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ORIGINAL ARTICLE

Endovascular thrombectomy for basilar artery occlusion stroke: Analysis of the German Stroke Registry-Endovascular Treatment

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Abstract

Background and purpose: Acute ischemic stroke due to basilar artery occlusion (BAO) causes the most severe strokes and has a poor prognosis. Data regarding efficacy of endovascular thrombectomy in BAO are sparse. Therefore, in this study, we performed an analysis of the therapy of patients with BAO in routine clinical practice.

Methods: Patients enrolled between June 2015 and December 2019 in the German Stroke Registry-Endovascular Treatment (GSR-ET) were analyzed. Primary outcomes were successful reperfusion (modified Thrombolysis in Cerebral Infarction [mTICI] score of 2b-3), substantial neurological improvement (≥8-point National Institute of Health Stroke Scale [NIHSS] score reduction from admission to discharge or NIHSS score at discharge ≤1), and good functional outcome at 3 months (modified Rankin Scale [mRS] score of 0–2).

Results: Out of 6635 GSR-ET patients, 640 (9.6%) patients (age 72.2 ±13.3, 43.3% female) experienced BAO (median [interquartile range] NIHSS score 17 [8, 27]). Successful reperfusion was achieved in 88.4%. Substantial neurological improvement at discharge was reached by 45.5%. At 3-month follow-up, good clinical outcome was observed in 31.1% of patients and the mortality rate was 39.2%. Analysis of mTICI3 versus mTICI2b groups showed considerable better outcome in those with mTICI3 (38.9% vs. 24.4%; $p = 0.005$). The strongest predictors of good functional outcome were intravenous thrombolysis (IVT) treatment (odds ratio [OR] 3.04, 95% confidence interval [CI] 1.76–5.23) and successful reperfusion (OR 4.92, 95% CI 1.15–21.11), while the effect of time between symptom onset and reperfusion seemed to be small.

Conclusions: Acute reperfusion strategies in BAO are common in daily practice and can achieve good rates of successful reperfusion, neurological improvement and good functional outcome. Our data suggest that, in addition to IVT treatment, successful and, in

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particular, complete reperfusion (mTICI3) strongly predicts good outcome, while time from symptom onset seemed to have a lower impact.

KEYWORDS
acute stroke, basilar artery occlusion, endovascular therapy, functional outcome, intravenous thrombolysis, ischemic stroke, mechanical thrombectomy

INTRODUCTION

While 10%–20% of acute ischemic strokes involve the posterior circulation, basilar artery occlusion (BAO) accounts for only approximately 1% of strokes but is strongly associated with a high mortality rate and a high risk of disability [1, 2]. The safety and effectiveness of endovascular thrombectomy (EVT) in large vessel occlusion (LVO) strokes of the anterior circulation have been reported in several randomized controlled trials [3]. However, patients with BAO and posterior circulation LVO in general were excluded from these studies. Therefore, high-quality level I data investigating the effectiveness of EVT in posterior circulation LVO stroke are rare. Most recently, the ATTENTION trial (trial of endovascular treatment of acute BAO) showed for the first time the superiority of EVT in BAO compared to standard of care, including intravenous thrombolysis (IVT) [4]. However, EVT was associated with increased rates of complications, especially intracerebral hemorrhage (ICH). Moreover, ATTENTION included only Chinese people with a much higher rate of intracranial stenosis compared to Western populations, limiting the transferability of these results. The recently published register study BASILAR, describing a large cohort of more than 800 patients, showed a benefit of EVT [5]. By contrast, the BEST trial (endovascular treatment versus standard medical treatment for vertebrobasilar artery occlusion trial), which analysed endovascular therapy plus standard medical therapy versus standard medical therapy alone in vertebrobasilar artery occlusion, showed no advantage for endovascular treatment regarding favorable outcome. However, that study was terminated early because of high crossover rate and poor recruitment after randomly assigning 131 patients [6]. Secondary prespecified analyses of the primary outcome, conducted to assess the effect of crossovers, showed higher rates of successful reperfusion and good outcome with modified Rankin Score (mRS) 0–3 at 90 days in patients who actually received the intervention compared to those who received standard medical therapy alone. In addition, the Basilar Artery International Cooperation Study (BASICS) [7] enrolled 300 patients over 9 years from 27 sites, showing no clear benefit of EVT [8]. Nevertheless, the very low enrollment rates and difficulties in patient recruitment complicate the interpretation of the results of that study. All in all, the majority of observational studies showed a benefit of EVT in LVO posterior circulation strokes [9–14]. A recent meta-analysis of 16 studies indicated comparable rates of successful reperfusion and good clinical outcome comparing anterior and posterior circulation strokes [15]. However, two large prospective observational studies did not support the superiority of EVT over IVT in patients with BAO, demonstrating relatively poor outcome despite successful reperfusion [2, 16]. These studies illustrate the challenges in obtaining high-quality data for BAO patients, as clinical equipoise no longer exists in the era of proven effectiveness of EVT in anterior circulation stroke, with clinicians faced with severely affected patients with poor prognosis if untreated. In summary, the standard treatment for BAO is still a matter of debate, and international guidelines from the European Stroke Organization (ESO) and the American Heart Association (AHA), as well as the national German guideline, state that there is uncertainty about the benefit of EVT in BAO [17–19].

