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ORIGINAL ARTICLE

Mechanical Thrombectomy in Basilar Artery Occlusion

Presence of Bilateral Posterior Communicating Arteries is a Predictor of Favorable Clinical Outcome

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Abstract

Background Mechanical thrombectomy (MT) of basilar artery occlusions (BAO) is a subject of debate. We investigated the clinical outcome of MT in BAO and predictors of a favorable outcome.

Material and Methods A total of 104 MTs of BAO (carried out between 2010 and 2016) were analyzed. Favorable outcome as a modified Rankin scale (mRS) ≤ 2 at 90 days was the primary endpoint. The influence of the following variables on outcome was investigated: number of detectable posterior communicating arteries (PcoAs), patency of basilar tip, completeness of BAO and posterior circulation Alberta Stroke Program early computed tomography score (PC-ASPECTS). Secondary endpoints were technical periprocedural parameters including symptomatic intracranial hemorrhage (sICH).

Results The favorable clinical outcome at 90 days was 25% and mortality was 43%. The rate of successful reperfusion, i.e. modified thrombolysis in cerebral infarction (mTICI) ≥ 2b was 82%. Presence of bilateral PcoAs (area under the curve, AUC: 0.81, odds ratio, OR: 4.2, 2.2–8.2; $p < 0.0001$), lower National Institute of Health Stroke Scale (NIHSS) on admission (AUC: 0.74, OR: 2.6, 1.3–5.2; $p < 0.01$), PC-ASPECTS ≥ 9 (AUC: 0.72, OR: 4.2, 1.5–11.9; $p < 0.01$), incomplete BAO (AUC: 0.66, OR: 2.6, 1.4–4.8; $p < 0.001$), and basilar tip patency (AUC: 0.66, OR: 2.5, 1.3–4.8; $p < 0.01$) were associated with a favorable outcome. Stepwise logistic regression analysis revealed that the strongest predictors of favorable outcome at 90 days were bilateral PcoAs, low NIHSS on admission, and incomplete BAO (AUC: 0.923, OR: 7.2, 3–17.3; $p < 0.0001$).

Conclusion The use of MT for BAO is safe with high rates of successful reperfusion. Aside from baseline NIHSS and incomplete vessel occlusion, both known predictors of favorable outcome in anterior circulation events, we found that collateral flow based on the presence or absence of PcoAs had a decisive prognostic impact.

Keywords Embolectomy · Collateral Circulation · Cerebral Stroke · Cerebrovascular Occlusion · Intracranial Thrombosis

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Background

In acute ischemic stroke (AIS) 6–10% of intracranial large vessel occlusions (LVO) are due to basilar artery occlusion (BAO) that is associated with the poorest outcome of all stroke subtypes, resulting in a morbidity and mortality rate of 70% even after treatment [1, 2]. To date, intravenous thrombolysis (IVT) with recombinant tissue plasminogen

activator remains the first-line therapy within 4.5 h after symptom onset, although the efficacy is very limited in LVO [3]. Intra-arterial administration of thrombolytic therapy is another treatment option, but reperfusion with pharmacological treatment alone can only be achieved in half of the patients [4]. The introduction of stent retriever-based mechanical thrombectomy (MT) showed increased rates of successful reperfusion and favorable outcome in the anterior circulation compared with the best medical treatment [5]. Experience about the safety and efficacy of such stent retriever treatment in posterior circulation stroke is limited to a few studies [6–16]; however, the ENDOSTROKE registry demonstrated that recanalization did not significantly predict clinical outcome in patients with BAO [17]. Several co-factors are known to be independent predictors of clinical outcome in BAO, such as lower age, lower scores in the National Institute of Health stroke scale (NIHSS) on admission, and a higher posterior circulation Alberta Stroke Program early computed tomography score (PC-ASPECTS) on pretreatment imaging [12, 18]. Furthermore, the impact of collateral status as assessed by pretreatment imaging, which is known to be a predictor of favorable outcome in LVO of the anterior circulation remains to be evaluated [19]. Overall, the data available suggest that outcome of endovascular treatment of BAO patients is influenced by clinical and radiological parameters, which may be of clinical importance for interdisciplinary decision making in AIS due to BAO. Therefore, we investigated the clinical outcome of MT for BAO and predictors of a favorable outcome.

