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Comprehensive classifications for the endovascular recanalization of vertebral artery stump syndrome

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ABSTRACT

Background: and purpose: To share our single-center vertebral artery stump syndrome (VASS) treatment experience and assess the role of comprehensive classification based on anatomic development, proximal conditions, and distal conditions (PAD).

Materials and methods: Data were retrospectively collected from patients who underwent endovascular thrombectomy (EVT) at the Stroke Center of the First Hospital of Jilin University between January 2016 and December 2021. Among patients with acute ischemic stroke in the posterior circulation, those with acute occlusion of the intracranial arteries and occlusion at the origin of the vertebral artery confirmed by digital subtraction angiography were selected. The clinical data were summarized and analyzed.

Results: Fifteen patients with VASS were enrolled in the study. The overall success rate of surgical recanalization was 80%. The successful proximal recanalization rate was 70.6%, and the recanalization rates for P1, P2, P3, and P4 were 100%, 71.4%, 50%, and 66.67%, respectively. The mean operation times for the A1 and A2 types were 124 and 120 min, respectively. The successful distal recanalization rate was 91.7%, and the recanalization rates for types D1, D2, D3, and D4 were 100%, 83.3%, 100%, and 100%, respectively. Five patients experienced perioperative complications (incidence rate: 33.3%). Distal embolism occurred in three patients (incidence rate: 20%). No dissection or subarachnoid hemorrhage occurred in any patient.

Conclusion: EVT is a technically feasible treatment for VASS, and comprehensive PAD classification can, to a certain extent, help initially estimate the difficulty of surgery and provide guidance for interventional procedures.

1. Introduction

In 2018, Hasan classified chronic internal carotid artery occlusion lesions based on the shape of the occluded vessels and compensation of the distal blood flow, which helped guide interventional surgery for recanalization.[1] Recently, angiographic classifications of intracranial occlusive lesions of the vertebral, middle cerebral, and carotid arteries, and extracranial occlusive lesions of the vertebral artery have been successively proposed using similar methods.[2–5] These have an important guiding role in selective surgery for neurointerventional endovascular revascularization. However, there is currently no angiographic classification for patients with acute ischemic stroke with posterior circulation tandem lesions.

Vertebral artery stump syndrome (VASS) is an acute ischemic event of the posterior circulation that occurs long after vertebral artery occlusion.[6] A previous study reported a 1.4% prevalence of VASS.[7] Traditionally, medication is the mainstay of treatment for VASS.[6–9] However, under the new diagnostic criteria for VASS, it is considered an embolic event involving large distal vessels, and endovascular thrombectomy (EVT) may be the most effective treatment method.[10] Actually, only a few previously reported cases of VASS are true VASS. In our previous study, which included most patients with VASS (n = 11), we found that VASS was common (11/211). [10] In patients with basilar artery occlusion, the proportion of tandem lesions is reportedly higher (24.6%).[11]Longer operative time and lower recanalization rates have been reported for tandem lesions than for basilar artery occlusion alone.[11,12] Therefore, angiographic classification of VASS is necessary to better assess the difficulty of surgery and guide the surgical strategy.

Based on the surgeon's perspective and the overall surgical process, we propose an anatomical development (A) classification to choose the

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approach, a proximal (P) classification to evaluate the difficulty of passing through the occluded vertebral artery, and a distal (D) classification to assess the difficulty of intracranial vascular thrombectomy. To facilitate the memory of classification, we placed A in the central position and named this the PAD comprehensive classification.

2. Materials and Methods

2.1. Patients

We retrospectively collected the medical records of 371 patients with acute ischemic stroke of the posterior circulation who underwent EVT at the Stroke Center of the First Hospital of Jilin University between January 2016 and December 2021. Patients were screened according to the selection criteria based on previously published articles.[10] The study design was approved by the appropriate ethics review board. The requirement for patient informed consent was waived for this retrospective study.

2.2. Surgical procedure and angiographic classification of VASS

The VASS procedure was performed as previously described (10). Comprehensive PAD classification was performed based on the presence or absence of a proximal (P) stump and regurgitation of compensatory

