useful information when devices used in mechanical thrombectomy are selected.

Keywords ▶ mechanical thrombectomy, Penumbra catheter, carotid siphon

Introduction

Recent trials and meta-analyses have proved the efficacy of mechanical thrombectomy over other types of treatment of large vessel occlusion in patients with acute ischemic stroke. Although the effectiveness of stent retrievers has been reported, Penumbra aspiration catheter (Penumbra Inc., Alameda, CA, USA) has been suggested as a good alternative device. Thrombectomy using Penumbra catheter such as a direct aspiration first pass technique (ADAPT) enables recanalization significantly faster than previously reported means of thrombectomy.[1)] There are many recent reports on adjunctive technique using Penumbra catheter. For example, Solumbra/Trenumbra techniques are reportedly useful as methods of reperfusion using a combination of Penumbra catheter and the stent-retriever (Solitaire FR device; Medtronic Neurovascular Irvine, CA, USA) or Trevo (Stryker Neurovascular Fremont, CA, USA).[2,3)] Continuous aspiration prior to intracranial vascular embolectomy (CAPTIVE) and stent-retriever-assisted vacuum-locked extraction (SAVE) technique which use a stent retriever with continuous aspiration by large-bore catheter are helpful to get successful recanalization and have shorter recanalization time.[4,5)] Proximal balloon occlusion together with direct thrombus aspiration during stent-retriever thrombectomy (PROTECT) using additional balloon guiding catheter showed excellent results.[6)]

Although aspiration catheters with larger catheter lumen have been developed to improve aspiration power, this also

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results in a larger profile and more difficulty in achieving distal navigation. Generally, larger Penumbra catheters often require the use of a coaxial technique to navigate into the site of the occlusion because of the 'ledge effect', being held up by bifurcation of the ophthalmic artery (OA).[7,8] Even if a coaxial technique was used, in some cases, we experienced that Penumbra catheter was unable to track to distal internal carotid artery (ICA) because of the anatomy of the carotid siphon (CS).

We investigated the anatomical characteristics of the ICA that render navigation of Penumbra catheters into the distal ICA through the CS challenging.

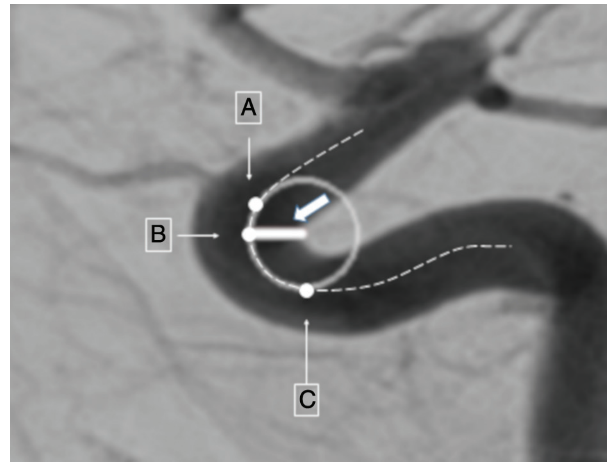

Fig. 1 Lateral angiography shows representative CS. Radius of the CS was defined as the diameter (white arrow) of the circle (white circle) passing the centerline of the CS through three points: (**A**) midpoint of the diameter in ICA at bifurcation of OA, (**B**) the vertex of ICA genu, and (**C**) the proximal C3 (white dots). CS: carotid siphon; ICA: internal carotid artery; OA: ophthalmic artery

Materials and Methods

Patient selection

We retrospectively reviewed clinical characteristics and radiographic imaging of patients with acute ischemic stroke who underwent mechanical thrombectomy using Penumbra system at our institution between January 2015 and March 2018. This study was approved by the Wakayama Medical University Ethics Committee.