In the present study, leveraging data from the German Stroke Registry-Endovascular Treatment (GSR-ET [20, 21]), we analyzed the neurointerventional periprocedural management, time management, complications, and functional outcome in EVT-treated patients with LVO due to BAO.

METHODS

Patients included in the GSR-ET (https://www.clinical- trials.gov; NCT03356392) were analyzed. For detailed information see Alegiani et al. [20] and Wollenweber et al. [21]. The GSR-ET is an open-label, academic, industry-independent, prospective, multicenter, and observational registry study. The registry was established in June 2015. Enrollment is ongoing, and there is no limit as to the number of participating centers. It is the aim of the GSR-ET to achieve area-wide coverage of EVT in Germany. Participating centers commit themselves to consecutively enrolling all patients receiving EVT at their site. Inclusion criteria are: clinical diagnosis of acute ischemic stroke; intention to perform EVT (i.e., initiation of an endovascular procedure); and age ≥18 years. There are no exclusion criteria. Patients, in whom angiography reveals no accessible vessel occlusion are also registered. Between June 2015 and December 2019, 6635 patients from 25 sites in Germany with acute ischemic strokes due to LVO who initiated EVT were included. The decision to perform mechanical thrombectomy was based on the interdisciplinary decisions of the treating physicians including clinical and imaging parameters according to national (German Neurological Society) and international guidelines (ESO, AHA) [17–19]. The decision to perform IVT, with 0.9 mg/kg body weight (10% as bolus) recombinant tissue plasminogen activator, was a clinical decision made locally by experienced neurologists based on individual patient data, clinically relevant functional deficits, and imaging according to national guidelines [22].

Stroke severity was assessed using the National Institute of Health Stroke Scale (NIHSS), and degree of dependence or disability was rated using the modified Rankin Scale (mRS) and the

premorbid mRS (pmRS), respectively. Site of occlusion was determined via computed tomography (CT) angiography, magnetic resonance angiography, or angiography. Reperfusion success was measured by the modified Thrombolysis in Cerebral Infarction (mTICI) score [23]; mTICI2b-3 was rated as successful reperfusion and mTICI3 as complete reperfusion. Evaluation of CT, magnetic resonance imaging (MRI) and angiography was performed by the local investigators (namely, the neuroradiologists). Acute stroke treatment, including treatment with IVT, followed standard of care and was not influenced in any way by the registry as there were no restrictions as to diagnostic or therapeutic procedures. In the GSR-ET, all source data were assessed and rated by the local neurointerventionalists and neurologists. All entered data underwent standardized quality checks that had been programmed to control for consistency, plausibility, and completeness. In cases of inconsistencies or missing data, queries were sent to the local centers [20, 21].

Outcome variables included: functional outcome defined by NIHSS score at discharge; mRS score at 3-month follow-up (assessed by trained neurologists, either by face-to-face or telephone interview); (peri-)procedural time intervals (dependent on times of last seen well [LSW]/symptom onset [SO] and groin puncture [GRO]/flow restoration [FLR]; time interval refers to the interval between SO/ LSW and FLR); ICH; and periprocedural and in-hospital complications.

Good outcome was defined as mRS score 0–2 according to the ESO definition (https://eso-stroke.org/outcome-measures-stroke-modified-rankin-scale-ordinal-logistic-regression/). Substantial neurological improvement was defined as a difference between admission and discharge NIHSS score of ≥8 points or discharge NIHSS score of ≤1, as described previously [24, 25]. ICH was defined as any hemorrhage in routine CT postinterventional imaging 24 h after EVT according to the European Cooperative Acute Stroke Study part II (ECASS II) definition, irrespective of the presence of new clinical symptoms.

Statistical analysis

Continuous variables were tested for normal distribution using the Kolmogorov–Smirnov test. Normally distributed data were presented as mean and standard deviation (±SD) and non-normally distributed data as median (interquartile range [IQR] 25%, 75% percentile) or counts and percentages. Clinical characteristics, imaging data, periprocedural time interval, and outcome parameters were compared in patients using the Kruskal–Wallis test or median test, as appropriate. Binary logistic regression analysis was performed for good clinical outcome (mRS score 0–2) and mortality at follow-up including variables that presented as significant in the univariate analysis or variables that were known outcome predictors (age, sex, pmRS score, NIHSS score at admission, IVT, successful reperfusion, ICH and time interval). We used binomial distribution and logit function to compare outcome variables. For all statistical testing, we used the Statistical Package for Social Science (SPSS Inc., 25.0 for Windows).