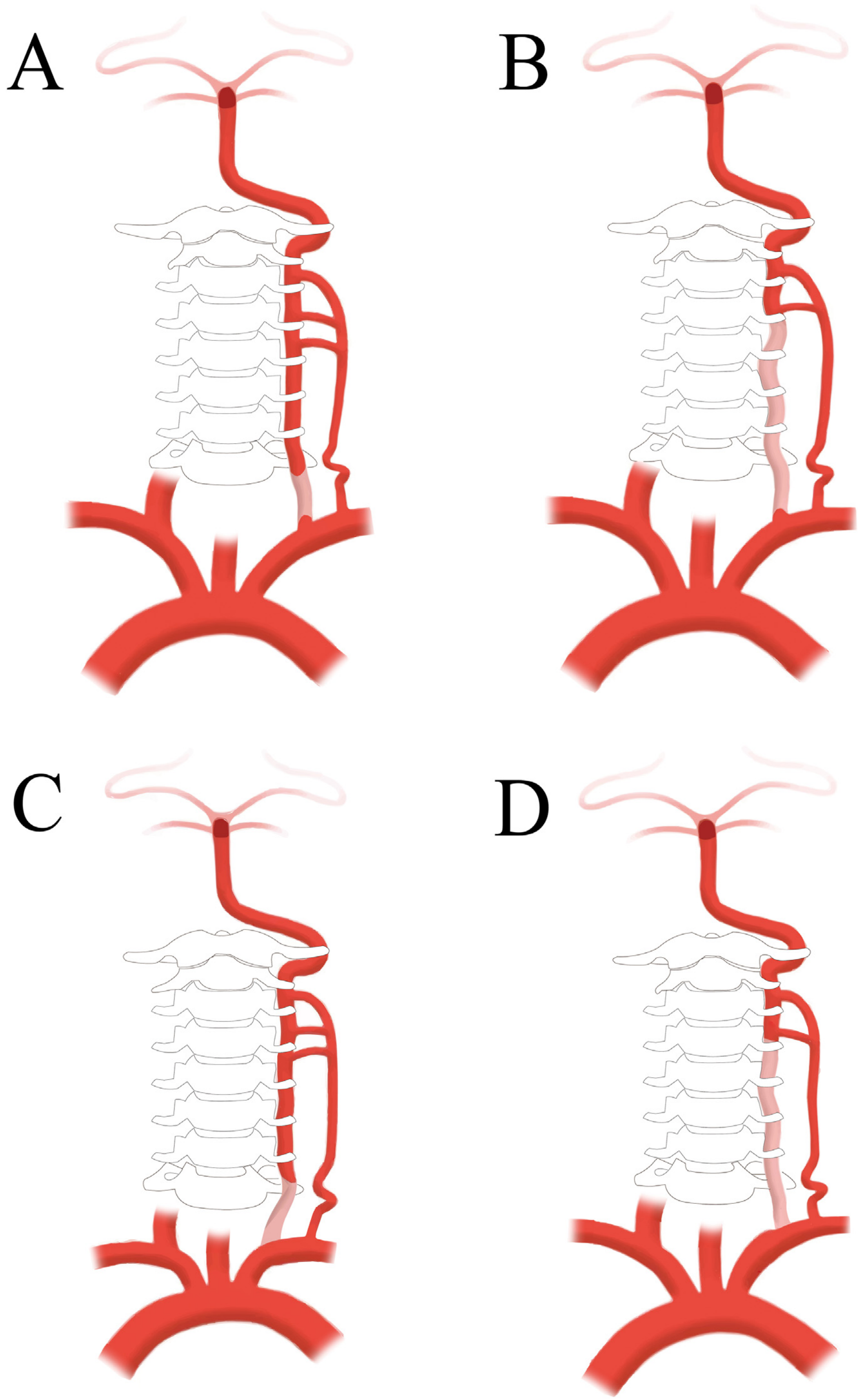

Fig. 1. Illustration of the proximal angiographic classification of vertebral artery stump syndrome.
(A) Type I: the stump exists and the compensatory blood flow can flow back to the level of the lower edge of the fifth cervical cone. (B) Type II: The stump exists, and the compensatory blood flow cannot flow back to the level of the lower edge of the fifth cervical cone. (C) Type III: The stump does not exist, but the compensatory blood flow can flow back to the level of the lower edge of the fifth vertebral body. (D) Type IV: The stump does not exist, and the compensatory blood flow cannot flow back to the level of the lower edge of the fifth cervical cone.

blood flow, anatomical (A) development of the bilateral vertebral arteries, and distal (D) thrombus load and tortuosity of the V4 segment of the vertebral artery on digital subtraction angiography images. VASS was classified into the following four types according to the presence or absence of the proximal (P) stump and regurgitation of compensatory blood flow: I) the stump exists, and the compensatory blood flow can flow back to the level of the lower edge of the fifth cervical cone; II) the stump exists, and the compensatory blood flow cannot flow back to the level of the lower edge of the fifth cervical cone; III) the stump does not exist, but the compensatory blood flow can flow back to the level of the lower edge of the fifth vertebral body; IV) the stump does not exist, and the compensatory blood flow cannot flow back to the level of the lower edge of the fifth cervical cone (Fig. 1). VASS was classified into two types according to the anatomical (A) development of the bilateral vertebral arteries: I) both vertebral arteries are anatomically normal with bilateral occlusion at the beginning of the vertebral artery, or one vertebral artery is anatomically normal but occluded at the beginning, and the other is hypoplastic; and II) normal anatomical development of both vertebral arteries, one of which is occluded at the beginning of the vertebral artery and the other is patent (Fig. 2). VASS was classified into four types