Patients with basilar/vertebral artery occlusion were excluded from this study. The inclusion criteria at our institution was as follows: (1) Symptoms were either moderate or severe, an admission National Institutes of Health Stroke Scale (NIHSS) score was at least 6. (2) Patients had a small territorial infarction by non-contrast CT, defined as an Alberta Stroke Program Early CT Score (ASPECTS) >6. (3) A modified Rankin Scale (mRS) prior to stroke onset score was 0, 1, or 2. (4) Patients with ICA and/or middle cerebral artery (MCA) occlusion identified by radiographic imaging underwent mechanical thrombectomy using Penumbra 60 (Almeda, CA, USA). (5) Clinical-diffusion mismatch existed. (6) The time from onset to puncture was within 6 hours. If the patients met the adaptation criteria of intravenous tissue plasminogen activator (IV-tPA), they underwent IV-tPA first. We divided these patients into two groups, 'ledge-effect group' in whom a Penumbra 60 could not be navigated into the distal ICA over the CS, and 'no ledge-effect group', those in whom a catheter was able to be navigated over the CS. In these groups, the patients whose OA could not be identified on angiography was excluded from radiographic analysis.

The case details were reviewed, including demographic data, medical history (atrial fibrillation, hypertension, diabetes mellitus, hyperlipidemia), history of smoking, comorbidity (cardiac artery disease, previous cerebral infarction, peripheral artery disease), NIHSS and CT-ASPECTs.

Means of confirming diagnoses

Less than 2 on the mRS was considered to be a favorable outcome. Thrombolysis in Cerebral Infarction (TICI) 2b-3 classification was used for evaluation of successful recanalization. The first pass effect (FPE) was defined as achieving a complete recanalization with the first pass.

Radiographic analysis

We evaluated the anatomical characteristics of CS by reviewing lateral angiography as follows: diameter of ICA, diameter of OA, OA/ICA ratio, and radius of CS between two groups. CS radius was defined as the diameter of the circle passing the centerline of the CS through three points, the midpoint of the diameter in the ICA at bifurcation of the OA, the vertex of the ICA genu, and the proximal C3 (**Fig. 1**). Smaller CS radius means greater elongation of the CS. These parameters were measured twice each by E.K. and Y.M.

Endovascular procedure

All endovascular therapies were performed on the angiosuite under local anesthesia. Generally, a 9F balloon-guiding catheter (Optimo, Tokai Medical products, Japan) was placed in the cervical portion of the ICA. Systematic heparin was intravenously injected during the procedure to keep the activating clot time between 250 and 350s. In case with IV-tPA, only 3000 units of heparin were injected after sheath insertion. The guiding catheter was continuously flushed with heparinized saline.

