Approaching the Boundaries of Endovascular Treatment in Acute Ischemic Stroke

Multicenter Experience with Mechanical Thrombectomy in Vertebrobasilar Artery Branch Occlusions

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Abstract

Purpose Little is known about catheter-based endovascular treatment of vertebrobasilar artery branch occlusion (VEBABO) in acute ischemic stroke (AIS). Nonetheless, the experience of mechanical thrombectomy (MT) in distal small sized arteries of the anterior circulation seems promising in AIS. In this multicenter study, we report the feasibility, efficacy and safety of MT in VEBABO.

Methods Retrospective analysis of consecutive AIS patients treated with MT due to VEBABO including posterior and anterior inferior cerebellar artery (PICA, AICA) and superior cerebellar artery (SCA) occlusions at seven tertiary care centers between January 2013 and May 2020. Baseline demographics and angiographic outcomes including recanalization success of the affected cerebellar arteries and procedural complications were recorded. Clinical outcomes were evaluated by the modified Rankin scale (mRS) at discharge and 90 days.

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Results Out of 668 endovascularly treated posterior circulation strokes we identified 16 (0.02%) cases with MT for VEBABO. Most frequently, MT of the SCA was done (13/16, 81%). Most VEBABOs occurred after MT of initial basilar/posterior cerebral artery occlusion (9/16, 56%). In 10/16 (63%) procedures, the affected VEBABO was successfully recanalized. Out of four patients three (75%) with isolated VEBABO had benefited from endovascular therapy. Subarachnoid hemorrhage was observed in 3/16 (19%) procedures. The rate of favorable outcome (mRS ≤2) was 40% at discharge and 47% at 90-day follow-up. Mortality was 13% (2/15).

Conclusion The use of MT for VEBABO is rare but appears to be feasible and effective; however, the comparatively high rate of procedure-related hemorrhage highlights that the indications for MT in these occlusion sites should be carefully weighed up.

Abbreviations

AICA	Anterior inferior cerebellar artery
AIS	Acute ischemic stroke
BA	Basilar artery
CT	Computed tomography
ENT	Emboli of new territory
IQR	Interquartile range
IVT	Intravenous thrombolysis
LVO	Large vessel occlusions
MT	Mechanical thrombectomy
mRS	Modified Rankin score
NIHSS	National Institutes of Health stroke scale
PCA	Posterior cerebral artery
pcASPECTS	Posterior circulation Alberta stroke program early CT score
PICA	Posterior inferior cerebellar artery
SAH	Subarachnoid hemorrhage
SCA	Superior cerebellar artery
TICI	Thrombolysis in cerebral infarction
VEBABO	Vertebrobasilar artery branch occlusion

Background

Mechanical thrombectomy (MT) is the gold standard treatment for acute ischemic stroke (AIS) caused by proximal large vessel occlusion (LVO) in the anterior circulation [1, 2]. With the rapid evolution of endovascular thrombectomy devices and technologies in recent years, catheter-based treatment even in occlusions of distal arteries with smaller vessel diameter have been made possible. Small-sized and medium-sized vessel MT including recanalization beyond the M2 segment or in segments of the anterior cerebral artery proved to be an effective and safe treatment option in AIS [3–5]. Studies analyzing the benefits of endovascular treatment in the posterior circulation are still limited [6]. The devastating effect of basilar artery (BA) occlusions (frequently including disability and death) is known; however, isolated infarcts of vertebrobasilar branches, such as superior cerebellar artery (SCA), anterior inferior cerebellar artery (AICA) or posterior inferior cerebellar artery (PICA), may also lead to significant clinical deficits [7–9]. Thus far, medical treatment with intravenous thrombolysis (IVT) is still regarded as the treatment of choice with respect to arterial branch occlusions of the posterior circulation [8, 9]. The role of endovascular treatment in such occlusions is unclear to date as experience remains scarce. We therefore conducted a multicenter study to report the feasibility, efficacy and safety of MT in vertebrobasilar artery branch occlusions (VEBABO) using modern MT devices and techniques.

