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Safety and Outcome of Intra-Arterial Treatment for Basilar Artery Occlusion

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IMPORTANCE After the many positive results in thrombectomy trials in ischemic stroke of the anterior circulation, the question arises whether these positive results also apply to the patient with basilar artery occlusion (BAO).

OBJECTIVE To report up-to-date outcome data of intra-arterial (IA) treatment in patients with BAO and to evaluate the influence of collateral circulation on outcome.

DESIGN, SETTING, AND PARTICIPANTS Single-center retrospective case series of 38 consecutive patients with BAO who underwent IA treatment between 2006 and 2015 at a comprehensive stroke center.

EXPOSURES Intra-arterial treatment by mechanical thrombectomy and/or IA thrombolysis.

MAIN OUTCOMES AND MEASURES Adequate recanalization was defined as a score of 2b or 3 on the Thrombolysis in Cerebral Infarction score. Favorable outcome was defined as a modified Rankin Scale of 0 to 3 at first follow-up. Imaging data on the patency of the vertebral arteries and posterior communicating arteries, as well as the presence of cerebellar arterial anastomosis, were recorded and posttreatment imaging results were reviewed.

RESULTS Of the 38 patients with BAO, mean (SD) age was 58 (16) years, and 21 (55%) were male. Twenty-seven patients (71%) were treated with intravenous thrombolysis before IA therapy. Mechanical thrombectomy was applied to 30 patients, and 7 patients received local urokinase without thrombectomy. The median National Institutes of Health Stroke Scale score was 21 (interquartile range [IQR], 15-32) points, and median time to IA treatment was 288 (IQR, 216-380) minutes. Adequate recanalization was achieved in 34 of 38 cases (89%). Functional outcome was favorable in 19 (50%) patients. No association between patent collateral circulation and favorable outcome was found. Symptomatic intracranial hemorrhage occurred in 2 patients (5%).

CONCLUSIONS AND RELEVANCE The proportion of patients reaching a favorable outcome in our study is comparable to the IA-treated group of the MR CLEAN trial and better than the results reported in the BASICS registry, suggesting that IA intervention in patients with BAO is an effective and safe treatment modality in daily clinical practice.

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In 2015, conclusive evidence emerged from multiple clinical trials for the efficacy and safety of intra-arterial treatment in patients with acute ischemic stroke in the anterior circulation caused by an intracranial large-vessel occlusion.[1] For the posterior circulation, the situation is less clear. There is a lack of data from randomized clinical trials to establish the best treatment for acute basilar artery occlusion (BAO). In the prospective registry from the Basilar Artery International Cooperation Study (BASICS), no difference in terms of functional outcome could be demonstrated for intra-arterial intervention (IA) as primary treatment compared with intravenous thrombolysis (IVT).[2]

The BASICS study group started a multicenter international study in 2013, aiming for a randomized clinical comparison between IVT alone and IVT followed by IA treatment in acute BAO.[3] The question remains whether this trial will reach its inclusion target, especially because some stroke clinicians are reluctant to include patients after the many positive results of trials for IA intervention in patients with anterior circulation stroke.

Moreover, the natural history and prognosis of BAO is worse compared with ischemic stroke in the anterior circulation: more than 80% of the patients with an initial severe deficit had an unfavorable outcome in the BASICS registry. Poor prognosis strongly correlates with failure to achieve recanalization of the occluded basilar artery.[4-7]

It took years and multiple clinical trials before the efficacy of IA treatment for anterior circulation strokes was proven in a randomized design. It is likely that the recent trials had positive results because of better patient selection, application of IA therapy in addition to IVT, and the improved treatment techniques with modern stent retrievers. In the BASICS registry, the IA-treated group did not receive IVT as first-line therapy and the new thrombectomy devices were not commercially available during the inclusion period. For BAO, a retrospective analysis indeed showed improvement of outcome after the implementation of the new thrombectomy devices.[8]

We report the outcome of patients with acute BAO who received IA treatment in a comprehensive stroke center, to compare these results with the older data from the BASICS registry. Furthermore, we evaluated prognostic factors, in particular collateral blood supply, because adequate collateral circulation has been associated with favorable outcome in anterior circulation strokes in patients treated with mechanical thrombectomy.[9,10] Finally, we evaluated the occurrence of intracranial hemorrhage and the clinical relevance of postprocedural computed tomography (CT) imaging findings.