Material and methods

Study Design and Patient Selection

Based on our prospectively captured database, all consecutive patients with AIS in the posterior circulation admitted to our hospital from October 2010 to December 2016 with indications for endovascular treatment were evaluated retrospectively on an intention-to-treat basis. The data collected included demographics, pre-existing cardiovascular risk factors and cerebrovascular events, comorbidities, metabolic parameters, and medication at the time of the stroke. The NIHSS and modified Rankin scale (mRS) parameters were assessed by a stroke neurologist.

Inclusion criteria for MT were as follows: (1) arterial occlusion in posterior circulation arteries as identified by computed tomography angiography (CT-A) or magnet resonance imaging angiography (MR-A), (2) any age, (3) neurological deficit attributable to posterior circulation stroke (no NIHSS limit), and (4) admission within 24 h of symptom onset. Patients were excluded when cerebral imaging revealed intracranial hemorrhage (ICH).

All patients received IVT if eligible, based on the judgement of the attending neurologist and in accordance with the clinical guidelines of the German Neurological Society at that point in time. If possible (i. e., no contraindications), MR imaging was regularly performed within 24 h after endovascular treatment, or immediately in the case of a new deficit, to determine the extent of stroke and to exclude postinterventional ICH. Symptomatic ICH (sICH) was defined as any apparent extravascular blood in the brain or within the cranium that was associated with clinical deterioration, as defined by an increase of ≥4 points in the NIHSS score [20].

The primary endpoint was a favorable clinical outcome (mRS $\leq$ 2) at 90 days. The influence of the following variables on clinical outcome was investigated: number of detectable posterior communicating arteries (PcoAs), patency of basilar tip, completeness of BAO, and PC-ASPECTS. Secondary endpoints were technical periprocedural parameters including sICH.

Analysis of Pretreatment Imaging

The exact location of BAO was defined according to Archer and Horenstein as proximal (involvement of the vertebrobasilar junction to the origins of the anterior inferior cerebellar arteries, AICA), mid-basilar (segment between the AICA and the origin of the superior cerebellar arteries, SUCA), and distal (segment distal to the SUCA), and refers to the clot's most inferior extent on CT-A or MR-A [21]. The location of the proximal face of the clot in the first angiogram of the basilar artery was then retrospectively compared with the pretreatment cross-sectional imaging and in cases of a subsequent different clot extension the digital subtraction angiography (DSA) series was used for further analysis. Persisting perfusion of the basilar tip independent of clot location was evaluated in CT-A or MR-A (Fig. 1). Collateral status was evaluated by CT-A or MR-A and defined as follows: 0 no PcoA, 1 unilateral PcoA and 2 bilateral PcoA, including the presence of an ipsilateral P1 segment of the posterior cerebral artery to ensure retrograde collateral flow. Collaterals were defined as "good" if bilateral PcoAs were present. Incomplete BAO was defined as incomplete occlusion at the target artery with no distal flow or incomplete occlusion at the target artery with distal flow. The PC-ASPECTS was assessed on CT-A source images or on diffusion-weighted imaging (DWI) as described previously [22, 23]. The presence of a hypoplastic/codominant vertebral artery (VA) and posterior inferior cerebellar artery (PICA) ending the VA was evaluated on CT-A, MR-A or DSA. All images were re-evaluated by the senior author, blinded to the clinical outcome and in an anonymous fashion.