Methods

We conducted a retrospective study of patients who were treated endovascularly for AIS caused by LVO in the posterior circulation at seven tertiary care centers between January 2013 and May 2020. We identified all patients who received MT due to vessel occlusions in vertebrobasilar branches including PICA, AICA and SCA. Mechanical thrombectomy of VEBABO was performed primarily in isolated occlusions (on baseline imaging or after fragmentation due to intravenous thrombolysis, IVT), secondarily as a residual occlusion after MT of a BA or posterior cerebral artery (PCA) occlusion, or as result of an embolization to a new territory (ENT). The indications and decision for VEBABO MT was left to the attending neuroradiologist's discretion. Baseline parameters, technical features, angiographic and clinical outcome were noted. The use of different thrombectomy techniques and intra-arterial thrombolysis, were left to the attending neuroradiologist's discretion. Endovascular treatment was performed with approved MT devices, using stent-retrievers or modern aspiration catheters or a combination of both. The patients received IVT according to neurological guidelines. Procedural angiograms were reviewed in the participating centers by an experienced interventional neuroradiologist

(≥4 years). Successful recanalization was defined as complete recanalization and restoration of the target artery with any distal flow. The reperfusion of the whole posterior circulation was measured with the thrombolysis in cerebral infarction (TICI) score. In addition, the rate of postinterventional subarachnoid hemorrhage (SAH), frequency of ENT, and the rate of peri-interventional perforation was recorded. Favorable outcome at discharge and after 90 days was defined as modified Rankin scale (mRS) score 0–2. All NIHSS and mRS grades were assessed by a consultant neurologist.

According to the guidelines of the respective local ethics committee, ethics approval was given when necessary for this anonymous retrospective study, which was conducted in accordance with the Declaration of Helsinki. The patients' consent for treatment was obtained (if possible) according to the individual institutional guidelines. Due to the retrospective nature of the study, additional informed consent was deemed unnecessary by the local ethics committees.

Results

In 7 participating tertiary stroke centers, 668 patients suffering from posterior circulation stroke were endovascularly treated from January 2013 to May 2020. The exact time period of each center is given in the Supplementary Table 1. Of those, 15 patients were treated for VEBABO. In total, 16 MT procedures were executed as 1 patient presented with bilateral SCA occlusion. Median age was 61 years (range 34–84 years) and 8/15 (53%) were male. In 10/15 (67%) patients, IVT was administered. Median baseline NIHSS was 13 (IQR 5–17) and median baseline posterior circulation Alberta stroke program early CT score (pcASPECTS) was 10 (IQR 8–10). One patient presented as a wake-up stroke. Detailed demographic, procedural and outcome parameters for each case are shown in Table 1.

The most frequent occlusion site was the SCA in 13/16 cases (81%). In two cases (13%) MT was performed in the AICA and in one (6%) in the PICA (Fig. 1). Most VEBABOs occurred secondary to MT of the initial BA/PCA occlusion (9/16; 56%); in 5/9 cases (cases 9, 12–15) as ENT and in 4/9 cases (cases 7, 8, 11 and 16) as residual occlusions. The primary occlusions were treated in 6/16 (38%) cases (cases 1–6; Fig. 2) and one SCA MT was done accidentally.

Median time from onset-to-groin puncture was 158 min (IQR 111–223 min) and the median time from groin-to-recanalization was 38 min (IQR 27–68 min). Median number of procedural attempts was 1 (range 0–2). Successful reperfusion (TICI ≥2b) of the whole posterior circulation at the end of the procedure was achieved in 13/15 (87%) patients and 5/15 (33%) patients were completely reperfused.