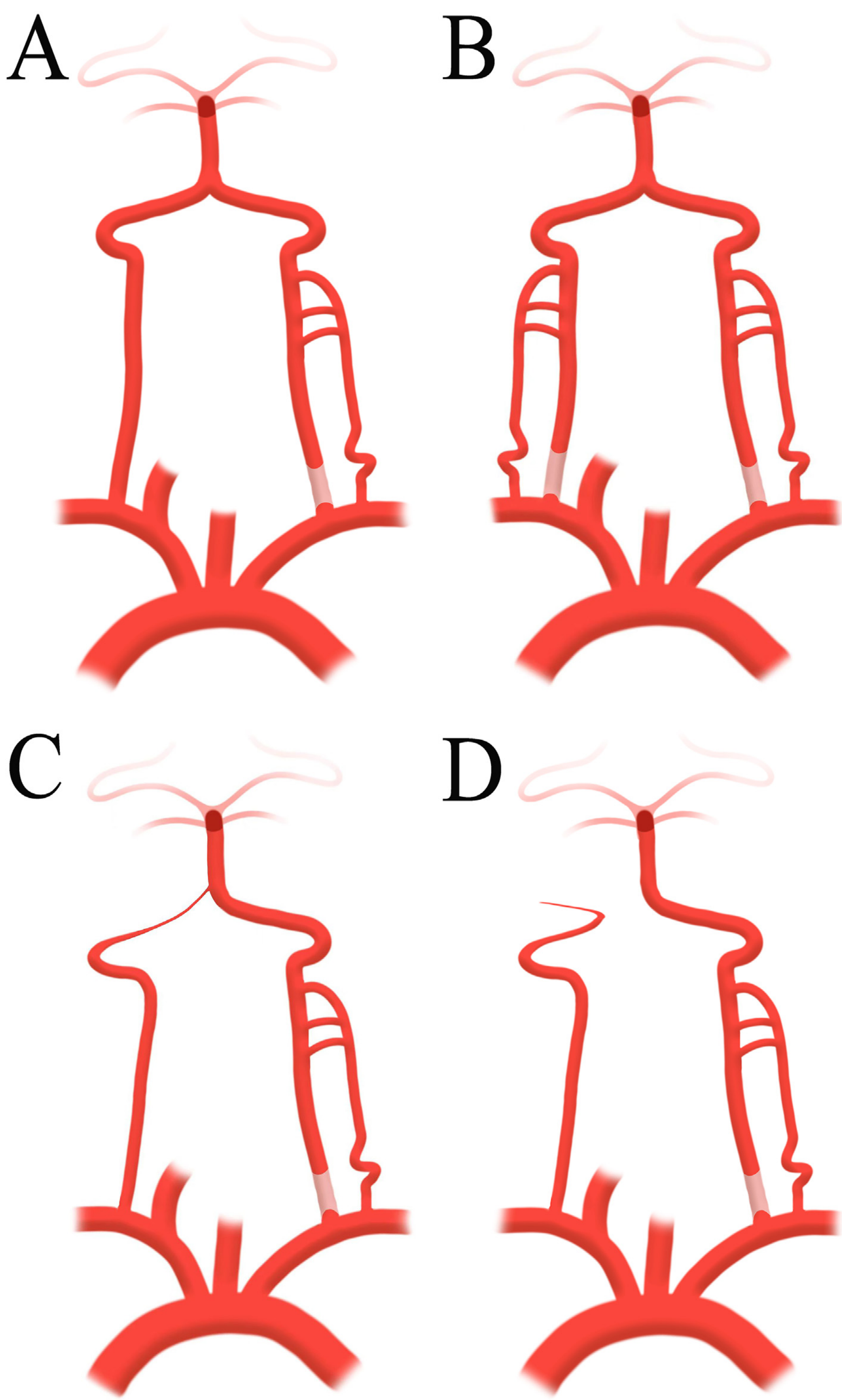

Fig. 2. Illustration of the anatomical angiographic classification of vertebral artery stump syndrome. (A) Type II, Normal anatomical development of both vertebral arteries, one of which is occluded at the beginning of the vertebral artery and the other is patent. B, (B)-(D) Type I: Both vertebral arteries are anatomically normal with bilateral occlusion at the beginning of the vertebral artery, or one vertebral artery is anatomically normal but occluded at the beginning and the other is hypoplastic.

according to the tortuosity of the V4 segment of the vertebral artery and the load of the distal (D) thrombus: I) the V4 segment is without severe tortuosity (angle >135°) and without large-load thrombus (single thrombus length ≤10 mm or the sum of the lengths of multiple thrombi ≤10 mm as determined by intraoperative imaging); II) the V4 segment of the vertebral artery is without severe tortuosity but with large-load thrombus (single thrombus length >10 mm or the sum of the lengths of multiple thrombi >10 mm as determined by intraoperative imaging); III) the V4 segment of the vertebral artery has severe tortuosity (angle ≤135°) but without large-load thrombus; and IV) severe tortuosity of the V4 segment of the vertebral artery with a large-volume thrombus (Fig. 3). The images of the comprehensive PAD classifications in digital subtraction angiography are shown in Figs. 4–6.

2.3. Outcomes

The primary outcomes of the study were as follows: successful recanalization of the distal vessels, defined as modified thrombolysis in cerebral infarction (mTICI) ≥2b; and successful recanalization of the proximal vessels, defined as residual stenosis of <50% post-treatment. The secondary outcomes were the number of passes, operative time, and complication rate.

3. Results

3.1. Baseline characteristics and surgery information

Among the 15 patients included, one was female, 14 were male, and the mean age was 65.7 (range, 45–79) years. Except for one patient who underwent intracranial artery embolization in the posterior cerebral artery, all patients underwent embolization at the basilar artery. Two patients (nos. 3 and 6) had bilateral occlusion of the vertebral artery origin. Of the 17 occluded vertebral arteries, nine were left occluded. The posterior communicating artery was open in eight of the 15 patients. Based on the P classification, there were three (17.6%), seven (41.2%), four (23.5%), and three (17.6%) cases of types I, II, III, and IV, respectively. Based on the type A classification, fourteen cases (93.3%) were type I and one (6.6%) was type II. According to the D classification, there were six (35.3%), seven (41.2%), two (11.8%) cases of types I, II, III, and IV, respectively (Table 1).