RESULTS

Patient characteristics

Out of 6635 patients in the GSR-ET, 640 patients (9.6%; age 72.2 ± 13.3, 43.3% female) experienced BAO. A tandem lesion with an additional occlusion was present in 21.4% of patients including the vertebral artery (10.2%) and the posterior cerebral artery (12.3%). The majority of patients were functionally independent pre-stroke (pmRS score 0–2: 87.4%) and had experienced severe strokes, with a median (IQR) NIHSS score of 17 (8, 27 [for further details see Table 1]).

Endovascular thrombectomy was performed mainly under general anesthesia (86.9%). The majority of patients (44.8%) were treated with a combination of aspiration and stent retriever, and 12.5% of patients were further treated with an acute stenting and/or percutaneous transluminal angioplasty. Periprocedural complications were reported in 120 patients (18.8%). Successful reperfusion was achieved in 88.4%. Substantial neurological improvement at discharge was attained by 45.5% of patients (291 of 640 patients), while 25.8% (152 of 589 patients) died during the hospital stay.

Functional outcome

At 3-month follow-up, good clinical outcome was observed in 31.1% (165 of 530 patients), while mortality was 39.2% (208 of 530 patients; 17.2% missing data for long-term follow-up). In binary logistic regression analysis (for 370 patients with all available data), all variables except sex were independently associated with good clinical outcome (Figure 1a). Regarding mortality, all variables except sex, pmRS score and time interval were associated with mortality (Figure 1b).

Impact of IVT treatment

Forty-five percent of patients (n = 285) received IVT. Patients treated with IVT were more likely to be functionally independent pre-stroke ($p < 0.001$). Time interval was substantially shorter in IVT-treated patients (281 vs. 406 min [$p < 0.001$]; median 125 min), and this was also true for time from admission to FLR (118 vs. 134 min; p = 0.001). Therefore, patient groups differed considerably, especially with regard to time variables. Patients treated with IVT performed better at 24-h follow-up (median NIHSS score 8 vs. 15; p = 0.009) and at 3-month follow-up with respect to good clinical outcome (33.7% vs. 19.4%; $p < 0.001$) and mortality (28.4% vs. 35.8%; p = 0.010 [Figure 2c]). ICH occurred more often in IVT-treated patients (11.2% vs. 6.5%; p = 0.033 [for further details see

TABLE 1 Characteristics of German Stroke Registry-Endovascular Treatment patients ($n = 6635$) with posterior circulation strokes and basilar artery occlusion ($n = 640$).

	GSR-ET posterior circulation strokes with BAO, $n = 640$ (9.6%)
Age, years ± SD	72.2 ± 13.3
Female, *n* (%)	277 (43.3)
Clinical characteristics at admission	
pmRS score, median (IQR)	0 (0, 1) (available in $n = 572$)
Baseline NIHSS score, median (IQR)	17 (8, 27)
Minor stroke (NIHSS score ≤5), *n* (%)	102 (15.9)
Wake up stroke/unknown onset, *n* (%)	158 (24.7)
Last seen well >4.5 h, *n* (%)	81 (12.7)
IVT, *n* (%)	285 (44.5)
Systolic BP at admission ± SD, mmHg	149.1 ± 28.3
Diastolic BP at admission ± SD, mmHg	80.6 ± 17.9
Etiology (according to TOAST classification)	
Cardioembolic, *n* (%)	240 (37.5)
Large artery sclerosis, *n* (%)	183 (28.6)
Other determined cause, *n* (%)	32 (5.0)
Stroke of undetermined cause, *n* (%)	185 (28.9)
Time intervals, median (IQR) min	
Time from SO/LSW to IVT	240.0 (163.5, 543.0)
Time from SO/LSW to GRO	
Time from admission to GRO	75.0 (48.0, 111.0)
Time from SO/LSW to FLR	323.0 (215.0, 509.8)
Time from SO to FLR ($n = 311$)	266 (194, 370)
Time from LSW to FLR ($n = 134$)	614 (410, 946)
Occluded vessels	
BAO	640 (100)
Tandem occlusion	144 (22.5)
+VA	79 (12.3)
+PCA	65 (10.2)
Anesthesia	
General anesthesia, *n* (%)	556 (86.9)
Conscious sedation, *n* (%)	84 (13.1)
Unknown, *n* (%)	5 (0.8)
Technical aspects/devices	
Aspiration catheter only, *n* (%)	120 (18.8)
Stent retriever only, *n* (%)	195 (30.5)
Aspiration and stent retriever, *n* (%)	287 (44.8)
Unknown	37 (5.8)
Acute stenting/PTA, *n* (%)	80 (12.5)
Number of passages ± SD	2.0 ± 1.5 (data available in $n = 587$)
Periprocedural medication, *n* (%)	225 (35.2) (data available in $n = 634$)
Heparin, *n* (%)	146 (64.9)
Heparin IU ± SD	4207 ± 2058
Tirofiban, *n* (%)	45 (20.0)
Treatment associated periprocedural complications, *n* (%)[a]	120 (18.8)
ICH	18 (15.0)
Vasospasm	41 (34.2)
Groin hematoma	7 (5.8)
Groin aneurysm	3 (2.5)
Device malfunction	3 (2.5)
Dissection/ perforation	27 (22.5)
Clot migration	25 (20.8)
Other	53 (44.2)
Successful reperfusion mTICI 2b/3, *n* (%)	554 (86.6)
mTICI 2b	150 (23.4)
mTICI 3	404 (63.1)
Unknown	13 (2.0)
Outcome at discharge (available in n = 589)	
NIHSS score, median (IQR)	4 (1, 11)
mRS score, median, (IQR)	4 (2, 6)
Substantial neurological improvement	291 (45.5)
Mortality (mRS score 6), *n* (%)	152 (23.8)
Hospital stay, days ± SD	10.7 ± 8.3
Complications, *n* (%)	208 (32.5)
ICH, *n* (%) in follow-up after 24 h in routine CT imaging	53 (8.3)
Outcome at 90 days follow-up (available in n = 530)	
Good clinical outcome (mRS score 0–2)	165 (25.8)
mRS score 0–3	223 (34.8)
Mortality	208 (32.5)