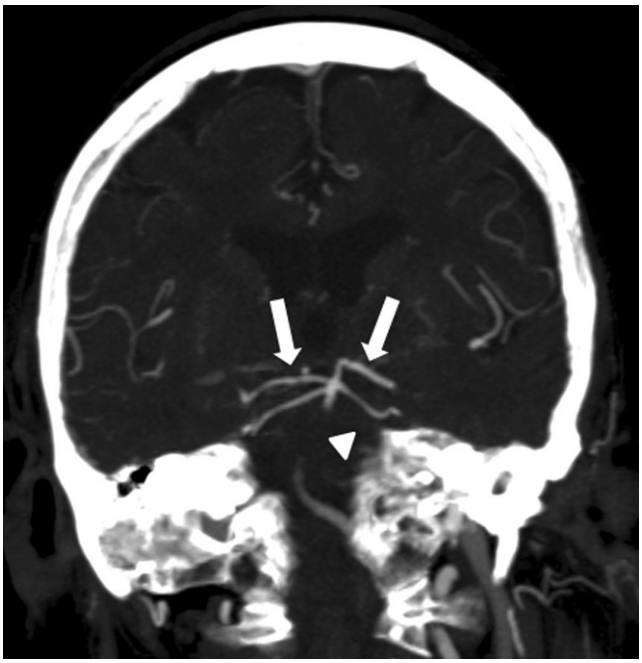

Fig. 1 Mid-basilar artery occlusion (*white arrowhead*) in a 61-year-old patient presenting with an initial NIHSS of 13. On pretreatment CT-A the presence of bilateral PcoAs (*white arrows*) and perfusion of the basilar tip and both superior cerebellar arteries are visible. After intravenous thrombolysis and stent retriever-based mechanical thrombectomy the patient recovered without any neurological deficits

Endovascular Procedure

Procedures were performed with the patient under general anesthesia. Femoral access was chosen in 95% of the cases. Different techniques of MT were executed over time. Based on a triaxial approach with a 6 F guiding catheter (Envoy, Cordis, Fremont, CA) in the VA, stent retrievers were used from the beginning in combination with an aspiration catheter (Distal Access Catheter, Concentric, Mountain View, CA; Navien, Covidien, Dublin, Ireland; Sofia, Microvention, Tustin, CA), which was placed distally in the VA. The stent retriever was then withdrawn into the aspiration catheter under suction with a 60 ml syringe (VacLok, Merit Medical Systems, South Jordan, UT) using different techniques of MT [24, 25]. These steps were repeated until the final reperfusion result was reached; the maximum number of attempts was up to the operator and did not exceed 10 in any case. The Trevo XP ProVue (Stryker, Fremont, CA) and the Solitaire AB/FR (Medtronic, Minneapolis, MN) devices were predominantly used in >90% of the procedures but from 2014 onwards the EmboTrap device (Neuravi, Galway, Ireland) was employed as well [26]. With ongoing research, we introduced the direct aspiration first-pass technique (ADAPT; [27, 28]), predominantly performed with a Sofia catheter as a large-bore aspiration catheter in 2014 [28, 29]. Intraprocedural use and choice of stent retriever(s) and/or aspiration catheter were left to the attending physician's discretion.

Statistical Analysis

Statistical analysis was conducted with JMP Software (V12, SAS Institute, Cary, NC). The Wilcoxon test and two-tailed Fisher's exact test were performed to determine the levels of significance. Statistical significance was defined as $p \leq 0.05$. Univariate and multivariate logistic regression was used to conduct receiver operating characteristic (ROC) analysis. Variables for multivariate logistic regression model were chosen by p-value. Significance between multivariate models was assessed with the deLong test. Partition regression analysis was conducted in order to rank association of clinical and imaging parameters with outcome variables as well as to provide decision trees for low-risk and high-risk groups. Descriptive parameters were given as median ± interquartile range (IQR).

Results

Baseline Characteristics

Over the defined period of 75 months, 570 patients received endovascular treatment for AIS in LVO. Of these 122 out of 570 (21%) had LVO of the posterior circulation, comprising 104/122 (85%) with BAO. Thereof, 84/104 (81%) had complete vessel occlusion and 20/104 (19%) incomplete BAO. Patient baseline and clinical characteristics are summarized in Table 1. In 85% of patients, CT-based stroke imaging was the preferred initial imaging modality.