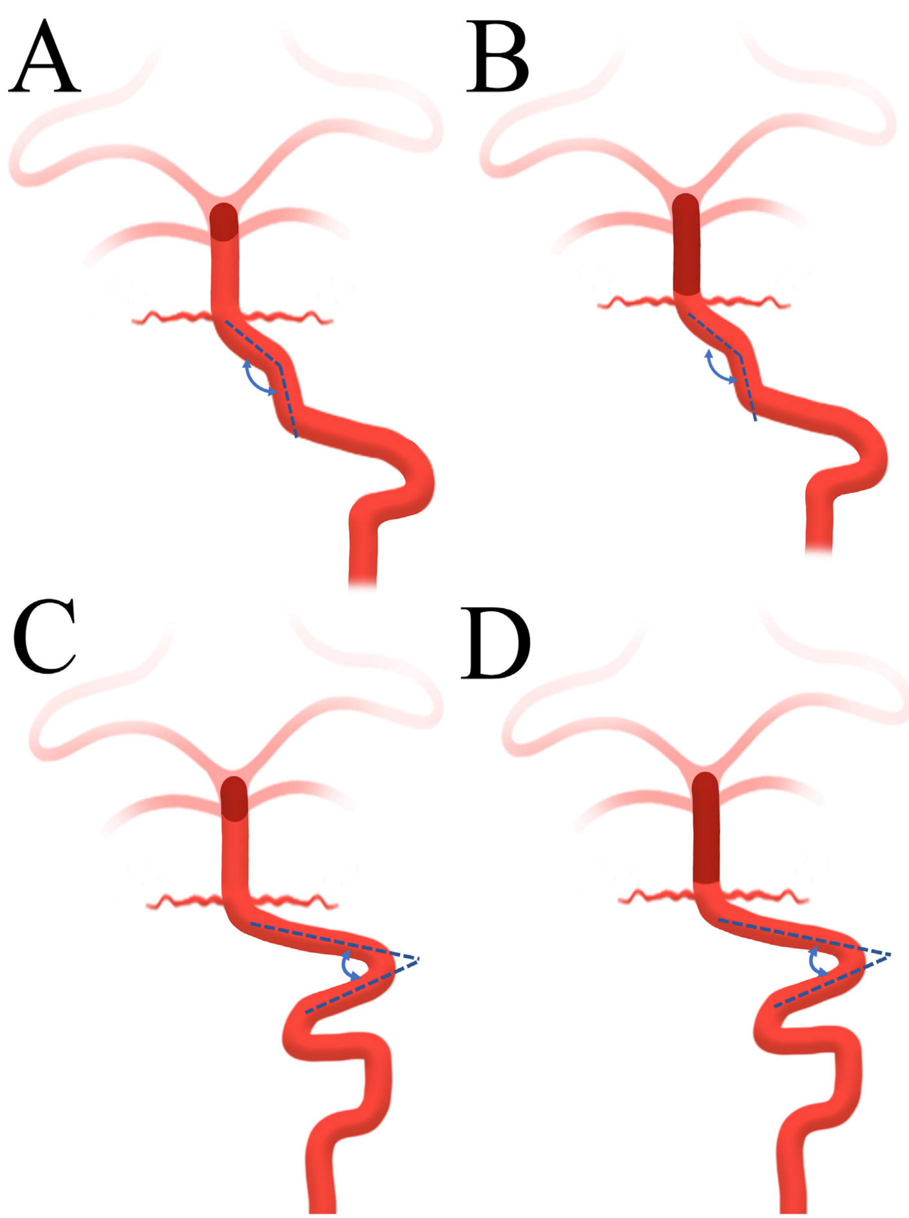

Fig. 3. Illustration of the distal angiographic classification of vertebral artery stump syndrome. (A) Type I: V4 segment without severe tortuosity (angle >135°) and large-load thrombus (thrombus length≤10 mm). (B) Type II: the V4 segment of the vertebral artery without severe tortuosity but with a large-load thrombus (thrombus length >10 mm). (C) type III: the V4 segment of the vertebral artery has severe tortuosity (angle≤135°) without a large-load thrombus. (D) Type IV: severe tortuosity of the V4 segment of the vertebral artery with a large-volume thrombus.

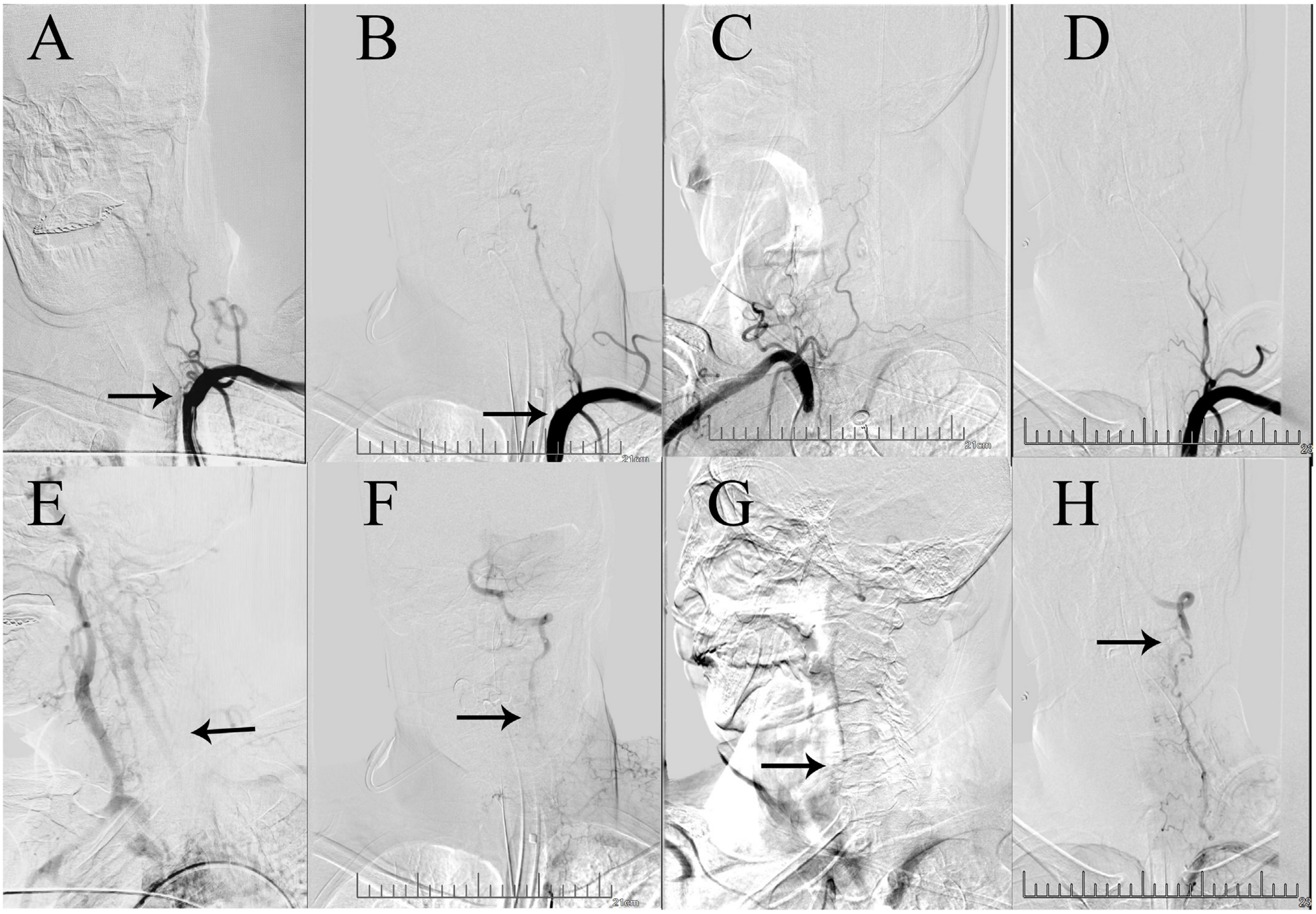

Fig. 4. Proximal angiographic classification of vertebral artery stump syndrome.
(A)-(D) show the morphology of the vertebral artery stump. (E)-(H) show regurgitation of the vertebral artery. (A) and (E) show Type I in the proximal classification, B and F show Type II in the proximal classification, (C) and (G) show Type III in the proximal classification, and (D) and (H) show Type IV in the proximal classification.