Key Points

Question How should we treat patients with acute basilar artery occlusion (BAO) in light of the conclusively positive results of intra-arterial treatment for ischemic stroke in the anterior circulation?

Findings In this case series of 38 endovascular-treated patients with BAO, 19 patients had a favorable outcome. These results are more advantageous than older data and comparable to those of recent thrombectomy trials in anterior circulation stroke.

Meaning Clinicians could consider providing additional intra-arterial treatment as part of standard care for patients with BAO.

Methods

Study Design and Patients

This is a single-center retrospective case series analysis of consecutive patients with a BAO who underwent IA treatment at the University Medical Center Groningen between January 1, 2006, and December 1, 2015. The University Medical Center Groningen is a comprehensive stroke center in the northern region of the Netherlands. It serves as both a primary and secondary referral center for acute IVT or IA treatment in stroke. Data were available by means of a local database. Additional information was obtained from the patients' medical records. Because of the retrospective study design, approval by a medical ethics committee was not mandatory according to the local regulation authorities.

After clinical evaluation, BAO was diagnosed with computed tomographic angiography or magnetic resonance angiography and subsequently confirmed with conventional angiography (digital subtraction angiography). Intra-arterial treatment consisted of IA thrombolysis, mechanical thrombectomy, or a combination of both, based on the judgment of the operator. Intra-arterial therapy was given either as primary treatment or add-on to intravenous therapy with recombinant tissue plasminogen activator. Intravenous recombinant tissue plasminogen activator was administered to eligible patients, in accordance with current management guidelines.

Patients with BAO were considered eligible for IA intervention based on the judgment of the treating stroke neurologist. Our local protocol for BAO recommends IA treatment up to 12 hours after symptom onset; however, under certain circumstances (eg, stuttering onset) longer onset-to-treatment times are allowed. In patients with initial mild symptoms and secondary worsening, clinically consistent with BAO, the moment of secondary worsening was taken as estimated time of occlusion. Start of the IA intervention was defined as the time of groin puncture.

Outcome Measures

Stroke severity was dichotomized as severe or mild to moderate. Neurological deficits consisting of coma, locked-in state, or tetraparesis were classed as severe, and all other deficits as mild to moderate. Neurological deficit was further evaluated with the Glasgow Coma Scale (GCS) and National Institutes of Health Stroke Scale (NIHSS) score before treatment. Outcome was measured with the modified Rankin Scale (mRS) at first follow-up (or at discharge if no follow-up had taken place). Favorable outcome was defined as mRS 0 to 3, unfavorable as mRS 4 to 6. This is in accordance with the definition used in the BASICS registry. Patients with mRS of 3 are not fully independent, requiring some help, but are able to walk without assistance. When the severity of the condition is taken into account, we judge it reasonable to categorize mRS scores of 3 among favorable outcome for BAO.