Pretreatment Imaging

In BAO 19 out of 104 patients (18%) had a proximal occlusion, 59 (57%) a mid-basilar occlusion, and the remaining 26 (25%) a distal occlusion. An overview of the between group results is provided in Table 2. For 90 BAO patients (87%) pretreatment imaging datasets were available for analysis. Good collaterals were noted in 46/90 patients (51%), 23/90 (26%) had a unilateral PcoA, and in 21/90 (23%) no PcoAs were found. In 14/90 cases (16%) the tip of the basilar artery was perfused via PcoA collaterals (Fig. 1). The basilar tip was found to be perfused in 8/14 patients (57%) with proximal BAO compared to 6/51 patients (12%) with mid-basilar occlusion ($p < 0.05$). Early signs of ischemia as expressed by a PC-ASPECTS ≥ 9 were present in 58/90 (64%). The vast majority (97/104) of patients (83%) had co-dominant VA and unilateral PICA ending was observed in 6 cases (6%).

Table 1 Clinical characteristics of all 104 patients with BAO

Baseline characteristics	
Age (mean ± SD), years	69.3 ± 15.6
Sex; female, *n* (%)	54 (51.9)
Risk factors	
Hypertension, *n* (%)	85 (81.7)
Coronary artery disease, *n* (%)	34 (32.7)
Atrial fibrillation, *n* (%)	53 (51)
PAOD, *n* (%)	8 (7.7)
Pulmonary disease, *n* (%)	13 (12.5)
Diabetes mellitus, *n* (%)	20 (19.2)
Chronic kidney disease, *n* (%)	13 (12.5)
Hyperlipidemia, *n* (%)	18 (17.3)
Obesity, *n* (%)	15 (14.4)
Smoker, *n* (%)	18 (17.3)
Etiology of stroke	
Thromboembolic, *n* (%)	47 (45.2)
PCSE, *n* (%)	34 (32.7)
Dissection, *n* (%)	9 (8.7)
Unknown, *n* (%)	32 (30.8)
Clinical characteristics	
Baseline NIHSS (mean ± SD; median, IQR)	13.9 ± 8.9; 11.5 (13)
IVT, *n* (%)	49 (47.1)

PAOD peripheral artery occlusive disease, *PCSE* potential cardiac source of embolism, *IVT* intravenous thrombolysis, *NIHSS* National Institute of Health stroke scale, *SD* standard deviation, *IQR* interquartile range

Angiographic Results

An IVT was admitted prior to the endovascular procedure in 49/104 patients (47%). The mean time from groin puncture to reperfusion was 73.6 min ± 60.3 (median 54 min, IQR 70 min). Mean onset to reperfusion time was 354.5 min ± 162 (median 310 min, IQR 163 min). In 76/104 patients (73%) stent retrievers were primarily used and in 17/104 patients (16%) the ADAPT technique was conducted as the first option. In the remaining cases, MT was aborted after groin puncture due to either disappearance of the target (i. e., spontaneous or IVT-induced recanalization, $n = 8$) or technical failure in reaching the target lesion due to underlying elongation in the access vessels ($n = 3$). The average number of stent retriever maneuvers for successful recanalization was 2.2 ± 2.5 and was lower in patients with good collaterals (2.1 ± 2 vs. 3.2 ± 2.9, $p = 0.15$). Reperfusion was successful in 85/104 cases (82%) with complete reperfusion (mTICI 3) in 50 patients (48%), with no significant difference between patients with good or poor collateral status.