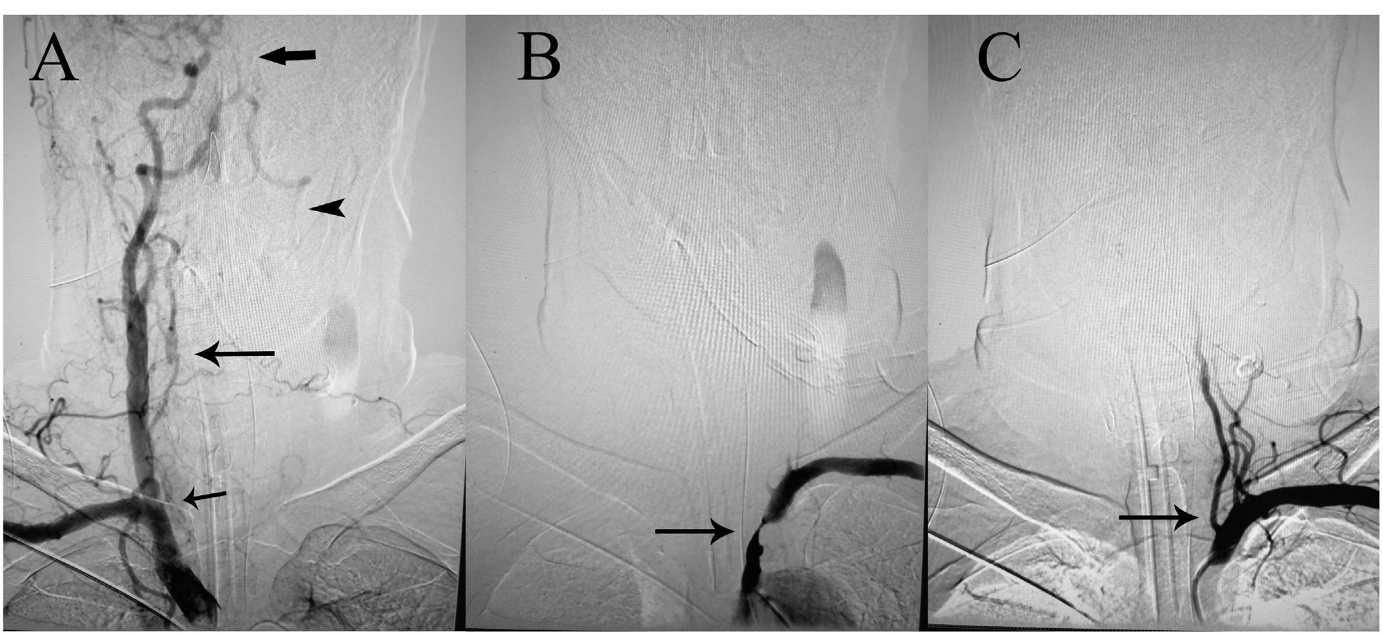

Fig. 5. Anatomical and developmental classification of vertebral artery stump syndrome Angiographic image of patient 10. (A) shows occlusion at the origin of the right vertebral artery (short arrow), vertebral artery regurgitation to mid-V2 (long arrow), basilar artery occlusion (thick arrow), and left vertebral artery steal (arrowhead); (B) shows severe stenosis of the left subclavian artery (arrow); (C) shows normal development of the left vertebral artery (arrow).

