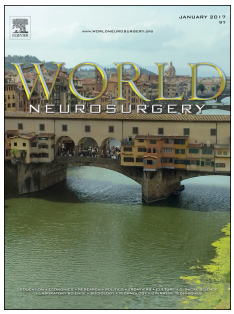

Endovascular revascularization of non-acute symptomatic proximal extracranial vertebral artery occlusion

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Title Page

Title: Endovascular revascularization of non-acute symptomatic proximal extracranial vertebral artery occlusion

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INTRODUCTION

Proximal extracranial vertebral artery occlusion (PEVAO) is considered as an uncommon cause of posterior circulation ischemia, and the pathophysiology involves hypoperfusion[1] and vertebral artery stump syndrome[2]. The incidence of posterior circulation ischemia due to PEVAO has not been determined till date. But the prevalence of vertebral artery stump syndrome accounted for 1.4% of acute posterior circulation stroke and showed an association with high risk of stroke recurrence and poor prognosis.[3] There are a variety of treatment modalities available for treating non-acute symptomatic PEVAO, which included antiplatelet agents[4], anticoagulants[3,5], hemodynamic improvement[6] and surgical bypass.[7,8] However, the optimal treatment for these patients still remained controversial and empirical.[9] With the development of endovascular intervention, there are few case reports that attempted to evaluate the feasibility of endovascular revascularization in such patients[10]. However, most of the reports are single cases, while the case series are rare.[11-18] The overall success and safety are still unclear. We herein reported 23 cases of endovascular revascularization of non-acute symptomatic PEVAO for evaluating the feasibility, success rate, safety, and the issues associated with the technique.

MATERIALS AND METHODS

Patient selection

Patients with non-acute symptomatic PEVAO were admitted to the stroke unit in the department of neurology at West China Hospital of Sichuan University between June 2011 and March 2018. Non-acute occlusion is defined as the presence of TICI 0 flow within the occluded segment, and with an estimated occlusion duration of more than 2 weeks. The duration of non-acute occlusion was estimated according to the symptoms duration, the previous doppler ultrasound, angiography, and current angiography. Symptomatic occlusion is defined as patients with recurrent stroke or transient ischemic attack associated with occluded artery. The indications of endovascular revascularization were as follows: (1) non-acute symptomatic PEVAO; (2) symptoms refractory to best medical treatment, including lifestyle modification, dual antiplatelet (not evaluated with PRU testing), statin therapy, management of blood pressure and glucose control; (3) unilateral extra-cranial vertebral artery occlusion combined with contralateral vertebral artery total occlusion or hypoplastic, or the normal contralateral vertebral artery, but the occluded side presented with vertebral artery stump syndrome; (4) the visible stump and distal V2 segment; (5) the bilateral sides of posterior communicating artery were aplastic or hypoplastic; and (6) patients refused to undergo bypass surgery. This study was approved by the Institutional Review Board of West China Hospital, Sichuan University.

Procedure

Endovascular revascularization was performed after obtaining the informed consent from the patients. All patients received dual antiplatelet medication (aspirin 100 mg and clopidogrel 75 mg) for more than 5 days before undergoing the procedure. After femoral or radial artery puncture, all patients were heparinized to achieve an activated clotting time of >250 s. After a 7F or 8F 80cm long sheath (Flexo, Cook Inc) was inserted into the femoral artery, a coaxial system of long sheath, 5F 100-125cm diagnostic catheter (Tempo, Cordis or JR4.0, Medtronic) and 0.035-inch guidewire (Glidewire, Terumo) were inserted into the left or right subclavian artery proximal till the vertebral artery ostium. In order to keep the system steady, a 0.018-inch sturdy guidewire (V-18, Boston Scientific) was inserted between the sheath and the diagnostic catheter as a supportive wire into the ipsilateral brachial artery. Coaxial assembly of microwire (Pilot, Miracle, Conquest *et. al*) and microcatheter (Excelsior SL-10, Stryker Neurovascular) were then advanced carefully. According to the resistance at the microwire tip, the microwire was rotated and turned in the direction of probing in order to smoothly traverse the occluded segment. If the microwire could not enter the distal lumen, then the “parallel wire” technique was considered. If the microwire and microcatheter have passed the occluded segment, then the microwire withdrawal and microcatheter angiography confirms distal lumen. A 0.014-inch exchange of 300cm length microwire (Hi-Torque, Abbott Vascular) was placed, and the microcatheter and diagnostic catheter were moved and exchanged to a 2.0×20mm balloon (Sprinter Legend, Medtronic) for pre-dilation in order to place a distal