Periprocedural Complications

Procedural complications occurred in 6 patients (6%): in 1 patient (1%) with a mid-basilar occlusion the aspiration catheter could not be advanced to the proximal face of the thrombus during the retrieval maneuver due to severe vessel elongation resulting in an embolization to new territory (ENT) with occlusion of a non-dominant PICA. The patient suffered from mild cerebellar ischemia without

Table 2 Imaging and clinical parameters of basilar artery occlusion according to the occlusion site

	Proximal	Mid-basilar	Distal	*P*-value
n (%)	19 (18.3)	59 (56.7)	26 (25)	–
Baseline NIHSS (mean ± SD)	12.4 ± 8.3	14.8 ± 9.7	14.9 ± 8.7	ns
IVT, *n* (%)	6/19 (31.6)	27/59 (45.8)	16/59 (61.5)	ns
Pretreatment imaging				
Good collaterals, *n* (%)	10/14 (71.4)	24/51 (47.1)	12/25 (48)	ns
Basilar tip patency, *n* (%)	8/14 (57.1)	6/51 (11.8)	0/25 (0)	0.0174
PC-ASPECTS ≥ 9, *n* (%)	8/14 (57.1)	34/51 (66.7)	16/25 (64)	ns
Hypoplastic vertebral artery	7/14 (28.6)	8/51 (15.7)	6/25 (24)	ns
PICA ending vertebral artery	2/14 (14.3)	0/51 (0)	4/25 (16)	ns
Angiographic and clinical results				
Groin puncture to reperfusion (mean ± SD)	67.8 ± 47.8 min	83.6 ± 63.7 min	69.5 ± 68.5 min	ns
Onset to reperfusion (mean ± SD)	347.1 ± 134.7 min	376.1 ± 181.8 min	358.3 ± 168.4 min	ns
Successful reperfusion, mTICI ≥ 2b, *n* (%)	15/19 (78.9)	48/59 (81.4)	22/26 (84.6)	ns
Favorable clinical outcome, mRS ≤ 2, *n* (%)	4/13 (30.8)	12/47 (25.5)	4/20 (20)	ns

NIHS National Institute of Health Stroke Scale, *SD* standard deviation, *IVT* intravenous thrombolysis, *PC-ASPECTS* posterior circulation Alberta Stroke Program early computed tomography score, *mTICI* modified thrombolysis in cerebral infarction, *mRS* modified Rankin Scale, *PICA* posterior inferior cerebellar artery, *IVT* intravenous thrombolysis, *PC-ASPECTS* posterior circulation Alberta Stroke Program early computed tomography score, *mTICI* modified thrombolysis in cerebral infarction, *mRS* modified Rankin Scale, *PICA* posterior inferior cerebellar artery