Abbreviations: BAO, basilar artery occlusion; BP, blood pressure; GRO, groin puncture; GSR-ET, German Stroke Registry-Endovascular Treatment; ICH, intracerebral hemorrhage; IU, international units; IQR, interquartile range; IVT, intravenous thrombolysis; LSW, last seen well; mTICI, modified Thrombolysis in Cerebral Infarction; mRS, modified Rankin Scale; *n*, number; NIHSS, National Institute of Stroke Scale; PCA, posterior cerebral artery; pmRS, premorbid mRS; PTA, percutaneous transluminal angioplasty; SD, standard deviation; SO, symptom onset; VA, vertebral artery.

[a]Multiple complications possible.

Table S1]). IVT treatment was independently associated with good clinical outcome (odds ratio [OR] 2.950, 95% confidence interval [CI] 1.719–5.062; $p < 0.001$ [Figure 1]).

Impact of grade of reperfusion (mTICI2b vs. mTICI3)

Successful reperfusion (mTICI2b and 3) was independently associated with good clinical outcome (OR 4.796, 95% CI 1.121–20.521 [Figure 1]) and was observed as mTICI2b in 150 patients (23.9%, mTICI score available for $n = 627$) and as mTICI3 in 404 patients

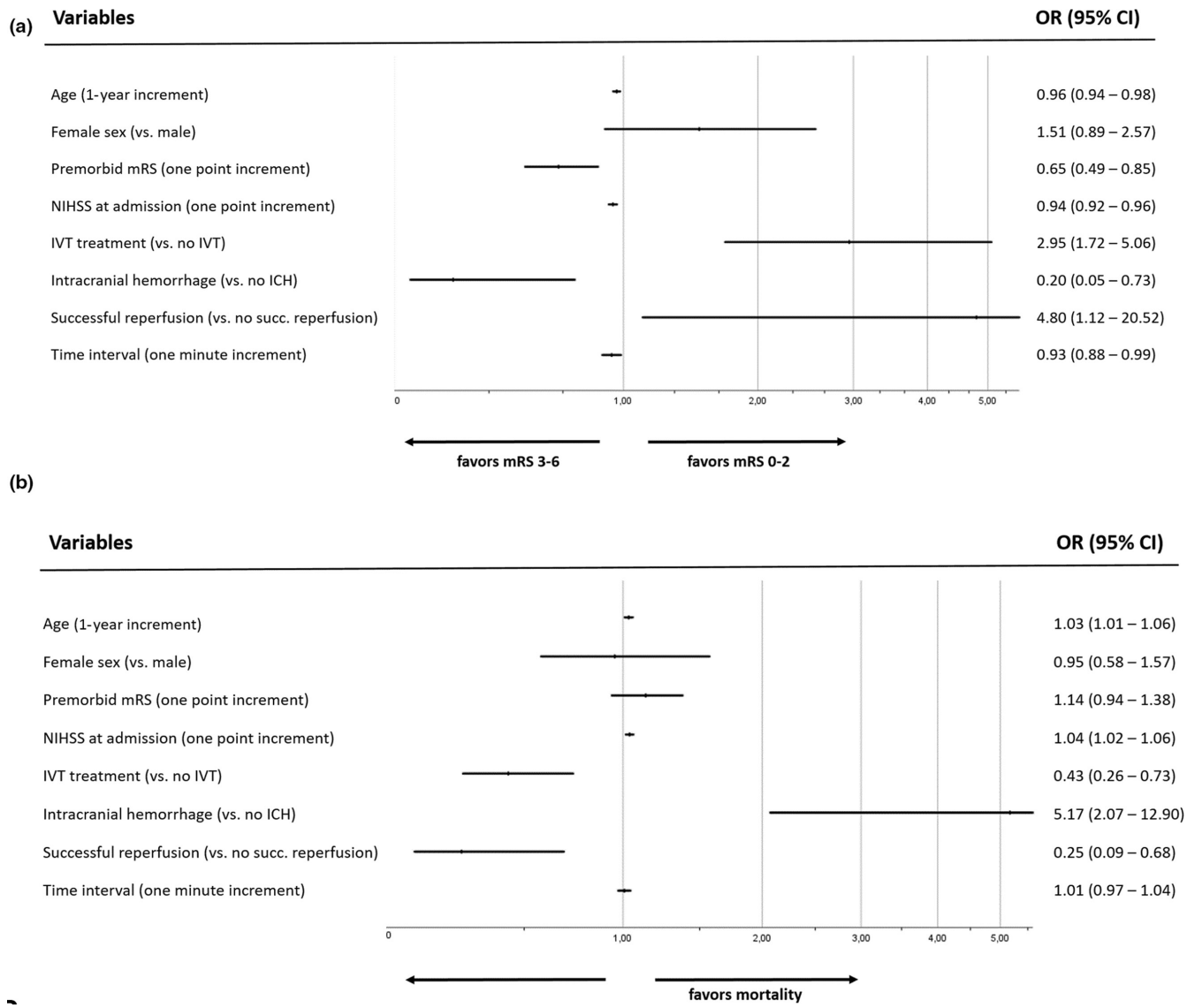

FIGURE 1 Forest plot of logistic regression analysis for good versus poor outcome and for mortality. (a) Odds ratios (ORs) and 95% confidence intervals (CIs) of binary logistic regression analysis: Factors such as time interval (symptom onset [SO] or last seen well [LSW] to flow restoration [FLR]), successful reperfusion, intracerebral hemorrhage (ICH), intravenous thrombolysis (IVT), National Institute of Health Stroke Scale (NIHSS) score at admission, premorbid modified Rankin Scale (pmRS) and age are