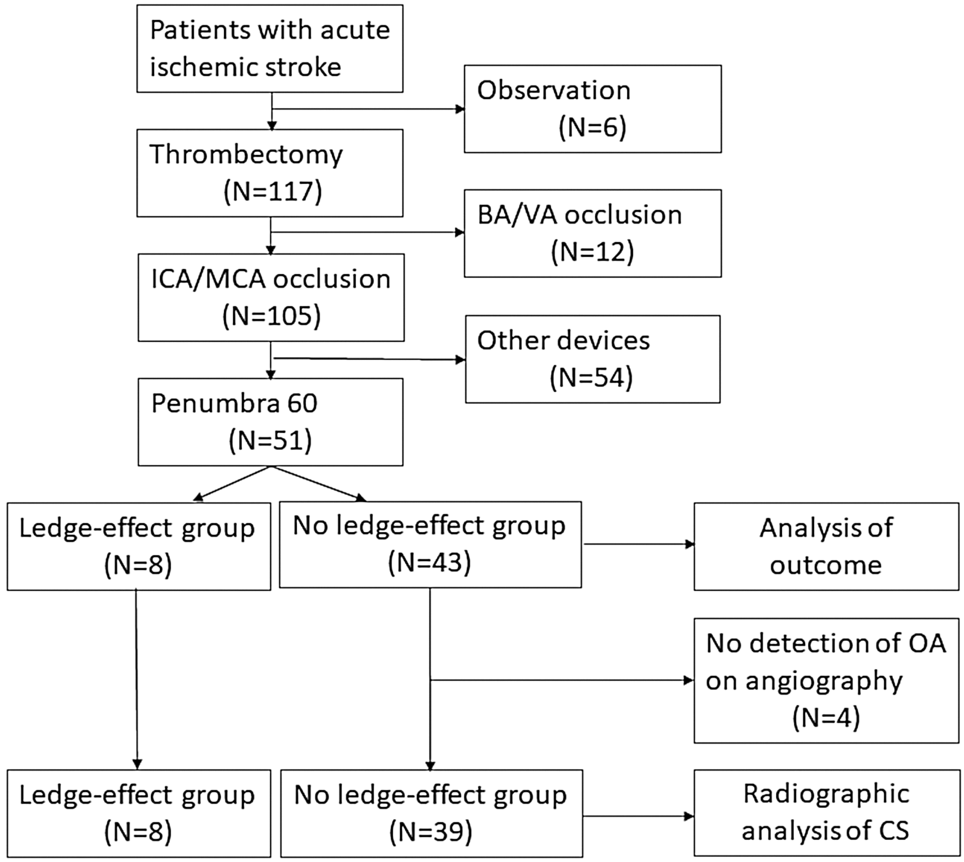

Fig. 2 Flowchart for exclusion and inclusion of the patients underwent thrombectomy in our study

Penumbra 60 was navigated just proximal to the thrombus over intermediate catheter, Penumbra 3Max (Alameda, CA, USA) or Marksman catheter (Covidien, Irvine, CA, USA) and a Chikai 0.014 inch microguidewire (Asahi Intecc, Aichi, Japan). After positioning, the catheters and microguidewires were withdrawn. After no retrograde blood was identified, pump aspiration was performed. Penumbra 60 was gently withdrawn under continuous aspiration. If this procedure was unsuccessful, the same procedure was tried once more. In unsuccessful aspiration procedures, use of a stent retriever was considered. In case, the Penumbra 60 was unable to be navigated over the CS, another method, such as using a stent retriever, was also considered.

Statistical analysis

ImageJ software (National Institutes of Health, USA) was used for anatomical measurements. JMP pro13 software (SAS Institute Inc., Cary, NC, USA) was used for statistical analysis. The chi-square homogeneity test and Student's t-test were used to compare categorical variables. P value of <0.05 was considered to be statistically significant. Cutoff value of the CS radius was calculated by receiver operating characteristic curve.

Results

Flowchart for exclusion and inclusion of the patients underwent thrombectomy in our study is shown in **Fig. 2**.

No ledge-effect group comprised 43 of 51 cases (83%), and the ledge-effect group comprised eight of 51 cases (17%). Patient characteristics are shown in **Table 1**. In all, 24 male patients (56%) were in the no ledge-effect group, six (76%) were in the ledge-effect group. Mean ages were 75.7 in the no ledge-effect group and 78.6 in the ledge-effect group. Risk factors and comorbidity were not significantly different between the two groups. Mean NIHSS scores were 17 and 15, respectively. Acute stroke severity assessed by the NIHSS and ASPECTs at presentation was not significantly different between the two groups.

The site of occlusion of the intracranial ICA was 18.6% (8/43) in the no ledge-effect group and 25% (2/8) in the ledge-effect group. The occlusion of the first segment of MCA (M1) was 76.7% (33/43) in the no ledge-effect group

Table 1 Characteristics of patients

		No ledge-effect group	Ledge-effect group	p
No. of patients (%)		43 (83)	8 (17)	0.3
Age (years) (SD)		75.7 ± 1.8	78.6 ± 4.4	0.94
Sex, male (%)		24 (56)	6 (75)	0.43
Af/pAf (%)		28 (65)	3 (38)	0.27
Risk factors (%)	Hypertension	26 (60)	6 (75)	0.69
	Hyperlipidemia	7 (16)	3 (38)	0.18
	Diabetes mellitus	8 (19)	4 (50)	0.08
	(Ex-)smoker	5 (31)	1 (13)	1
Comorbidity (%)	CAD	9 (19)	2 (20)	0.62
	Previous CI	12 (28)	2 (20)	1
	CKD	2 (4)	0 (0)	1
	PAD	1 (2)	0 (0)	1
NIHSS (mean)		17	15	0.29
CT-ASPECTs (mean)		9	9	0.85