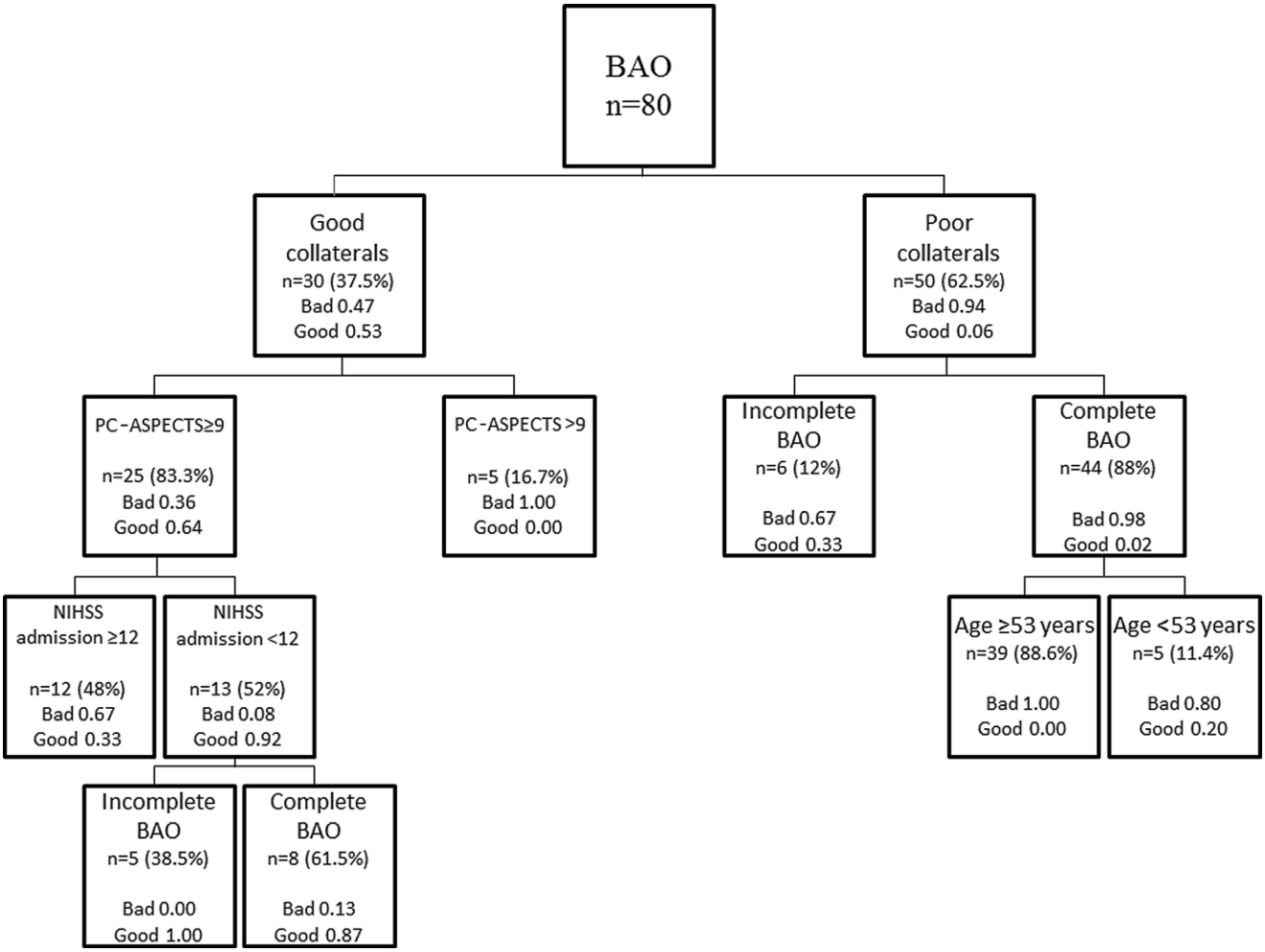

Fig. 2 Partition regression model showing priority of significant predictors of clinical outcome. *BAO* basilar artery occlusion, *PC-ASPECTS* posterior circulation Alberta Stroke Program early computed tomography score, *NIHSS* National Institute of Health Stroke Scale

any additional functional deficit. In 5 patients (5%) an iatrogenic dissection of the VA was observed, necessitating subsequent stenting in 2 cases.

Clinical Outcome

The follow-up data after 90 days were available for 80 BAO patients (77%) whereby 20 (25%) had favorable clinical outcome (mRS 0–2) and 27 (34%) had a moderate outcome (mRS 0–3). Mortality rate was 43% (with 35 patients deceased). There was no significant difference with respect to the occlusion site. Of the 20 patients 15 (75%) with favorable outcome exhibited good collaterals and 19 out of 20 patients (95%) showed a PC-ASPECTS of ≥9 on pretreatment imaging. Univariate analysis revealed that 5 predictors were significantly associated with favorable outcome at 90 days: presence of good collaterals (AUC: 0.81, OR: 4.2, 2.2–8.2; $p < 0.0001$), lower NIHSS on admission (AUC: 0.74, OR: 2.6, 1.3–5.2; $p < 0.01$), PC-ASPECTS ≥ 9 (AUC: 0.72, OR: 4.2, 1.5–11.9; $p < 0.01$), incomplete BAO (AUC: 0.66, OR: 2.6, 1.4–4.8; $p < 0.001$), and basilar tip patency (AUC: 0.66, OR: 2.5, 1.3–4.8; $p < 0.01$). Lower age also tended to be associated with better outcome but this did not reach significance (AUC: 0.63, $p = 0.09$). Using stepwise logistic regression analysis, the strongest predictors of favorable outcome were good collaterals, NIHSS on admission, and incomplete BAO (AUC: 0.923, OR: 7.2, 3–17.3; $p < 0.0001$). The partition regression model for 80 patients with BAO and available 90 day mRS data showed a significant relationship between clinical outcome and the presence of good collaterals, high PC-ASPECTS, and low NIHSS on admission (Fig. 2). In our cohort, all patients with good collaterals showed a favorable clinical outcome (mRS < 2), if PC-ASPECTS was 9 or higher, NIHSS on admission was <12, and vessel occlusion was incomplete ($n = 5$). In contrast, all patients presenting with bilateral PcoAs but significant brainstem lesions (defined as PC-ASPECTS