associated with good clinical outcome (modified Rankin Scale [mRS] score 0–2) at 90-day follow-up. (b) ORs and 95% CIs of binary logistic regression analysis: Factors such as successful reperfusion, ICH, IVT, NIHSS score at admission and age are associated with mortality at 90-day follow-up.

(64.4%). As mTICI is not perfectly applicable to posterior circulation because of the difficulty in addressing residual side branch occlusions [26], we additionally compared mTICI3 ("complete reperfusion") with TICI2b patients ("good reperfusion" [Table 2 and Figure 2b]). In this analysis, mTICI3 patients had markedly better outcomes regarding substantial neurological improvement (38.7% vs. 54.0%; $p = 0.002$) and good outcome at follow-up (24.4% [29 of 119 patients] vs. 38.9% [129 of 332 patients]; $p = 0.005$). In logistic regression analysis, mTICI3 was independently associated with good clinical outcome (OR 2.000, 95% CI 1.007–3.717), but not with mortality (OR 0.670, 95% CI 0.3861.164; $p = 0.156$). In addition, the mTICI3 and mTICI2b groups differed in several other important and possibly interconnected variables, as indicated in Table 2. In brief, periprocedural time management showed that time from GRO to FLR as well as time from admission to FLR was shorter in mTICI3 patients (53 vs. 37 min and 143 vs. 117 min, respectively; $p < 0.001$ and $p = 0.004$). Interventionalists needed more passages in mTICI2b patients (2.7 vs. 1.7; $p < 0.001$) as well as more additive medication (46.0% vs. 32.0%; $p = 0.003$), and periprocedural complications occurred twice as often in mTICI2b than in mTICI3 patients (27.3% vs. 13.1%; $p < 0.001$).