Af: atrial fibrillation; ASPECTs: Alberta Stroke Program Early CT Score; CAD: cardiac artery disease; CI: cerebral infarction; PAD: peripheral artery disease; pAf: paroxysmal atrial fibrillation; NIHSS: National Institutes of Health Stroke Scale

Table 2 Sites of occlusion and methods for mechanical thrombectomy

		No ledge-effect group	Ledge-effect group	p
ICA occlusion		8	2	0.25
MCA occlusion	M1	33	4	0.25
	M2	2	2	
Tandem occlusion		4	1	1
Side	Left	26	2	0.06
IV-tPA		8	1	1
Inner catheter	3MaxACE	6	2	0.76
	Marksman	35	6	
	Others	2	0	
Other system	Solitare	14	4	0.04
(Stent)	Trevo	7	4	
	Revive	10	0	
	None	10	1	
Number of passes		2	2	0.79
Number of FPE		15	3	0.33

FPE: first pass effect; ICA: internal carotid artery; IV-tPA: intravenous tissue plasminogen activator; MCA: middle cerebral artery

and 50% (4/8) in the ledge-effect group, the occlusions of the second segment of MCA (M2) were 4.7% (2/43) and 25% (2/8), respectively. The tandem occlusion was 9.3% (4/43) in the no ledge-effect group and 12.5% (1/8) in the ledge-effect group. There was one case (12.5%) with embolism from carotid artery occlusion requiring carotid artery stenting (CAS) in the ledge-effect group. There were four cases (9.3%) with embolism due to carotid artery stenosis or occlusion requiring CAS or percutaneous transluminal angioplasty (PTA) in the no ledge-effect group. The simple aspiration method was used in 23.3% (10/43) of the no ledge-effect group and 12.5% (1/8) in the ledge-effect group. In the former group, other five5 cases with M1 distal occlusion required additional stent retrievers (Solitaire, Trevo and/or Revive [Codman, Raynham, Massachusetts, USA]) to achieve recanalization because of the difficulty for navigation of Penumbra 60. The ADAPT method using 3MAX was performed in the latter one case. IV-tPA was conducted 18.6% (8/43, no ledge-effect group) and 12.5% (1/8, ledge-effect group), respectively. The difference of inner intermediate catheters of Penumbra 3MAX and Marksman demonstrates no significant difference in trackability of Penumbra 60. Mean pass times to recanalization were 2.0 in both groups. FPE was achieved in 34.5% (15/43) and 37.5% (3/8), respectively ($p = 0.33$). Results are shown in **Table 2**.

The rates of successful recanalization (TICI grade ≥2b) were 86.0% (37/43, no ledge-effect group) and 100% (8/8,

Table 3 Outcome of procedure

		No ledge-effect group	Ledge-effect group	p
TICI	3	19	6	0.22
	2b	18	2	
	2a	4	0	
	1	0	0	
	0	2	0	
TICI	2b–3 (%)	37(86)	8(100)	1
Puncture to recanalization (min)		61	73.5	0.34
mRS 0–2 at 30 days (%)		17(39.5)	3(37.5)	1

mRS: modified Rankin Scale; TICI: Thrombolysis in Cerebral Infarction

Table 4 Anatomical results

	No ledge-effect group	Ledge-effect group	p
Diameter of ICA (mm)	4.53	4.06	0.11
Diameter of OA (mm)	1.08	1.11	0.78
OA/ICA ratio	0.22	0.23	0.11
Radius (mm)	4.19	2.92	0.0019

ICA: internal carotid artery; OA: ophthalmic artery

ledge-effect group), respectively. ($p = 0.22$). Puncture to recanalization times were 61.0 and 73.5 minutes in each group ($p = 0.34$). Favorable outcome was 39.5% and 37.5% (17/43 and 3/8), considered to be without significant difference (**Table 3**).