Successful VEBABO recanalization was reached in 10/16 (63%) procedures. Thromboaspiration was the most frequently used thrombectomy technique in 7/16 (44%) procedures, followed by stent-retriever only technique in 4/16 (25%) and a combined approach in 3/16 (19%). With the latter approach the aspiration catheter was placed within the BA in two patients with SCA occlusion during the retrieval maneuver and in one case the tip of the catheter was successfully navigated directly at the affected SCA ostium. In one case intra-arterial thrombolysis (a dose of 1 mg recombinant tissue plasminogen activator) was successful and administered selectively over a microcatheter due to a SCA occlusion. In all procedures, a microwire was necessary to navigate the MT devices into the affected branch. A detailed overview about the equipment used is shown in Table 1.

Procedure-related SAH occurred in 3/16 (19%) thrombectomies. In one patient with a baseline BA occlusion the stent retriever was accidentally deployed in the left SCA (case 10). In this case, the recanalization of the SCA failed, but the BA could be recanalized after correct positioning of the stent retriever within the BA and contralateral PCA. The patient suffered from mild SAH on postinterventional computed tomography (CT) but died due to progressive brain infarction. In another patient (case 11) who suffered from a residual SCA occlusion after IVT and BA MT, navigation of the affected SCA with a microwire led to a perforation of the vessel. This was treated with a coil occlusion of the proximal SCA to sacrifice it due to ongoing bleeding. The patient sustained a serious SAH and died during the hospital stay. One individual (case 1) presented with tandem occlusion including a dissection of a dominant vertebral artery and a single SCA occlusion. Initially, the dissection was treated with stenting and 500 mg aspirin was given. Subsequently, a recanalization of the SCA failed with the first attempt using an aspiration only technique. Successful recanalization was achieved with a second maneuver using a stent retriever; however, the patient suffered from massive SAH on postinterventional CT and was discharged with an mRS of 5.

Favorable outcome (mRS ≤ 2) was achieved in 6/15 (40%) patients at discharge and in 7/15 (47%) at 90 days follow-up, while 2 (13%) patients died. In patients with isolated VEBABO, the 90-day outcome was favorable in 3 out of 4 patients.

Discussion

Acute cerebellar ischemia due to posterior circulation branch occlusions including the PICA, AICA and SCA are rare and account for about 2% of all acute brain infarcts in some series [10]. Medical treatment with IVT is consid-

Table 1 Detailed demographic, procedural and outcome parameters

Case	Occlusion site	Initial LVO	IVT	Baseline ASPECTS	NIHSS admission	Onset to groin-puncture (min)	Groin to recanalization (min)	Final TICI for whole posterior circulation	Successful recanalization of affected VEBABO	Number of VEBABO MT maneuvers	Thrombectomy technique	Used devices	Complications	NIHSS discharge	mRS discharge	mRS 90 days
1	SCA	N/A	No	9	4	146	58	3	Yes	2	Aspiration only, second approach with SR + aspiration	3MAX, pRESET 3 × 20	SAH	13	5	4
2	SCA	N/A	Yes	10	2	220	40	3	Yes	1	Aspiration only	3MAX	No	1	1	1
3	SCA	N/A	Yes	10	13	165	35	3	Yes	1	SR only	Catch 4 × 20	No	7	2	1
4	SCA	N/A	Yes	10	6	160	N/A	2b	No	1	Aspiration only	3MAX	No	5	2	2
5	Left SCA	BA	Yes	10	5	Wake-up	72	2b	Yes	1	Aspiration only	3M	No	7	4	N/A
6	Right SCA								No	2	Aspiration only	3MAX	No			
7	AICA	BA	Yes	6	9	90	15	2b	Yes	1	SR only	Trevo 3 × 20	No	N/A	4	4
8	PICA	BA	No	8	14	156	36	2b	Yes	2	SR only	Trevo 3 × 20	No	N/A	4	2
9	SCA	BA	Yes	7	23	240	35	2b	Yes	1	SR only	Trevo 3 × 20	No	N/A	4	4
10	SCA	BA	No	9	21	118	164	2a	No	2	SR + aspiration	Solitaire 4 × 20, pRESET Lite 4 × 20, Sofia 5F	SAH	N/A	6	6
11	SCA	BA	Yes	10	17	181	66	2a	No	0	N/A	N/A	Perforation	N/A	6	6
12	SCA	BA	Yes	10	13	270	43	2b	No	2	SR + aspiration	Catch 4 × 20, 5MAX ACE	No	5	2	1
13	SCA	BA	Yes	10	15	145	27	2b	Yes	1	Intra-arterial thrombolysis	Prowler	No	4	3	3
14	SCA	BA	Yes	10	12	85	20	3	Yes	1	Aspiration only	3MAX	No	3	2	2
15	AICA	PCA	No	9	0	233	27	3	Yes	1	SR + aspiration	Catch Mini 3.5 × 15	No	0	0	0
16	SCA	BA	No	8	25	89	115	2b	No	1	Aspiration only	Sofia 5F	No	16	4	4