Table 1. Baseline Characteristics

Characteristic	All (N = 38)	Severe (n = 23)	Mild/Moderate (n = 15)	*P* Value[a]
Age, mean (SD), y	58 (16)	62 (14)	52 (17)	.08
Male sex, No. (%)	21 (55)	13 (57)	8 (53)	.85
Hypertension, No. (%)	19 (50)	10 (44)	9 (60)	.32
Diabetes mellitus, No. (%)	4 (11)	3 (13)	1 (6)	>.99
Hyperlipidemia, No. (%)	19 (50)	8 (35)	11 (73)	.02
Smoking, No. (%)	15 (40)	7 (30)	8 (53)	.16
Antithrombotic treatment,[b] No. (%)	7 (18)	4 (17)	3 (20)	>.99
National Institutes of Health stroke scale score, median (IQR)	21 (15-32)	31 (22-34)	14 (9-16)	<.001
GCS sum score,[c] median (IQR)	10 (6-11)	7 (5-10)	11 (11-14)	<.001
IVT, No. (%)	27 (71)	16 (70)	11 (73)	>.99
Time to IVT, median (IQR), min	155 (120-180)	158 (135-194)	120 (90-160)	.03
Time to IAT, median (IQR), min	288 (216-380)	255 (195-320)	340 (255-480)	.20
Stroke etiology, No. (%)				
Atherosclerosis	19 (50)	12 (52)	7 (47)	.74
Cardioembolic	6 (16)	3 (13)	3 (20)	.66
Other	7 (18)	4 (17)	3 (20)	>.99
Unknown	6 (16)	4 (17)	2 (13)	>.99

Abbreviations: GCS, Glasgow Coma Scale; IAT, intra-arterial treatment; IQR, interquartile range; IVT, intravenous thrombolysis.

[a] $P < .05$ was considered significant. *P* values are derived with independent-samples *t* test from means of scale variables and χ^2 test or Fisher exact test where appropriate for nominal variables.

[b] Both platelet inhibitors and anticoagulation.

[c] Sum score of the Eye (1-4), Motor (1-6), and Verbal (1-5) score of the GCS, with a minimum of 3 and maximum of 15 points. Locked-in state with obeying of ocular commands was scored as Motor, 6.

Imaging and Collateral Flow Assessment

All the imaging data before, during, and after IA treatment were reevaluated for this study. Postprocedural recanalization was assessed with the Thrombolysis in Cerebral Infarction (TICI) score on the final digital subtraction angiography run and adequate recanalization was defined as a TICI score of 2b or 3.[11] To determine the quality of collateral circulation, we assessed the patency of 3 potential collateral vessels on pretreatment digital subtraction angiography and/or computed tomographic angiography, that is, the vertebral arteries, the posterior communicating arteries, and the anastomosis between the posterior cerebellar artery (PICA) and the superior cerebellar artery (SCA). For each vertebral artery, no patency was defined as the presence of 1 of the following: complete occlusion, PICA termination, aplasia or clear hypoplasia (vessel diameter of ≤2 mm at V_1 and V_2 segment), or a high-grade stenosis of more than 70% in the course of the vessel. For each posterior communicating artery, no patency was defined as absence of arterial contrast between the top of the carotid artery and the posterior cerebral artery (when contrast supply was doubtful, this was scored as no patency). For the PICA-SCA anastomosis, (functional) patency was defined as retrograde contrast filling of the SCA from the PICA on either side, and no patency by the absence of this. In addition, we assessed whether the PICA-SCA and posterior communicating artery collaterals provided (retrograde) filling of the basilar tip. For each collateral subgroup, and for various combinations, the influence of patency on functional outcome was investigated.

Brain CT scans obtained within 36 hours after the IA procedure were reevaluated for the presence of evident ischemic changes in or around the pontine region, evident hemorrhage, or evident intraparenchymal contrast staining (as a sign of a disrupted blood-brain barrier). We defined symptomatic hemorrhage as any clinical deterioration in the presence of intracranial hemorrhage at radiological evaluation.

Statistical Analysis

χ^2 tests or Fisher exact tests were used to evaluate the influence of collateral vessel patency and other prognostic factors on outcome. χ^2 tests were further used to study the association between postprocedural imaging results and outcome. We did not perform multivariate analysis because of small sample sizes. All *P* values are 2 sided, and $P < .05$ was considered significant. IBM SPSS statistics, version 22, was used.