embolic protection device (Spider Fx, EV3) successfully. The diameter and length of the occluded vertebral artery were measured by using digital subtraction angiography (DSA). If the occluded length was shorter than 20mm, then a balloon-expandable stent was placed. If not, a serial balloon-expandable stents or combined with self-expandable stent(s) were placed to scaffold the occlusion according to the diameter and length, and the number of stents should be less than 3. Finally, the stent delivery catheter and protection device were carefully retracted (Figure 1). If the attempts were repeated, the microwire and microcatheter could not pass the occluded segment and enter the distal true lumen, stopping the procedure.

Post-intervention and follow up

After the endovascular procedure, patients were monitored by placing them in the neurological stroke unit for 24 hours. All patients, except who had failed endovascular revascularization received dual antiplatelet therapy for at least 6 months after the procedure, thereafter continuing with only 100 mg aspirin per day. The clinical and radiological follow-ups were scheduled at 1, 3, 6, and 12 months after the procedure.

Illustrative case

A 56-year-old man with a history of hypertension and diabetes presented to our hospital with diplopia. Brain MRI was negative for detecting infarction in posterior

circulation. Neck CT angiography revealed occlusion of the right vertebral artery during its origin, and the left vertebral artery was hypoplastic. He was placed on aspirin 100mg daily, clopidogrel 75mg daily and rosuvastatin 10mg every night. Two months later, the patient had blurred vision and weakness in the right side limbs. Neurological examinations revealed bilateral right homonymous hemianopia, and muscular strength of 2/5 in the right limbs. Brain MRI demonstrated acute infarction in left thalamus and bilateral occipital lobes. Finally, DSA and endovascular revascularization were successfully performed. The patient was discharged home and prescribed aspirin 100mg daily and clopidogrel 75mg daily for at least 9 months, and then with aspirin 100mg daily. At 5-year follow-up, the patient did not report any ischemic events, and the modified Rankin scale (mRS) score was 1, the brain MRI did not reveal any new infarctions and the CTA revealed mild re-stenosis in the stent (Figure 2).

Statistical analysis

Descriptive statistics were performed and presented as means, standard deviations, percentages, and ranges. The analysis was carried out using IBM SPSS Statistics for Windows, Version 24.0.

Results

A total of 23 patients (17 men) were enrolled, with a mean age of 59 years old (42-77 years old). Among the patients, 18 patients had hypertension, 10 patients had diabetes, and 3 patients had hyperlipidemia. All patients underwent the procedure through transfemoral approach, except 1 patient who underwent the procedure through transradial route, and 1 patient underwent through transfemoral and transradial approaches. Endovascular revascularization for PEVAO has been succeeded in 21 patients. Two patients failed as the microwire could not enter the distal true lumen. Distal protection device has been used in 20 patients and thrombosis was seen in 6 distal protection devices by the naked eye. There were no neither wire-induced vascular perforations nor vessel ruptures during the procedures. However, acute stent thrombosis and basilar artery embolism were seen in 1 patient (i.e., case 5), and the patient was treated using intra-arterial recombinant tissue plasminogen activator and tirofiban thrombolysis, but postoperative brainstem hemorrhage occurred and the patient died after 72 hours. No new neurologic deficits occurred in remaining 22 patients during the peri-procedure period. During the 3-month follow-up period, no ischemic episode occurred in 20 patients who underwent successful revascularization. The recanalized vertebral arteries were patented without restenosis in 20 patients who underwent CTA.