pRESET Lite: Phenox, Bochum, Germany; Trevo: Stryker Neurovascular, Fremont, California, USA; Solitaire: Medtronic, Irvine, California, USA; Catch and Catch Mini: Balt, Montmorency, France; Prowler: Codman Neuro, West Chester, Pennsylvania, USA; 3MAX: Penumbra, Alameda, California, USA; 5MAX Ace: Penumbra, Alameda, California, USA; Sofia 5F: MicroVention, Aliso Viejo, California, USA

AICA anterior inferior cerebellar artery, *ASPECTS* Alberta Stroke Program Early CT score, *BA* basilar artery, *F* female, *IVT* intravenous thrombolysis, *LVO* large vessel occlusion, *M* male, *min* minutes, *MT* mechanical thrombectomy, *mRS* modified Rankin score, *N/A* not applicable, *NIHSS* National Institutes of Health stroke scale, *PCA* posterior cerebral artery, *PICA* posterior inferior cerebellar artery, *SCA* superior cerebellar artery, *SR* stent retriever, *TICI* thrombolysis in cerebral infarction, *SAH* subarachnoid hemorrhage, *VEBABO* vertebrobasilar artery branch occlusions

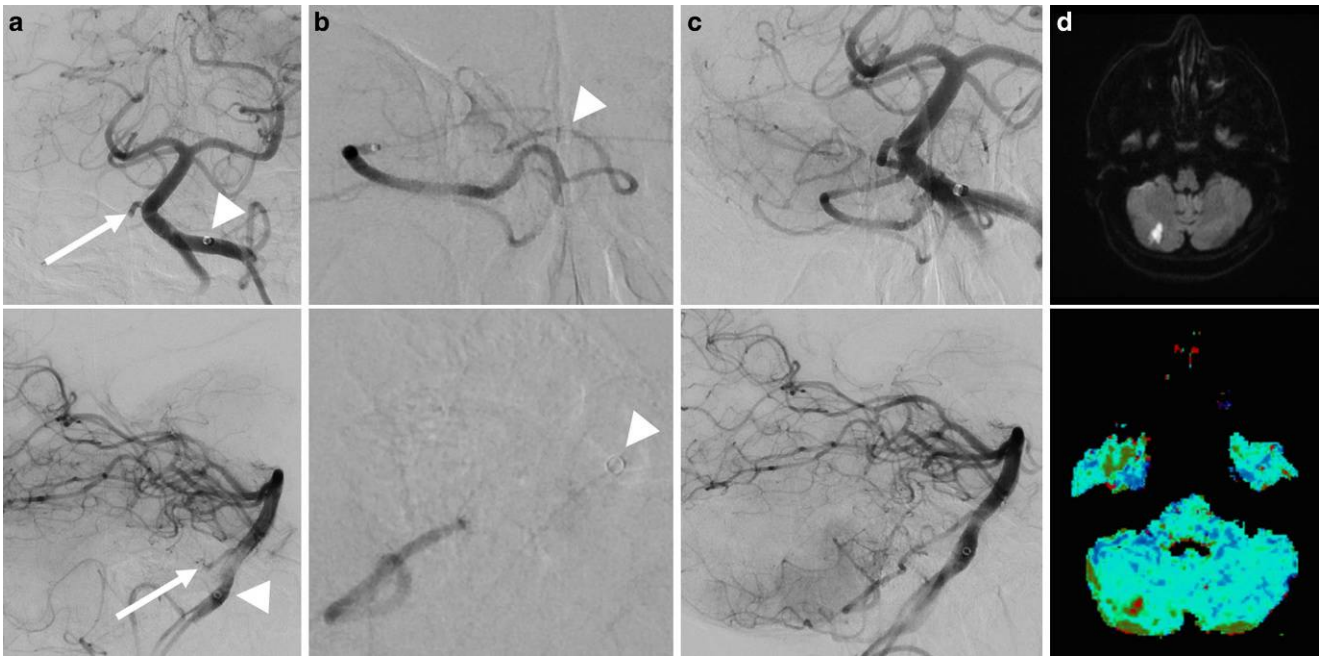

Fig. 1 **a** Residual occlusion of the right anterior inferior cerebellar artery (AICA, arrow) after mechanical thrombectomy of an initial occlusion of the posterior cerebral artery (case 15). A combined apporach with stent-retriever and aspiration thrombectomy was used. The aspiration catheter was placed in the distal left vertebral artery (*arrowhead*). **b** After navigating the microcatheter distal to the lesion, regular distal flow was observed. **c** Final angiogram showed successful recanalization of the dominant AICA after one thrombectomy maneuver with stent retriever and aspiration. **d** A small infarction in the right cerebellar cortex was seen in postprocedural magnet resonance angiography (diffusion weighted imaging and perfusion imaging) (upper row **a**–**c** posterior-anterior angiograms, lower row **a**–**c** lateral angiograms, upper row **d** diffusion weighted imaging, lower row **d** perfusion imaging)

ered the treatment of choice for cerebellar ischemic strokes [1]. In our study, we reviewed an alternative approach for cerebellar ischemic strokes using endovascular treatment and revealed several findings: (1) the overall incidence of MT for VEBABO is very low in clinical practice (0.02%), (2) the procedure seems feasible leading to rapid flow restoration in the occluded arteries in the majority of cases and (3) favorable outcomes at least for isolated VEBABOs were promising and overall results comparable to the current literature regarding BA occlusions.