< 9) on pretreatment imaging died (n = 5). Patients with poor collaterals predominantly exhibited a favorable outcome if BAO was incomplete (33%). In the case of a complete vessel occlusion within this cohort the likelihood of a poor clinical outcome (mRS 5/6) was 98% (n = 39).

Discussion

We conducted a multivariate analysis assessing putative prognostic factors in order to provide a better rationale for informed decision making. This may be helpful for both clinicians, when deriving interdisciplinary decisions with respect to best treatment in an individual situation, and patients/caregivers of patients, when discussing an intended therapy with them. Aside from known prognostic factors, such as baseline NIHSS and age, the presence of good collateral flow based on the anatomical presence of PcoAs was a strong predictor for a favorable clinical outcome in our study.

The efficacy of stent retrievers in LVO in the anterior circulation has been shown in several randomized clinical trials (RCT; [5]); however, data on the significance of MT in the posterior circulation remain scarce and to date, no prospective randomized study exists. A multicenter registry and a few retrospective case series with small sample sizes focusing exclusively on BAO have reported first experiences for the use of stent retrievers in these patient cohorts [6–17]. The successful reperfusion rate of 82% in our study is comparable to those of previous case series (64–83%; [6–16]) and the ENDOSTROKE registry, which reported a TICI 2b/3 rate of 79% [17]. Comparable to the aforementioned studies, patients from our cohort showed a favorable clinical outcome in 25% but also an overall mortality of 43%, despite high rates of reperfusion, suggesting that other variables exert a decisive influence on the clinical course of BAO.

One key factor for clinical outcome may be the time from onset to reperfusion as shown in the BASICS study, which reported a decrease of good clinical outcome with ongoing reperfusion time [30]; however, other series failed to establish a clear time dependency [6, 17, 31]. Our median groin puncture-to-reperfusion time (54 min) was similar to the ENDOSTROKE registry (56 min), considerably faster than in the study of Möhlenbruch et al. (77 min) and slower in comparison to the study of Baek et al. (30 min; [6, 16, 17]); our median onset-to-reperfusion time (310 min) was slightly faster compared to most series [12].

Another factor known to impact on outcome irrespective of reperfusion is infarct size on pretreatment imaging. In a study of 50 BAO patients it has been demonstrated that all patients with a DWI PC-ASPECTS of at least 9 had a good outcome [18]. Similarly, in a series of 24 BAO cases who underwent CT-A a significantly better outcome was associated with a PC-ASPECTS ≥ 9 [6]. In our study 95% of patients with favorable outcome exhibited a PC-ASPECTS ≥ 9, which corroborates the notion that significant brainstem lesions prior to the endovascular procedure indicate poor prognosis.