The radius of CS in ledge-effect group was significantly smaller than that in the no ledge-effect group ($p = 0.0019$). The other parameters, diameter of ICA, OA, and OA/ICA ratio, between the two groups showed no significant difference (**Table 4**). Cutoff value of the radius was 3.62 mm.

A representative case, a 72-year-old female, with occlusion of ICA top had small CS radius and was in the ledge-effect group (**Fig. 3**). Small radius indicates that the vertex of CS is severe. First, Penumbra 60 with Penumbra 3MAX intermediate catheter into 9F balloon guide catheter was applied. It failed to be passed through CS because of the ledge effect. Marksman microcatheter was navigated to the distal thrombus through Penumbra and stent retriever (Trevo 4 × 20 mm) was deployed across the thrombus and the microcatheter was removed completely. After waiting for 5 minutes, continuous aspiration was started and the stent was retrieved into the aspiration catheter. After two passes of same the procedure, full recanalization was shown on final angiography.

Discussion

In our study, the CS radius was independent factor in unsuccessful navigation of Penumbra catheter into the distal ICA. Generally, ledge effect is reported to render navigation of the catheter into the distal ICA both challenging and time-consuming.[7] Therefore, we evaluated CS anatomy influencing the ledge effect and focused on the diameter of ICA, OA, OA/ICA ratio, and radius of CS for the following reasons.

Diameter of ICA

The average diameter of the cavernous part of the ICA was reported to be 3.68 mm on the right, 3.85 mm on the left.[9] In the no ledge effect and ledge-effect group, these averages were 4.53 mm and 4.06 mm, respectively. It was slightly larger than that previously reported. Small diameter of ICA was assumed to make navigation of the Penumbra catheter challenging, but in this study, the average ICA diameter was not significantly small.

Diameter of OA

A larger diameter of the OA would create a larger ledge effect to advance the Penumbra catheter through the CS. OA is the first branch of the ICA immediately after it arises from the cavernous sinus and enters the cranial cavity. Its diameter ranges between 0.7 and 1.8 mm.[10,11] The average OA diameter in this study was not significantly different between groups: 1.08 and 1.11 mm, reference value range. OA could be measured except in four cases and be located in supraclinoid segment of the ICA. Recanalization was not necessary in one of the cases. OA was not detected in the other three cases with successful recanalization.