Discussion

Over the last several decades, bypass surgery is regarded as a useful method for

patients with posterior circulation ischemia caused by PEVAO. The bypass method included: occipital artery to the V3 segment, occipital artery to the posterior inferior cerebellar artery, the occipital artery to the anterior inferior cerebellar artery, the external carotid artery to the V2 segment and so on. The procedure of bypass is complex and time consuming, and the complications associated with different bypass methods included: vocal cord paralysis, laryngeal nerve palsy, accessory nerve palsy, superficial wound infection, upper brachial plexus weakness, Horner's syndrome, and so on.[9,19]

Endovascular revascularization is less invasive and is increasingly used in chronic total occlusions of the coronary artery. However, the role of endovascular intervention in non-acute symptomatic PEVAO requries further elucidation. Our study demonstrated that the technical success rate was 91.3% and perioperative complication rate was 4.3% using endovascular revascularization in treating patients with posterior circulation ischemia caused due to PEVAO. Therefore, endovascular revascularization might seem to be a promising strategy for selective patients and experienced interventional physicians.

To perform the procedure, there are major concerns regarding patient selection, the unsteady supporting system, inability to traverse the occluded segment and distal embolization. Therefore, the following important technical strategies should also be

taken into consideration.

It is extremely important initially to perform a systematic pre-procedural evaluation for identifying proper patients and lesion characteristics that imply high success rates. In theory and clinical practice, a tapered stump of the occlusion, a short and straight occlusion length, mild or absence of calcification and distally patented lumen with collateral filling from the branches are considered as predictors of technical success in endovascular treatment for chronic total occlusion.[20-22]

Second, the steady supporting system is crucial during the procedure, and the supporting system might be unsteady because of the short distance between the innominate artery and the vertebral artery ostium and resistance due to microwire manipulation. A variety of techniques have been used to obtain stability of the supporting system. An 8 F long sheath, a 5F diagnostic catheter in the subclavian artery and an additional sturdy guidewire were selected for insertion between the sheath and diagnostic catheter into the ipsilateral brachial artery. The advantage of the supporting system is to provide a stable platform and retention of the ability to manipulate the microwire and angulate the head of diagnostic catheter in the subclavian artery for performing revascularization procedures. Moreover, the steady supporting system is the key to successful recovery of distal protection device.

Third, it is important to select the proper microwire for crossing the occluded segment to the distal vessel. The soft tip, polymer-jacketed tapered microwire is the most commonly chosen one for crossing, and if it fails to cross, then a stiff, polymer-jacketed wire or a stiff, tapered wire could be used. After crossing the proximal cap, soft tip polymer-jacketed wire can be used to direct the microwire into the distal true lumen. If the microwire enters the subintimal space, then the re-entry to the true lumen was achieved by using a “parallel wire” technique.

Fourth, the protective device more critically assists in reducing the posterior circulation embolic events. The posterior circulation embolization is the most concerned as it may lead to severe disability and death during the procedure. As Iwata et al [11] have first reported the use of combination technique of reverse flow and downstream filtering in endovascular revascularization of PEVAO, many other clinicians have used different protecting devices, such as distal balloon, Spider FX and so on. In our study, 20 patients have used distal protection devices Spider FX to effectively prevent embolisms, and none of the patients experienced posterior circulation stroke.

Last but not the least, it is extremely important to know when to quit. Not every patient could undergo such a procedure successfully and not every lesion could be treated with endovascular technique. If the risk associated with endovascular

revascularization remains too high or if the potential for success is too low, other alternatives (such as bypass surgery) should be considered. Therefore, to reduce the complications, three rules such as the procedure time of less than 3 hours; the maximal contrast and the radical dose should be vitally followed.[23,24]

Limitations

The present study has some limitations due to its retrospective nature, nonrandomized, single-center design and small sample size. Besides, the follow-up period is short, and the imaging modality involved is the noninvasive CTA. Also a longer follow-up period is warranted in future. These limitations reflect the need for further research in this area.