Some technical specifics should be considered: (1) the use of a microwire is always required, (2) currently, there are no approved stent retriever devices for these small-sized target vessels although a new generation of very small clot retrievers (e.g. Tigertriever 13, Rapid Medical, Yokneam, Israel) recently enter the market awaiting clinical large-scale evaluation, (3) the ADAPT technique might potentially be a more safer option than stent retriever technique as 2 out of 3 cases with periprocedural SAH in our series occurred after stent retriever withdrawal [11]. Nevertheless, the presented number of patients is too low to draw definitive conclusions regarding superiority of a particular thrombectomy technique. In our study, thromboaspiration was predominantly performed; however, consistent with studies evaluating MT for distal artery occlusions (including M2) the combined approach also appeared to be feasible and effective [3, 5]. If a combined technical approach is employed it might be better to place the aspiration catheter at the ostium of the vessel to reduce the probability of distal thrombus fragmentation towards the basilar tip. The risk of iatrogenic emboli in previously unaffected or distally located territories in the posterior circulation are reported to be higher than in anterior circulation stroke, which might be due to the maintenance of antegrade blood flow by at least one of the vertebral arteries during the retrieval maneuver [12, 13]; however, in our case series no distal embolization during MT for VEBABO was observed.

The rate of recanalization of the affected vertebrobasilar branches in our study was promising with 63%, which was similar to the TICI 3 reperfusion rate of 45% and TICI ≥2b rate of 65–83% in recent studies evaluating anterior circulation MT in distal vessel occlusions [3–5]; however, the TICI score in isolated VEBABO cannot be applied, which makes it difficult to compare our recanalization results to LVO strokes in the anterior circulation. Up to now there has only been one individual case report presenting a patient with AICA occlusion who was treated successfully with stent retriever MT [14].