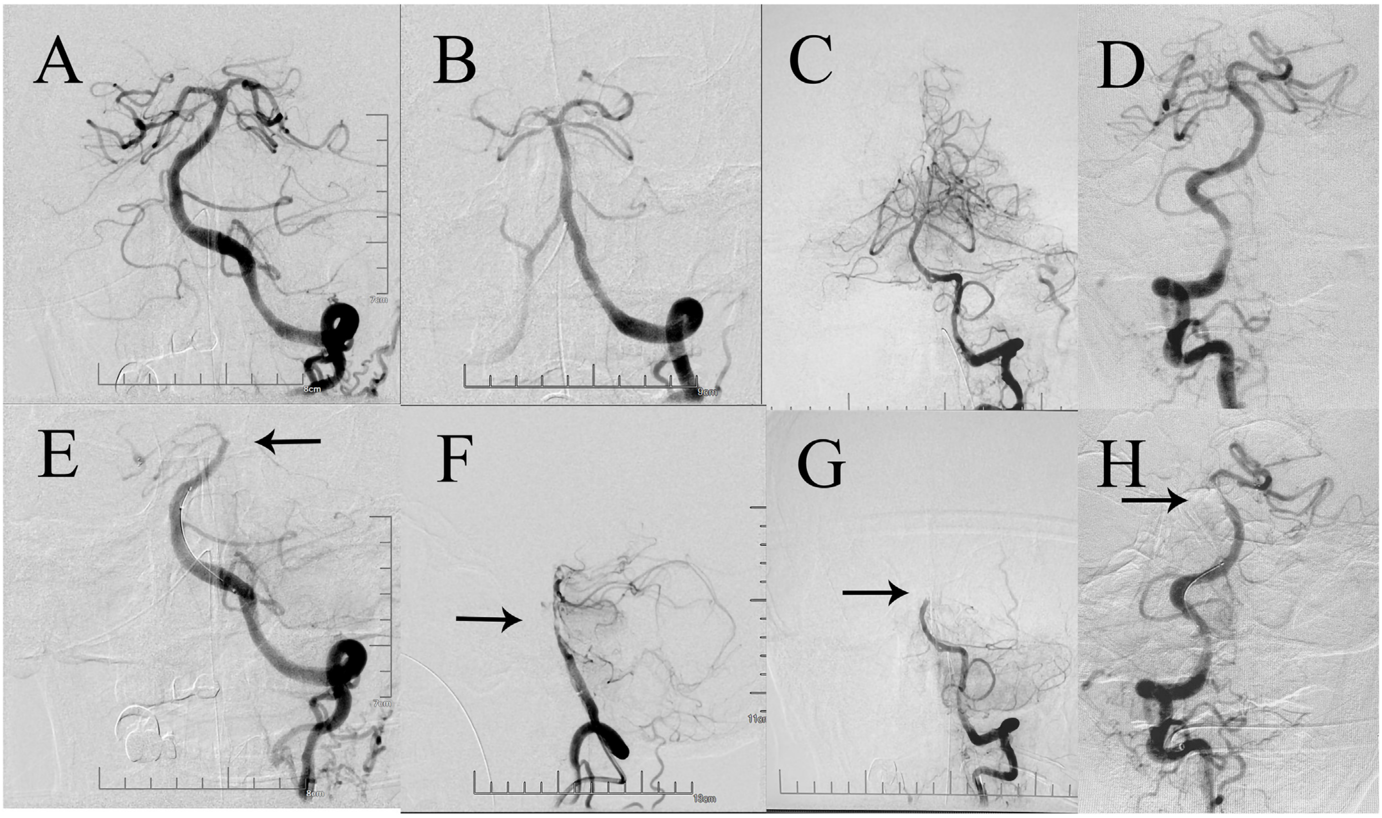

Fig. 6. Distal angiographic classification of vertebral artery stump syndrome.
(A)-(D) show the tortuosity of the V4 segment of the vertebral artery; (E)-(H) show the thrombus burden; (A) and (E) show type I in the distal classification; (B) and (F) show type II in the distal classification; (C) and (G) show type III in the distal classification; and (D) and (H) show type IV in the distal classification.

In five of the 17 occluded vertebral arteries, the guidewires could not be passed at the occlusion site. Among the 12 vertebral arteries that were passable by the microguidewire nine were stented at the beginning of the vertebral artery (75%). In patient 15, the left approach was chosen because the right vertebral artery stump could not be passed through. Owing to severe stenosis of the left subclavian artery, one stent was implanted in the proximal subclavian artery following distal thrombectomy. Among the 15 patients, three chose arterial thrombolysis (20%), while 12 underwent mechanical thrombectomy (80%). Fourteen stent retrievers were used in 12 patients who underwent distal thrombectomy. The double-stent thrombectomy technique was used in two patients (Nos. 4 and 12) (Table 1).

3.2. Outcomes

The acutely occluded arteries were successfully recanalized in 12 of the 15 patients (80%). In 12 of the 17 occluded vertebral arteries, occlusion recanalization was achieved (70.6%), and the recanalization rates were 100% (3/3), 71.4% (5/7), 50% (2/4), and 66.67% (2/3) for P1, P2, P3, and P4, respectively. Eleven patients underwent mechanical thrombectomy of the intracranial arteries through 12 vertebral arteries, with a success rate of 91.7%, including a recanalization rate of 100% (3/3), 83.3% (5/6), 100% (1/1), and 100% (2/2) for D1, D2, D3, and D4, respectively. The mean operative time was 123.6 (range, 80–180) min in the 11 patients who underwent distal thrombectomy, 124 min (range, 80–180)min) for type A1, and 120 min for type A2 (Table 2).

Eleven patients underwent distal thrombectomy through 12 vertebral arteries, and the mean number of passes was 2.1 (range, 1–4), including mean pass numbers of 2.3, 1.3, 1, and 3.5 for D1, D2, D3, and D4, respectively. Five patients (33.3%) developed perioperative complications. Distal embolisms occurred in three of these patients (20%).

The incidence of complications on D1, D2, D3, and D4 was 33.3%, 33.3%, 100%, and 50%, respectively. No dissection or subarachnoid hemorrhage occurred in any patient (Table 2).

4. Discussion

VASS is a posterior circulation ischemic event that occurs long-term following vertebral artery occlusion.[6] According to previously proposed diagnostic criteria, VASS is an embolic event of the intracranial artery in the posterior circulation following vertebral artery occlusion.[10] Therefore, EVT is considered the most direct and effective treatment modality. However, as a special tandem lesion, VASS makes surgery more difficult. To assess the degree of surgical difficulty and better guide surgery, we proposed a preliminary comprehensive PAD classification using the VASS. To the best of our knowledge, this is a novel comprehensive classification of the VASS and tandem lesions.

The Basilar trial is currently the largest clinical study of patients who underwent posterior circulation thrombectomy, and the successful recanalization rate with endovascular therapy was 80.7%. The good prognosis rate was 32%, while the mortality rate was 46.2%.[13] The recanalization success rate in the present study was 80%, with a good prognosis rate of 40% and a mortality rate of 46.7%. The results of the present study are similar to those of the Basilar trial, and endovascular therapy can be considered feasible and effective for patients with VASS.

Emergency thrombectomy should be performed as soon as possible to recanalize occluded vessels and restore blood perfusion in the brain tissue.[14] Based on the special bilateral vertebral artery supply in the posterior circulation, surgeons should first consider the choice of surgical approach. If the contralateral vertebral artery is anatomically well-developed and patent in a patient with VASS, thrombectomy should be chosen first to restore blood flow as soon as possible. In our group of patients, only Patient 13 belonged to type A2. Although the contralateral vertebral artery was anatomically well-developed and patent, the

Table 1
Angiographic characteristic and surgical treatment details of vertebral artery stump syndrome.