Retrograde filling of the basilar artery may help to sustain the blood supply to penumbral tissue, thereby potentially reducing the final infarct volume. The presence of good collaterals on pretreatment CT-A is associated with greater neurological improvement during hospitalization in BAO patients; however, Goyal et al. failed to demonstrate a higher rate of 90 day functional independence in a multivariate analysis, probably due to the small sample size of 21 patients [32]. This is consistent with a series of 31 patients demonstrating bilateral PcoAs on baseline imaging in 61%, with a trend towards a better clinical outcome [10]. Van der Hoeven et al. recently developed a CT-A based posterior circulation collateral score (PC-CS) that predicted poor outcome at 1 month; however, the elaborated 10-point grading system involved the presence of PICA, AICA, and SUCA, which in our opinion are not always reliably detectable on CT-A due to vessel size [33]. Furthermore, they showed that the presence of at least one PcoA is accompanied by a lower risk for poor outcome after 30 days. In our study a good collateral status based on the presence of bilateral PcoAs was strongly associated with a favorable clinical outcome at 90 days and thus a relevant prognostic factor in stepwise logistic regression. Our data are supported by Alqadri et al. who applied a DSA grading of collateral formation in the posterior circulation in BAO patients [34]. They reported that a retrograde filling of the basilar artery via the posterior cerebral artery with filling of at least one SUCA resulted in a lower incidence of comatose presentation and a higher rate of good outcome compared to the presence of bilateral anastomoses of cerebellar or posterior cerebral arteries. This is in accordance with our finding that a retrograde perfusion of the basilar tip on pretreatment imaging was associated with favorable outcome of the cases and more frequently so if the proximal part of the basilar artery was occluded. The most parsimonious explanation for this finding is that the resulting collateral flow to the perimesencephalic arteries reduces paramedian mesothalamic ischemia, thereby preventing main functional deficits and impaired consciousness [35]. The ENDOSTOKE registry underlined the importance of good collaterals in DSA; however, the American Society of Interventional and Therapeutic Neuroradiology/Society of Interventional Radiology (ASITN/SIR) collateral grading system is basically executed in anterior circulation LVO, which limits the generalization of this finding [17, 36].

The stroke severity on admission was a strong predictor of a favorable outcome and not dependent on occlusion

site, which is in line with the results of the ENDOSTROKE and BASICS registries [17, 37]. In our partition regression model, the optimal NIHSS threshold was 12 in the case of bilateral PcoAs. A higher NIHSS was associated with poor outcome in 67% of this subgroup.

Previous authors reported age as a predictor of outcome [12, 38]. In our study, age showed a trend towards constituting a prognostic factor but failed to reach statistical significance; however, younger patients presenting with incomplete BAO more frequently showed a favorable clinical outcome compared to older patients. The influence of an incomplete LVO independent of age and baseline NIHSS on clinical outcome was demonstrated recently [39].

The strengths of our study include the large number of consecutive patients all of whom were treated by modern endovascular means, and the robust statistical results, which were a consequence of the magnitude of the differences observed. A limitation of our study is the retrospective design with its potential selection bias, for example, patients that we did not intend to treat were not included in this study. Furthermore, although evaluation of pretreatment imaging parameters was re-assessed in a blinded fashion, results could still be less favorable after core laboratory adjudication.

Conclusion

The results of our study demonstrate that MT performed with current technologies in patients with BAO is a safe and feasible method that yields high rates of successful reperfusion. Furthermore, our results emphasize the importance of individual pretreatment characteristics for patient outcome. Our data suggest that a pretreatment, i. e. individual risk assessment is feasible, which may provide a better rationale for the selection of patients, interdisciplinary decision making, and the counseling of patients/caregivers. Particularly a good collateral flow seems to be an important prognostic factor of favorable clinical outcome, which can be approximately predicted based on the presence or absence of the PcoAs on pretreatment imaging. Future prospective studies are warranted to validate the impact of such variables.

Compliance with ethical guidelines

Conflict of interest V. Maus, A. Kalkan, C. Kabbasch, N. Abdullayev, H. Stetefeld, U.B. Barnikol, T. Liebig, C. Dohmen, G.R. Fink, J. Borggrefe and A. Mpotsaris declare that they have no competing interests.

Ethical standards The study was approved by the local ethics committee (Registration ID: 16-347) and was conducted in accordance with the Declaration of Helsinki.

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