From a technical point of view, it is important to mention that an accidental stent retriever positioning within the SCA might occur in cases with a distal BA occlusion due to poor vessel opacification and misinterpreting the course of the

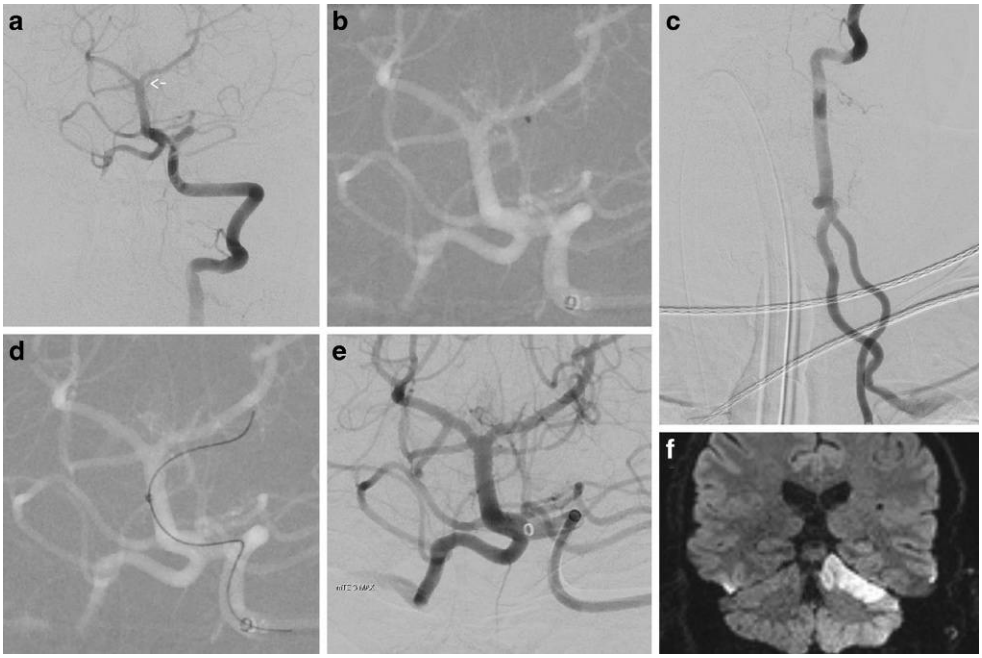

Fig. 2 **a** Initial angiogram during mechanical thrombectomy of an isolated occlusion of the left superior cerebellar artery (SCA, white arrow) due to a dissection of the right vertebral artery. **b** The aspiration catheter was placed distally in the left vertebral artery and a microwire was navigated through the occlusion site in the left SCA. **c** A 3MAX reperfusion catheter was advanced to the proximal clot face. **d** After one maneuver with thromboaspiration successful recanalization of the SCA was achieved. **e** Due to a rare variant of the left vertebral artery with proximally duplicated arteries, a biaxial approach was applied with a large bore aspiration catheter without using a conventional guiding catheter (not shown). **f** Postinterventional diffusion weighted imaging showed cerebellar infarction in the left SCA territory. Nevertheless, clinical symptoms of the patient improved with residual ataxia (case 2)

PCA and SCA, as happened in one of our patients. Therefore, evaluating the presence/absence of bilateral posterior communicating arteries on preinterventional CT angiography is essential and shaping the distal tip of the microwire into a "J" configuration is reasonable.