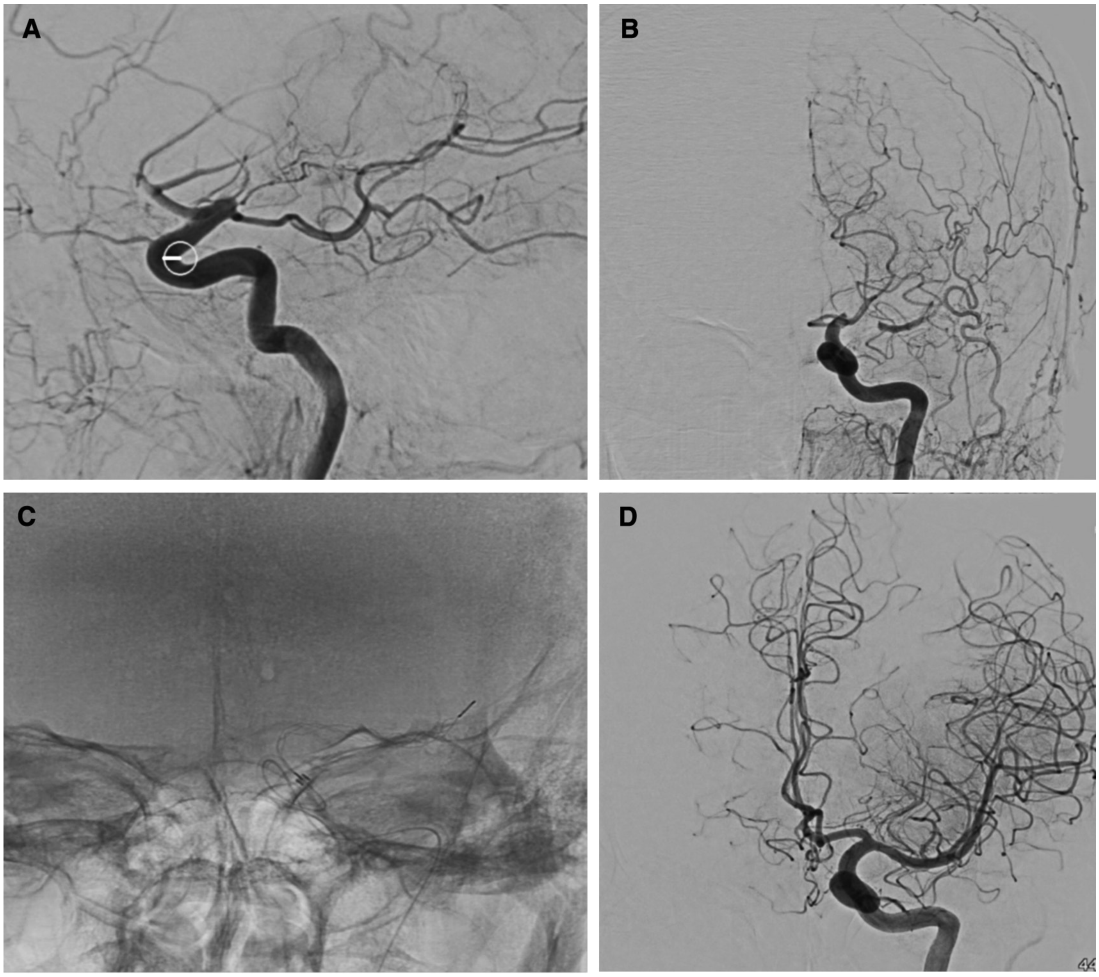

Fig. 3 (**A**) Representative case, a 72-year-old female, with small radius of CS (3.54 mm) and ledge-effect group is shown. Small radius indicates severe bending of the CS. Diameter of ICA is 5.46 mm, diameter of OA is 0.94 mm, and OA/ICA ratio is 0.17. (**B**) Diagnostic angiography shows the occlusion of ICA top. (C) Stent retriever Trevo 4 × 20 mm was deployed across the thrombus. Penumbra catheter was navigated just proximal of Trevo. Trenumbra was conducted. (**D**) Two passes of the same procedure showed full recanalization on final angiography. CS: carotid siphon; ICA: internal carotid artery; OA: ophthalmic artery

OA/ICA ratio

If the OA/ICA ratio is smaller, it means a relatively smaller diameter of OA. Smaller ratio is expected to facilitate the navigation of Penumbra catheter into distal ICA through CS. In our study, however, there was no difference between the two groups.

Radius of CS

Previous reports on radius of ICA reported that bending of the CS resembles the circle. Chi Zhang et al. (2013) reported geometric classification of the CS and defined the osculating circle (OC) as the curvature radius fitting to the bend of centerline of CS.[12–14] We defined radius of the CS as the diameter of the circle passing the centerline of CS through three points including midpoint of the diameter in ICA at bifurcation of OA, vertex of the genu of ICA, and midpoint of the proximal C3. Radius of the CS means relatively the tortuosity. Smaller radius shows severe elongation of the vessel which can make advancement of a catheter challenging. In our study, only this parameter had significant difference between the two groups. It proved the bending of the CS in the ledge-effect group affected feasibility to navigate Penumbra over CS.