Impact of time intervals until flow restoration

In multivariate analysis time intervals until FLR showed an independent association with patient outcome. This finding was to be

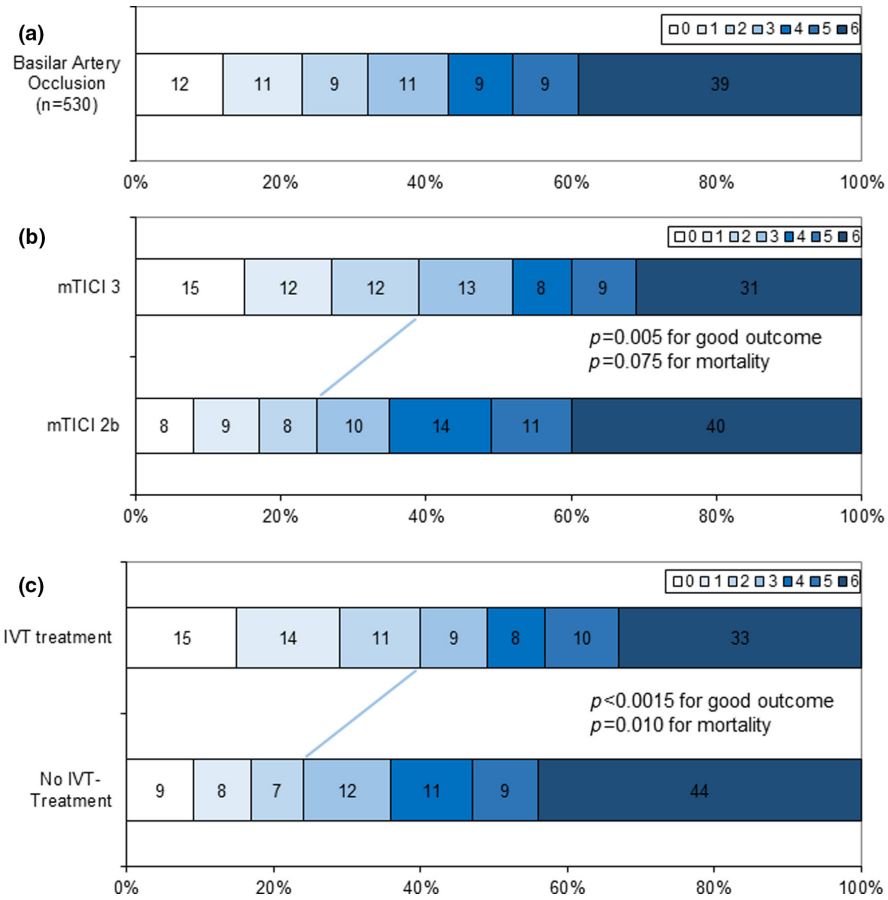

FIGURE 2 Distribution of functional clinical outcome in basilar artery occlusion (BAO) patients. (a) Clinical outcome in all BAO patients. (b) Comparison of clinical outcome in good reperfusion (modified Thrombolysis in Cerebral Infarction [mTICI]2b) versus complete reperfusion (mTICI3). (c) Comparison of clinical outcome in patients with intravenous thrombolysis (IVT) treatment versus those without IVT treatment.

expected as longer ischemic time increasingly damages brain tissue. However, this result was based on data not distinguishing between "time since SO" (available for $n = 311$, median [IQR] 266 [194, 370] min) and "LSW" (available for $n = 134$, median [IQR] 614 [410, 946] min). When particular attention was paid to the different available time intervals (SO or LSW until GRO or FLR [Figure S1]), no obvious time difference between the outcome groups was visible. Reperfusion success measured by mTICI showed no obvious association with the different presented time intervals.

A trend can be described for the patients with available data on time interval between LSW and successful reperfusion: patients with bad clinical outcome despite successful reperfusion (LSW to GRO: mean 698 ± 548 min) tended to present with longer time intervals than patients with good clinical outcome (LSW to GRO: mean 605 ± 381 min; $p = 0.3$), without a statistically significant difference. This trend was absent for patients with available time intervals since SO: within the timeframe in which reperfusion was confirmed in the existing cohort (SO to GRO: median [IQR] 222 [149, 324] min), no time difference was observed for the outcome groups in case of successful reperfusion.

DISCUSSION

In this study, we present one of the largest analyses of daily life practice in BAO acute treatment with EVT with / without IVT in a multicenter German stroke registry. Our key findings that are highly relevant for clinical practice in treating patients with BAO are as follows. First, EVT was safe and effective in treating BAO. Nearly half of our patients showed substantial neurological improvement after mechanical thrombectomy and nearly one third had a good outcome at follow-up. Nearly 40% died during the follow-up period. Second, complete reperfusion (mTICI3) was found to be an independent predictor of good outcome, in contrast to mTICI2b, suggesting that complete reperfusion might be of special importance for functional outcome. However, this could be explained by the higher impact of also smaller infarcts in the posterior circulation and brainstem. Third, IVT plus EVT also seemed to be safe and effective and to be associated with better functional outcome. Fourth, the negative effect of time delay in the group of patients with known SO appeared to be small. In the group of patients with unknown SO (the very late time window), the impact of time seemed to become relevant, suggesting additional imaging should be considered for these patients.