NO.	Sex/ Age	Arterial lesion	Contralateral vertebral artery	Vertebral regurgitation	Stump	Stump shape	PComA	Tortuous V4	Massive clots	Approach	Retriever/ Thrombo-lytics	GP IIb/IIIa	Stent/ Balloon (mm)
1	M/ 65	LVAO BAO	Tortuous, V4 slim	LV2 distal segment	+	Bump	Left open	–	–	L	6 × 30 Solitaire FR	N	3.5 × 18 Apollo
2	M/ 63	LVAO BAO	V4 slim	LV2 distal segment	+	Bump	Left open	+	+	L	6 × 30 Solitaire FR	N	4.0 × 19 Express Vascular SD
3	M/ 71	RVAO BAO	Occlusion at the beginning	RV2 middle segment	+	Bump	–	–	–	R	–	N	–
		LVAO		LV2 distal segment	–	Plane	–	–	–	L	–	N	–
4	M/ 64	LVAO BAO	Occlusion after PICA	LV1 segment	–	Plane	–	–	–	L	4.5 × 30 Aperio/6.0 × 30 Solitaire FR	Tirofiban	5.0 × 19 Express Vascular SD
5	M/ 45	LVAO BAO	Occlusion at the beginning, occlusion after PICA	LV1 segment	–	Plane	Both open	–	–	L	600000U urokinase via LICA and 600000U urokinase via LTCA	N	–
6	M/ 71	RVAO BAO LVAO	Occlusion at the beginning	RV2 distal segment	+	Bump	–	–	+	R	6 × 30 Solitaire FR2	Eptifibatide	3.0 × 30 Sterling
				LV2 distal segment	–	Plane	–	–	+	L	6 × 30 Solitaire FR2	Eptifibatide	5.0 × 19 Express Vascular SD
7	F/ 54	LVAO BAO	Inferior, V4 slim	LV2 proximal segment	–	Plane	Right open	–	+	L	4 × 20 Solitaire FR	Tirofiban	3.0 × 30 Sterling
8	M/ 67	RVAO BAO	Inferior, From the aortic arch, slender and tortuous	RV2 proximal segment	–	Plane	Left open	–	+	R	300000U urokinase via LVA	N	–
9	M/ 73	RVAO BAO	Occlusion after PICA	RV2 middle segment	–	Plane	Right open	–	+	R	4 × 20 Solitaire FR	N	4.0 × 23 Apollo
10	M/ 68	RVAO BAO	Inferior	RV2 distal segment	+	Bump	–	–	+	R	6.0 × 30 Solitaire FR	N	4.5 × 15 mm RX Herculink Elite
11	M/ 79	RVAO BAO	Inferior, From the aortic arch, slender and tortuous	RV2 proximal segment	+	Bump	–	–	+	R	6.0 × 30 Solitaire AB	Tirofiban	5.0*20 Drug eluting vertebral artery stent
12	M/ 68	LVAO RPCAO	Inferior, conclusion after entering the skull	LV1 segment	+	Bump	–	+	–	L	200000U urokinase via RPCA	N	5.0 × 15 Express Vascular SD
13	M/ 67	LVAO BAO	Occlusion after entering the skull	LV2 proximal segment	+	Bump	Both open	+	–	L	6 × 30 Solitaire FR	Tirofiban	2.5 × 30 Ultra-soft SV
14	M/ 55	RVAO BAO	Occlusion after PICA	RV2 distal segment	+	Bump	–	+	+	R	6.0 × 30 Solitaire FR/4 × 20 Solitaire FR	Tirofiban	4.0 × 23 Apollo
15	M/ 75	RVAO BAO	Inferior, Steal flow	RV2 middle segment	+	Bump	Right open	+	+	R	6.0 × 40 Aperio	N	9.0 × 39 Omnilink

Abbreviation: PComA, posterior communicating artery; GP IIb/IIIa, Glycoprotein IIb/IIIa; LVAO, left vertebral artery occlusion; RPCAO, right posterior cerebral artery occlusion; RVAO, right vertebral artery occlusion; BAO, basilar artery occlusion; LICA, left internal carotid artery; LTCA, left thyroid carotid artery; PICA, posterior inferior cerebellar artery; LPCAO, left posterior cerebral artery occlusion.

subclavian artery had severe stenosis; therefore, the preferred access route was not the left side, and the left side was chosen for thrombectomy only when the right vertebral artery could not be passed. However, the average surgical time for type A2 was shorter than that for type A1. This is consistent with the findings of Cohen et al., in which the operative time was shorter in patients who underwent the clean approach than in those who underwent the dirty approach.[15]

For EVT of the VASS, the key to the procedure is the successful passage through the occluded vertebral artery. Therefore, we propose a P-type classification based on the presence or absence of a stump and regurgitation of the vertebral artery. This seems to be similar to the classification proposed by Gao et al. [4] However, we did not focus on the morphology of the stump because the occlusion of the proximal vertebral artery in the VASS is longer, mostly chronic, and without significant morphological differences; therefore, we differentiated only according to the presence or absence of the stump. In addition, based on the

Table 2
Endovascular treatment outcomes for vertebral artery stump syndrome.

No.	Type	Distal recanalization	Proximal recanalization	Arterial dissection	Distal embolization	Hyperperfusion	SAH	Pass	PRT (min)
1	P_2 A_1 D_1	+	+	–	–	–	–	1	120
2	P_2 A_1 D_1	+	+	–	–	–	–	2	85
3	P_2 A_1 D_1	–	–	–	–	–	–	0	120
	P_4 A_1 D_1	–	–					0	
4	P_3 A_1 D_1	+	+	–	+	–	–	3 + 1*	180
5	P_3 A_1 D_1	–	–	–	–	–	–	0	145
6	P_2 A_1 D_2	–	+	–	–	–	–	2	130
	P_4 A_1 D_2	+	+					1	
7	P_3 A_1 D_2	+	+	–	+	–	–	1	140
8	P_3 A_1 D_2	–	–	–	–	–	–	0	185
9	P_4 A_1 D_2	+	+	–	–	–	–	1	80
10	P_2 A_1 D_2	+	+	–	–	+	–	2	100
11	P_1 A_1 D_2	+	+	–	–	–	–	1	120
12	P_1 A_1 D_3	+	+	–	–	–	–	0	190
13	P_1 A_1 D_3	+	+	–	+	–	–	1	110
14	P_2 A_1 D_4	+	+	–	–	–	–	3 + 1*	175
15	P_2 A_2 D_4	+	–	–	–	+	–	3	120