Greater difference in diameters between inner diameter of Penumbra 60 and outer diameter of intermediate catheter (Penumbra 3MAX or Marksman microcatheter) causes greater ledge effect. The coaxial advancement technique was reported previously. If a microguidewire is just used for advancing the Penumbra 60, the gap between the two devices is expected to be large and this could result in difficulty controlling the catheter. The coaxial advancement technique was used to reduce the gap between the inner diameter of Penumbra 60 and the outer diameter of intermediate catheter so to allow navigation of the Penumbra 60 into distal portion over CS.[15] However, in our study, the difference of intermediate catheter was not significant. The outer diameter of Penumbra 3MAX is 0.050 inch. On the other hand, that of Marksman microcatheter is 0.037 inch. This difference of 0.013 inch was negligible for navigation of Penumbra 60 through CS. When comparing the Penumbra 60 with the intermediate catheter, the ledge effect (inner diameter of Penumbra 60 [0.060 inch] – outer diameter of intermediate catheter), is 0.010 inch for Penumbra 3Max and 0.023 inch for Marksman microcatheter. This difference could be negligible from our result.

Previous reports detailed other methods of navigation of Penumbra catheter through CS smoothly.

One method of navigating the Penumbra catheter through the CS is by steam-shaping the tip of the Penumbra catheter. It allows easy navigation through the CS. In the previous reports, there were three types of "simple-curved" steam shaping; a 45° curve, a 90° curve, and J-shape curve. In most cases, advancement is more smoothly achieved using a steam-shaped catheter tip with a 45° curve. However, in some cases with extreme tortuosity or severe atherosclerotic stenosis, a 90° curve or J-shape can be occasionally used.[16] Therefore, if tortuosity of CS is severe, although in our study steam-shaping was not performed, it may be better to shape the Penumbra catheter before puncture. The disadvantage of this proposal is that it is time-consuming and shaping might induce the malformation of tip of the Penumbra catheter.

Another means of navigating the Penumbra catheter through the CS is by the so-called 'buddy wire' technique. It means introducing a supportive microguidewire. This can be used to support the Penumbra catheter and provide added stability. This method is usually used for percutaneous coronary intervention (PCI), CAS, stenting of the vertebral artery, and other endovascular therapies.[17–19] Double wires might enable reduction of the gap between microguidewire and microcatheter and improve usability of the catheter by reducing the ledge effect.

More recently, Sofia Non-wire Advancement techniKE (SNAKE) is reported benefit for mechanical thrombectomy. Because the distal end of the Sofia catheter is extremely soft, it could be safely advanced into the intracranial vessels without any microcatheter or microguidewire. This technique may be one method to overcome the challenging of the ledge effect.[20]

Successful recanalization with TICI 2b or 3 was achieved in 75–87% with ADAPT in other reports.[21] The reperfusion rate of TICI2b or 3 in no ledge effect and ledge-effect group was 86% and 100%, respectively. These results were similar to those of previous reports.[22] The mean reperfusion times were 61.0 and 73.5 minutes, respectively ($p = 0.33$). There was no difference in pass times or in treatment for cervical lesion between both groups. Ledge-effect group had tendency for longer reperfusion time. Consequently, change of devices in cases of unsuccessful navigation of Penumbra catheter through CS may be required, and more patients in the ledge-effect group would result in difference between these groups.

In this study, in unsuccessful navigation through CS, correct selection of devices could reduce reperfusion time. Furthermore, aspiration catheters with larger lumen that could improve power of aspiration are under developed. These catheters could produce greater ledge effect, however. Therefore, this study is meaningful for mechanical thrombectomy using Penumbra catheters.

A limitation of our study is that, because of limited resources, this was a retrospective study and it was conducted in a single institution. Actually CS radius would rely on a completely orthogonal view of the CS but lateral angiograph is not completely orthogonal to the skull. To reduce the influence, strict lateral angiography with the acoustic meatus at same level was obtained. The tortuosity of femoral artery and arch of aortic artery might affect navigation of Penumbra catheter to thrombus. However, inflation of balloon guiding catheter not only stop flow of ICA but also support anchoring ability for navigation of Penumbra catheter. As a results, this inflation of balloon could minimize elongation of femoral artery and aortic arch.

Conclusion

The main factor in ability to navigate a Penumbra catheter through the CS was the radius of the CS. This measurement could be helpful for selection of devices for mechanical thrombectomy.

Disclosure Statement

There is no conflict of interest for the first author and coauthors.

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