Outcomes in our study were comparable to former analyses. However, a good outcome (mRS score 0–2) was very good in comparison to the ATTENTION study (mRS score 0–2: 33% vs. 31.1% in the GSR-ET), but was less often observed than in the BEST trial (mRS score 0–2: 39% vs. 31.1% in the GSR-ET) or BASICS (mRS 0–2 35.1% vs. 31.1% in the GSR-ET) [6]. This notion is further supported by the fact that good outcome in our cohort was even more often observed than in the BASILAR registry (mRS score 0–2 27.4%

TABLE 2 Good reperfusion (mTICI2b) versus complete reperfusion (mTICI3) in patients with basilar artery occlusion.

	GSR-ET posterior circulation strokes with BAO, *n* = 640 (9.6%)		*p* value
	mTICI 2b *n* = 150 (23.4%)	mTICI 3 *n* = 404 (63.1%)	
Age, years ± SD	71.0 ± 14.2	71.9 ± 13.3	0.857
Female, *n* (%)	65 (43.3)	171 (42.3)	0.832
Clinical characteristics at admission			
pmRS score, median (IQR)	0 (0, 1)	0 (0, 1)	0.493
Baseline NIHSS score, median (IQR)	18 (9, 28)	15 (11, 26)	0.029
IVT, *n* (%)	59 (39.3)	184 (45.5)	0.191
Etiology (according to TOAST classification)			0.441
Cardioembolic, *n* (%)	52 (34.7)	163 (40.3)	
Large artery sclerosis, *n* (%)	48 (32.0)	108 (26.7)	
Other determined cause, *n* (%)	8 (5.3)	21 (5.2)	
Stroke of undetermined cause, *n* (%)	42 (28.0)	112 (27.7)	
Time intervals, minutes, median (IQR)			
Time from admission to FLR	143.0 (101.0, 177.0)	117.0 (82.0, 163.5)	0.004
Time from GRO to FLR	53.0 (31.5, 85.0)	37.0 (23.0, 60.0)	<0.001
Time from SO/LSW to FLR	332.5 (238.0, 523.5)	313.0 (201.0, 507.0)	0.128
Acute stenting/PTA, *n* (%)	22 (14.7)	46 (11.4)	0.337
Occluded vessels			
BAO, *n* (%)	150 (100)	404 (100)	
Tandem occlusion	42 (28.0)	74 (18.3)	0.013
+VA	22 (14.7)	42 (10.4)	0.163
+PCA	25 (16.7)	34 (8.4)	0.005
Technical aspects/devices			
Aspiration catheter only, *n* (%)	22 (14.7)	84 (20.9)	0.111
Stent retriever only, *n* (%)	33 (41.3)	124 (30.7)	0.612
Aspiration and stent retriever, *n* (%)	39 (26.0)	183 (45.3)	0.425
Periprocedural medication, *n* (%)	69 (46.0)	133 (32.9)	0.003
Number of passages ± SD	2.7 ± 1.7	1.7 ± 1.1	<0.001
Treatment associated periprocedural complications, *n* (%)	41 (27.3)	53 (13.1)	<0.001
ICH	5 (3.3)	5 (1.2)	0.100
Vasospasm	14 (9.3)	23 (5.7)	0.128
Outcome at discharge (available in n = 507)			
NIHSS, median (IQR)	5 (2, 12)	3 (1, 9)	0.006
mRS, median, (IQR)	5 (3, 6)	4 (2, 5)	0.003
Substantial neurological improvement, *n* (%)	58 (38.7)	218 (54.0)	0.002
Mortality (mRS score 6), *n* (%)	35 (23.3)	71 (17.6)	0.094
Outcome at 90 days follow-up (available in n = 451)			
Good clinical outcome (mRS score 0–2), *n* (%)	29 (19.3)	129 (31.9)	0.004
mRS score 0–3, *n* (%)	49 (32.7)	143 (35.4)	0.937
Mortality, *n* (%)	48 (32.0)	104 (25.7)	0.075

Abbreviations: BAO, basilar artery occlusion; GRO, groin puncture; GSR-ET, German Stroke Registry-Endovascular Treatment; FLR, flow restoration; ICH, intracerebral hemorrhage; IQR, interquartile range; IVT, intravenous thrombolysis; LSW, last seen well; mTICI, modified Thrombolysis in Cerebral Infarction; mRS, modified Rankin Scale; NIHSS, National Institute of Stroke Scale; PCA, posterior cerebral artery; pmRS, premorbid mRS; PTA, percutaneous transluminal angioplasty; SO, symptom onset; VA, vertebral artery.

Shaded values indicate significant results.

vs. 31.1% in the GSR-ET). Of note, good outcome was less often observed than in our previously published analysis in a smaller cohort (n = 225, mRS score 0–2: 37.7%) [21]. This might in part be attributable to a larger group of patients who were lost to follow-up than in the previous analysis (17.2% vs. 12.0%); if more patients are lost to follow-up, this might hint towards a possible underestimation of good outcome rates.