Abbreviation: SAH, subarachnoid hemorrhage. *Indicates that the single-stent thrombectomy was performed 3 times, and the double-stent thrombectomy was successfully recanalized once.

regurgitation of the vertebral artery, we can roughly estimate the location of the beginning of the vertebral artery and the length of the occlusion. To implement the classification simply and intuitively during the operation, we did not propose a specific occlusion length to define the classification, as in Gao. However, we used a typical bony landmark, the lower edge of the fifth vertebral body, for the classification. In this group of patients with VASS, the recanalization rates were 100%, 71.4%, 50%, and 66.67% for P1, P2, P3, and P4, respectively. We believe that the reason why the recanalization rate of P4 was higher than that of P3 may be the small sample size in each group. It was observed that the proximal end of the P1 type was the easiest to pass by the guidewire. The presence of the stump allowed the microguidewire to find the point of force smoothly, and a closer regurgitation indicated a shorter occlusion section. Both are favorable for the microguidewire to pass through a vertebral artery occlusion. To increase the stability and passability of the head end, all microguidewires used coaxial technology with different microcatheters. If the microguidewire could not pass through the occluded segment after repeated attempts, we tried a loach guidewire and a stiffened loach guidewire. If it is still unable to pass through the VA-occluded segment after a long attempt, intra-arterial thrombolysis should be selected for remedial treatment or the operation should be ended to avoid serious complications. Some researchers believe that arterial thrombolysis is the last option for treating VASS when the stump is not visible.[16] Of the three patients in our group with proximal non-passage, two chose arterial thrombolysis, one had a good prognosis, and one had a poor prognosis. As rescue therapy, intra-arterial thrombolysis may improve patient outcomes.

Mechanical thrombectomy of occluded vessels in the distal intracranial arteries is the most important procedure. It has been shown that the thrombus load and retrieval route are important factors for successful recanalization.[17,18] Accordingly, we used the thrombus load and tortuosity of the V4 segment of the vertebral artery to perform the D classification for distal thrombectomy. Among the nine patients who underwent distal thrombectomy in this group, only patient 6 underwent bilateral thrombectomy via bilateral approaches. However, the contralateral approach was chosen after two unsuccessful thrombectomies because of the thin diameter of the V4 segment of the right vertebral artery. Consequently, the recanalization rate of D2 was 83.3%.

Regarding the number of passes, the D1, D2, D3, and D4 types had 2.3, 1.3, 1, and 3.5 passes, respectively. Owing to the smaller size of the stent retriever used in patient 4, four thrombectomies were performed, which eventually increased the mean number of thrombectomies for the D1 type. Regardless, the D4 type had the highest number of thrombus retrievals. Tortuous V4 combined with a large-load thrombus inevitably increases the difficulty of thrombus retrieval. In this case, we believe that there are two methods to choose from to achieve occlusion recanalization as soon as possible and reduce the number of mechanical thrombectomies. First, an intermediate catheter can be used during thrombectomy. Compared with the guide catheter, the intermediate catheter can be sent to the V4 segment or even further, and the suction effect can be fully exerted. Studies have shown that the use of an intermediate catheter can increase the success rate of thrombectomy.[19] The other option is the double-stent thrombectomy technique. Several case reports have shown that double-stent thrombectomy is safe and effective.[20–22] Two patients in the present study achieved successful recanalization by choosing the double-stent thrombectomy technique following three thrombectomy failures and no related complications occurred. This technique is also feasible for the VASS. However, the disadvantage is that it not only requires the operator to have considerable experience in interventional surgery, but also increases the cost of surgery.

None of the patients in this group underwent dissection or subarachnoid hemorrhage. Distal embolism (P2 or P3 segments) occurred in only three patients during the operation, and one of the three patients died. Brain herniation due to hyperperfusion was the cause of death. In this study, complications mainly occurred in D3 and D4, and it was found that large thrombus load and tortuous V4 segment made thrombus escape more likely and increased the risk of postoperative hyperperfusion syndrome.Complications such as distal embolism should be tolerated to avoid irreversible and serious complications from perfect recanalization. All patients with distal embolisms were treated with platelet glycoprotein (GP) IIb/IIIa receptor antagonists. Studies have shown that platelet GP IIb/IIIa receptor antagonists can increase the recanalization rate and improve the functional prognosis of patients undergoing thrombectomy.[23]

Our study has some limitations. First, this was a retrospective, single-center clinical study. Although this is the largest number of patients with VASS included to date, the sample size was small, and there was no statistical significance between the different angiographic types. Therefore, prospective studies with larger sample sizes are required to confirm our findings. Second, a good surgical path (including the aortic arch type and subclavian artery angulation)[24] is essential for successful surgery. For simple and intuitive classification, the angiographic classification used in this study did not consider the surgical route. A more detailed classification of the VASS with a larger sample size is required in the future.

5. Conclusions

EVT is a technically feasible treatment for the VASS, and a comprehensive PAD classification can, to a certain extent, initially estimate the difficulty of surgery and provide guidance for interventional procedures.

Author contributions

Wenbin Zhang and Chao Li framed the study concept, analyzed and interpreted the data, and drafted and revised the manuscript. Mingchao Shi contributed to the imaging analysis and offered insightful suggestions for this concept. Jie Zhou, Feixue Yue, and Kangjia Song contributed to data collection and revised the manuscript. Shouchun Wang conceptualized the study, interpreted the data, and revised the manuscript.

Declaration of competing interest

The authors have no potential conflicts of interest to disclose.

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