The procedure-related complication rate including SAH and vessel perforation in our case series was comparatively high with respect to the aforementioned studies dealing with distal vessel occlusions in the anterior circulation (19% vs. 0–8.5%) [3–5]. One explanation might be the essential usage of a microwire in the small-sized vessels. The angle of nearly 90° between the main trunk and the vertebrobasilar branches makes the microwire indispensable in order to catheterize the target arteries [15]. As a result, there might be a higher risk of vessel perforation and SAH as previously shown [16]. We furthermore strongly recommend superselective injection of contrast medium before placing the stent retriever to prove an intraluminal position. Considering the fact that two out of five patients who required two maneuvers suffered from SAH illustrates that any further attempts after one maneuver should be pursued with caution and requires individualized assessment. If IVT or intravenous aspirin is administered, the indication for ongoing thrombectomy maneuvers should also be carefully weighed against the risk of the procedure (as seen in case 1). In anterior circulation MT, the probability of both favorable outcome and recanalization decreases with increasing thrombectomy attempts [17].

In line with the results of the multicenter ENDOSTROKE registry, favorable outcome (mRS ≤2) in our case series was comparable (38% vs. 34%), with a lower mortality rate (13% vs. 35%) [6]. This can be explained by the inclusion of even isolated VEBABO patients with clinically mild strokes; however, most VEBABOs occurred secondarily after initial BA/PCA occlusion and therefore the efficacy of VEBABO MT with respect to clinical outcome has to be interpreted with caution. Nevertheless, in three out of four cases with primary VEBABO, the clinical symptoms improved during the hospital stay and clinical outcome was favorable.

Finally, it remains unclear whether MT for VEBABO should be considered as a therapeutic alternative to medicinal treatment. In endovascular treatment of dissecting distally located cerebellar aneurysm, parent vessel occlusion is a treatment option and the associated ischemic sequelae are often well-tolerated [18–20]. Even though the usual course of cerebellar infarctions is benign, a minority of patients (up to approximately 10%) present with severe neurological deficits and disturbance of consciousness, indicative of brainstem involvement [7, 10]. Previous studies showed that the prognosis of cerebellar infarcts might be related to the presence and grade of consciousness disturbance and

functional disability was most frequently seen in SCA infarcts compared to other single cerebellar infarcts [7, 10]. These highly selected patients with potential brainstem involvement, particularly if not eligible for IVT, might benefit from an endovascular therapeutic option. The first results of the recent Basilar Artery International Cooperation Study (BASICS) trial shows that a stratification by the NIHSS might be useful to select patients in order to pursue an endovascular approach in BA occlusions [21].

A limitation of our study is the retrospective nature including inherent selection bias and the usage of different thrombectomy equipment and techniques. The lack of a control group is a further limitation. As highlighted previously, the presented number of patients is too low to draw definitive conclusions. It is difficult to evaluate the potential benefit of clinical outcome, especially in cases with residual VEBABO after initial BA occlusion; however, this multicenter study demonstrates the expanding frontiers in thrombectomy and includes the largest number of endovascularly treated VEBABOs described in the literature so far.

Conclusion

Mechanical thrombectomy for VEBABO is rare but appears to be feasible and effective with a promising rate of successful recanalization; however, considering the potential risk of procedure-related hemorrhage, the indications for the procedure should be very carefully weighed and individually assessed.

Author Contribution Conception and design: VM; acquisition of data: VM, SF, LY, CM, NA, AK, DL, JK; analysis and interpretation of data: VM, HS, LY, BT, AB, CK, PP, CC, EP, JK; drafting the article: HS, VM. All authors have read and approved the manuscript.

Compliance with ethical guidelines

Conflict of interest H. Styczen, S. Fischer, L.L. Yeo, B. Yong-Qiang Tan, C.J. Maurer, A. Berlis, N. Abdullayev, C. Kabbasch, A. Kastrup, P. Papanagiotou, C. Clajus, D. Lobsien, E. Piechowiak, J. Kaesmacher and V. Maus declare that they have no competing interests relevant to this work.

Ethical standards According to the guidelines of the respective local ethics committee, ethics approval was given when necessary for this anonymous retrospective study, which was conducted in accordance with the Declaration of Helsinki. The patients' consent for treatment was obtained (if possible) according to the individual institutional guidelines. Due to the retrospective nature of the study, additional informed consent was deemed unnecessary by the local ethics committees.

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