The median NIHSS score in our study was substantially lower than in the other above-mentioned studies. In the GSR-ET, all patients with BAO were included and therefore our analysis included all of these patients irrespective of baseline NIHSS score, whereas BASICS and ATTENTION only included patients with an NIHSS score ≥10 points. As a result of this, our study shows a trend towards better outcome.

In our BAO population, 20% of the patients presented with concomitant occlusions of the vertebral artery or the posterior cerebral artery (tandem lesion). Treatment approaches in these patients with tandem lesions were heterogeneous. Half of the patients were treated with IVT, while 13% received acute stenting and 13% were treated with a combined intervention with aspiration catheters and stent retrievers.

Overall, we observed successful reperfusion in the vast majority of patients (86.6%), with complication rates comparable or even lower than those observed after EVT in patients with anterior circulation strokes from our registry [27]. The strongest predictors of good outcome were IVT treatment and successful reperfusion—again comparable with anterior circulation strokes [21]. Compared to non-IVT-treated patients, those who underwent IVT had a better functional outcome—despite higher rates of ICH. IVT treatment is recommended for LVO in anterior circulation strokes within a 4.5-h time window in combination with EVT [17–19]. The results from ATTENTION [4] are not generally transferable to a European population. Furthermore, our study was an analysis of real-world data and not a controlled study; therefore, our study offers insights into BAO treatment beyond those obtained from the ATTENTION study, suggesting that, in a real-world setting, IVT plus EVT is effective and safe for the treatment of BAO.

Complete reperfusion (mTICI3) was found to be an independent predictor of good outcome, in contrast to mTICI2b, suggesting that complete reperfusion might be of special importance for functional outcome and therefore mTICI3 should definitely be strived for. The most probable explanation for the magnitude of the observed effect—which is to a lesser extent also reported for anterior circulation strokes—may be the close proximity of functionally important areas in the brainstem and midbrain, where small infarctions also lead to relevant deficits [28]. However, the groups were not well balanced with respect to stroke severity and technical aspects of the intervention.

Several publications, including the BASILAR registry study, suggest that the time window for BAO reperfusion might not be as narrow as in the anterior circulation [29]. These speculations seem to be supported by our data; although we found a small negative effect of time on outcome in the overall cohort, taking a closer look, it seems that the group of patients with unknown SO in particular—who predominantly represent the group in the very late time window—is responsible for this effect, whereas in the group of patients with known SO the time effect is almost negligible. Based on this, additional MRI for patients with unknown SO and very late time window is supported by our findings.

Our study has several limitations. The observational study design, with an absence of controlled and randomized data, and the absence of a control group do not allow conclusions to be drawn about causality. The follow-up rate was 82.8%, which might have led to bias regarding outcome and mortality. We cannot rule out a selection bias caused by the multicenter design with respect to major clinical procedures such as IVT treatment or acute stenting. With respect to complications, we can provide neither radiological criteria for the ICH nor an evaluation of the clinical relevance of ICH.

Furthermore, the selection by treating physicians of the patients to receive or not to receive EVT, with or without IVT, may have biased our findings. This is especially applicable to the low time effect in our study.

Overall, EVT for BAO in daily routine practice appears to be safe and effective. IVT treatment and successful reperfusion predict good outcome, with mTICI3 showing a clear advantage over mTICI2b. Pooled data from large national or international multicenter registries would be the best option to gain additional evidence in the near future for this highly clinically relevant entity. Future clinical trials should address different reperfusion strategies in acute BAO patients.

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CONFLICT OF INTEREST STATEMENT

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. Katharina Feil received funding for research from Boehringer Ingelheim outside of this study (Lexi Study), speaker honoraria from Pfizer outside of this study, and internal funding program/applied clinical research AKF Program (No. 496-0-0)/ANNES. Maria Teresa Berndt, Moriz Herzberg, Steffen Tiedt, Clemens Küpper, Sonja Schönecker, Johannes Wischmann, Konstantin Dimitriadis, Marianne Dieterich, and Claus Zimmer report no disclosures. Thomas Liebig consults for Stryker Neurovascular GmbH and has received speaker honoraria from Pfizer, Covidien, Phenox, and Microvention outside of this study. Lars Kellert has received funding for travel or speaker honoraria from Alexion, AstraZeneca, Bayer Vital, Boehringer Ingelheim, Bristol-Meyer-Squibb, Daiichi Sankyo, and Pfizer outside of this study. Tobias Boeckh-Behrens received speaker honoraria from Philips and Phenox outside of this study.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

The study was conducted in accordance with the Declaration of Helsinki and was centrally approved by the Institutional Review Board of the Ludwig-Maximilians Universität, Munich, Germany (protocol No. 689-15). Further approval was obtained from local institutional review boards according to local regulations.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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APPENDIX

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