Conclusions

Endovascular revascularization of non-acute symptomatic PEVAO is feasible and is associated with high rate of procedural success with minimal procedural complications. A large, multi-center, randomized study is warranted to further confirm these findings.

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Conflict of interest disclosure: The authors declared no conflicts of interest.

Figure legends:

Figure 1: Diagram showing the endovascular revascularization process

A, proximal extracranial vertebral artery occlusion; B, placement of steady supporting system; C, the microwire and the microcather tried to pass through the occluded segment; D, small balloon pre-dilation; E, placement of Spider FX; F, balloon expansion, G, stent placement; and H, the last morphology.

Figure 2:

A, DSA showed right proximal vertebral artery occlusion and the stump is blunt; B and C, Post successful stenting; D, 5-years later, and the CTA showed mild restenosis in the stent.

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Table 1: Summary of patients with endovascular revascularization

Patient No	Gender	Age	Presented symptoms	Risk factor	Diagnosis (PCI)	NIHSS	mRS
1	Male	52	Dizziness, blurred vision, dysarthria	Hypertension	Ischemic stroke	3	2
2	Male	56	Dizziness and blurred vision	Hypertension, DM	Ischemic stroke	4	1
3	Male	49	Dizziness and dysarthria	Hypertension	TIA	8	2
4	Female	52	Dizziness	Hypertension, DM hyperlipidemia	Ischemic stroke	0	1
5	Male	71	Dizziness	Hypertension	TIA	0	1
6	Female	47	Dizziness and blurred vision	Hypertension, DM	Ischemic stroke	2	1
7	Male	77	Dizziness and fatigue	Hypertension	Ischemic stroke	5	2
8	Male	44	Right side limbs numbness	DM	Ischemic stroke	1	1
9	Male	69	Dizziness	Hypertension	TIA	0	1
10	Male	66	Dizziness	Hypertension, DM, hyperlipidemia	TIA	0	1
11	Male	49	Dizziness, blurred vision and left limbs weakness	Hypertension	Ischemic stroke	6	2
12	Male	75	Dizziness	Hypertension	TIA	0	1
13	Male	62	Dizziness and left limb numbness	Hyperlipidemia	Ischemic stroke	0	1

14	Female	70	Dizziness	DM	TIA	0	1
15	Male	61	Cerebellar ataxia	Hypertension	Ischemic stroke	1	2
16	Male	56	Dizziness	Hypertension, DM	TIA	0	1
17	Female	64	Blurred vision	Hypertension	Ischemic stroke	1	1
18	Male	61	Dysarthria	Hypertension, DM	Ischemic stroke	2	2
19	Male	42	Lightheadness and fatigue	Hypertension	Ischemic stroke	2	2
20	Male	51	Episode of disturbance of consciousness	DM	TIA	0	1
21	Male	64	Hemianopia	Hypertension	Ischemic stroke	2	1
22	Female	61	Cerebellar ataxia	DM	Ischemic stroke	1	2
23	Female	63	Right side limbs numbness	Hypertension	Ischemic stroke	1	1

DM: diabetes mellitus; TIA: transient ischemic attack

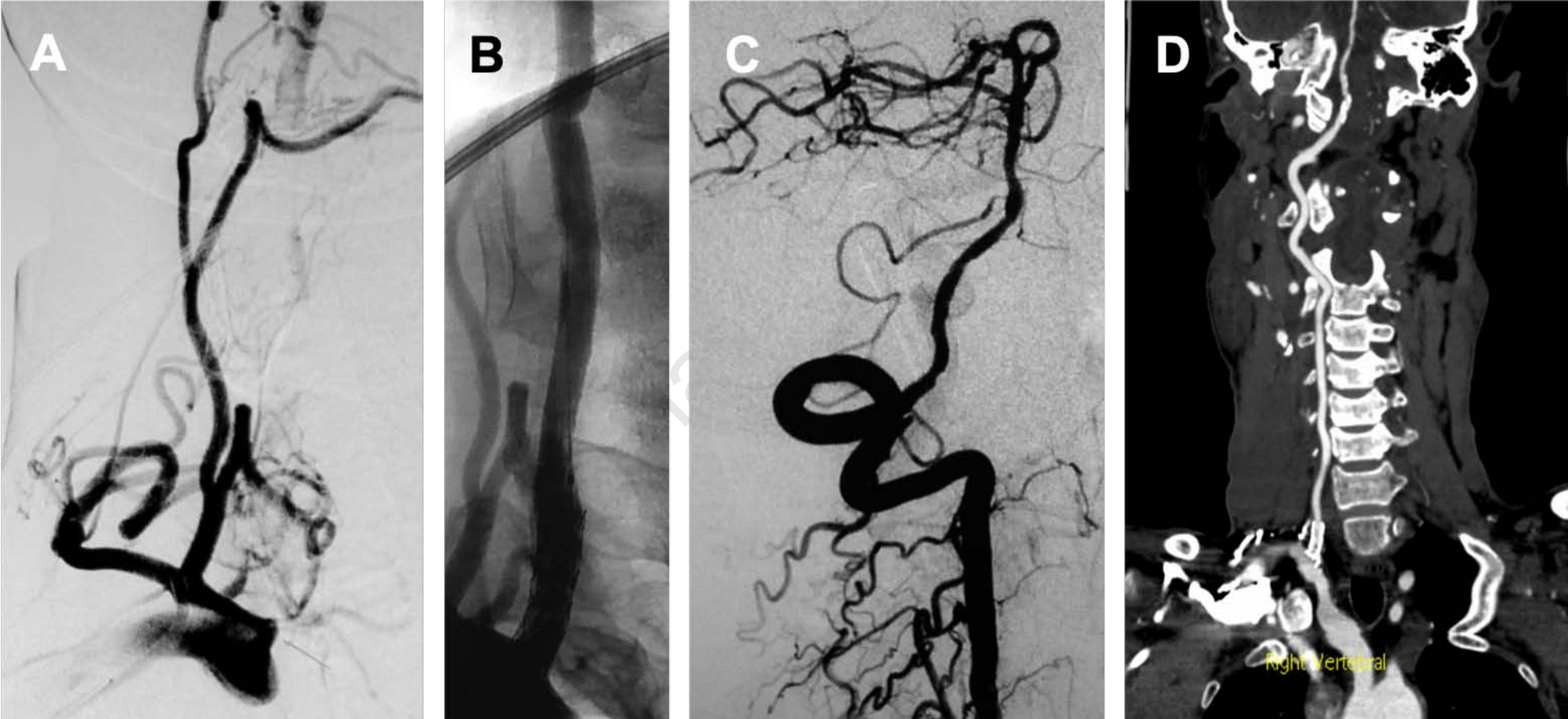
Patient No	Treat side	Contralateral side	Success	Microwire Selection	Distal protection	Embolism in protection	Complication
1	R	Hypoplastic	Yes	Synchro	Yes	No	No
2	R	Occluded	Yes	Pilot 150	Yes	No	No
3	R	Hypoplastic	Yes	Pilot 150	Yes	Yes	No
4	R	Hypoplastic	Yes	Pilot 150	Yes	No	No
5	R	Hypoplastic	Yes	Pilot 50	Yes	No	Acute stent thrombosis
6	L	Hypoplastic	Yes	Pilot 50	Yes	No	No
7	L	Normal	Yes	Pilot 50	Yes	No	No
8	R	Occluded	Yes	Pilot 200, Conquest, Miracle 12	Yes	Yes	No
9	L	Hypoplastic	Yes	Pilot150, Miracle 12, Conquest,	Yes	Yes	No
10	R	Hypoplastic	Yes	Pilot 50, Synchro, Miracle 3	Yes	No	No
11	R	Hypoplastic	Yes	Pilot 50	Yes	No	No
12	R	Occluded	Yes	Pilot 50, Miracle 3	Yes	No	No
13	L	Occluded	Yes	Pilot 150, Miracle 12, Conquest	Yes	Yes	No
14	L	Hypoplastic	Yes	Synchro, Miracle 3	Yes	No	No
15	L	Occluded	Yes	Pilot 150	Yes	No	No

16	R	Hypoplastic	Yes	Pilot 50, Miracle 3	Yes	Yes	No
17	R	Hypoplastic	No	Pilot 150, Miracle 12, Conquest	No	-	No
18	R	Occluded	Yes	Pilot 50, Miracle 3	Yes	No	No
19	L	Hypoplastic	Yes	Pilot 150, Miracle 3	Yes	No	No
20	R	Hypoplastic	Yes	Pilot 150, Miracle 12, Conquest	Yes	No	No
21	R	Hypoplastic	Yes	Pilot 150	Yes	No	No
22	R	Occluded	Yes	Pilot 150, Miracle 12, Conquest	Yes	Yes	No
23	R	Occluded	No	Pilot 150, Miracle 12, Conquest	No	-	No

Note: Distal protection devices: Spider.

Abbreviations

PEVAO Proximal extracranial vertebral artery occlusion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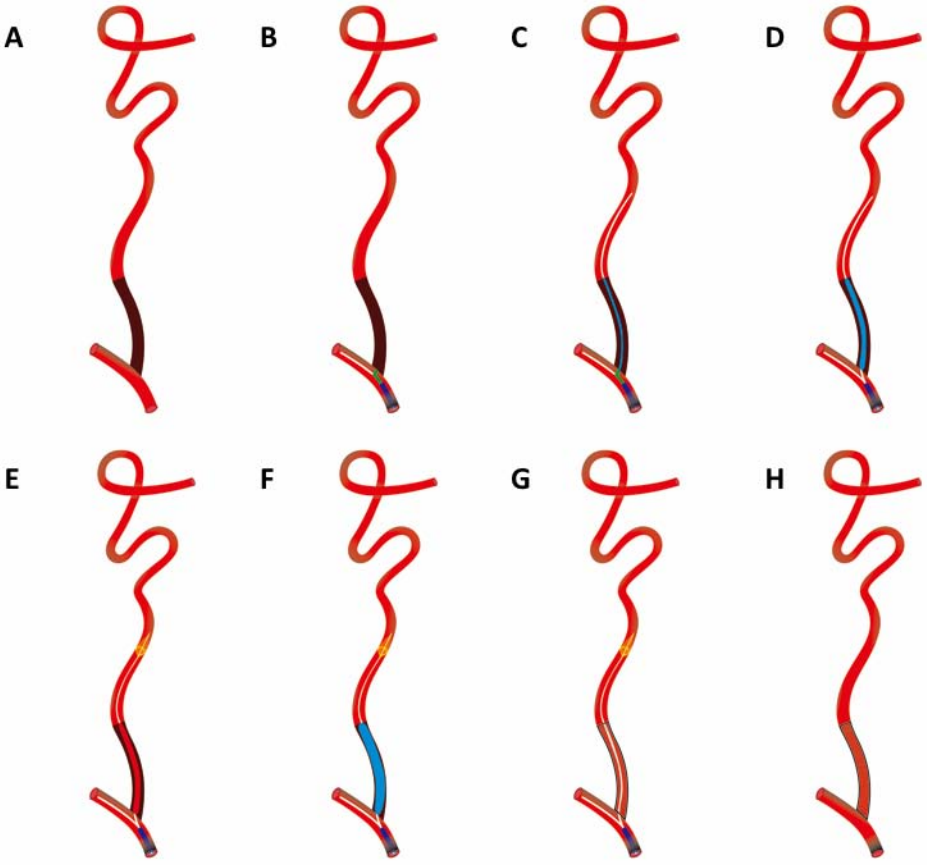
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