Results

Baseline Characteristics

Thirty-eight consecutive patients received IA treatment for BAO between January 1, 2006, and December 1, 2015. Baseline characteristics are presented in **Table 1**. Median NIHSS score was 21 (interquartile range [IQR], 15-32) and median GCS sum score, 10 (IQR, 6-11). Seventeen patients had a GCS of 8 or less, of whom 10 met the formal criteria for coma (eye/motor response/verbal 1-5-2 or lower). Furthermore, 5 patients presented with quadriparesis and GCS sum score greater than 8. Median time to IA treatment was 288 (IQR, 216-380) minutes. Twenty-seven patients (71%) received IVT before IA treatment. Mean time to IVT was significantly shorter for the mild-to-moderate group. All patients were treated under general anesthesia except 1. During the study period, 9 patients with proven BAO did not receive IA treatment in our center for various reasons (eTable 1 in the Supplement).

Periprocedural Characteristics

Periprocedural characteristics are presented in **Table 2**. A thrombectomy device was used in 30 patients (79%), of whom 15 received a combination with IA pharmacological therapy. In total, 32 devices were used, mostly the Trevo stent retriever (19 patients), and furthermore the Merci (7), ReVive (3),

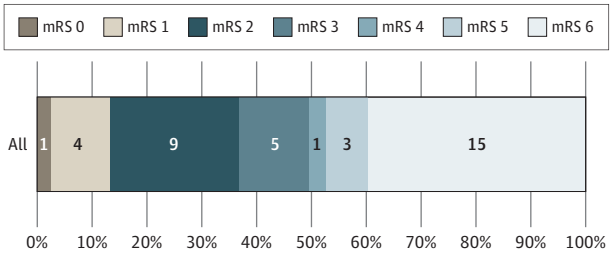
Table 2. Periprocedural Characteristics

Characteristic	Patients, No. All (N = 38)	Severe (n = 23)	Mild to Moderate (n = 15)
Type of intra-arterial treatment			
Pharmacological	7	4	3
Thrombectomy	15	10	5
Combination	15	9	6
No treatment[a]	1	0	1
Localization of occlusion[b]			
Complete	9	8	1
Proximal	4	1	3
Midbasilar	6	2	4
Distal	8	5	3
Proximal plus mid	6	3	3
Mid plus distal	5	4	1
Thrombolysis in Cerebral Infarction score			
0	3	2	1
1	1	0	1
2a	0	0	0
2b	13	8	5
3	21	13	8

[a] In this case the intra-arterial catheter could not be maneuvered into the vertebral arteries.

[b] Complete indicates basilar artery occlusion from the fusion of the vertebral arteries to the division into posterior cerebral arteries; proximal, from fusion of the vertebral arteries to anterior inferior cerebellar arteries; mid, from anterior inferior cerebellar arteries to superior cerebellar artery; distal, from superior cerebellar artery to the division into posterior cerebral arteries.

Figure. Outcome for the Total Group



Data are total numbers. Modified Rankin Score (mRS) was measured at first follow-up (median, 3 months [range, 1-5 months]).

Solitaire (2), and Catch (1). In 7 patients, only pharmacological therapy was applied with IA urokinase. In 1 case, mechanical thrombectomy could not be performed because of extensive tortuosity of the vertebral artery and no IA treatment was administered. Adequate recanalization (TICI 2b or 3) was achieved in 34 cases (89%).

Outcome

Favorable outcome (mRS 0-3) was seen in 19 patients (50%), and 15 patients died (39%). Fourteen patients (37%) reached mRS 0 to 2. The **Figure** shows full outcome results. Of the patients with initial severe neurological deficit, 9 of 23 had a favorable outcome (39%), vs 10 of 15 (67%) patients with mild-to-moderate deficit (P = .10). When only patients treated with a thrombectomy device were analyzed, favorable outcome was seen in 15 patients (50%).

Table 3. Influence of Collateral Circulation on Functional Outcome

Parameter	Patients, No. Favorable Outcome[a]	Unfavorable Outcome	P Value
Patent VAs, No.			
0	5	10	
1	5	4	.23
2	9	5	
Patent VAs (binary), No.			
0	5	10	.10
1 or 2	14	9	
Patent PICA-SCA anastomosis[b]			
No	10	7	.15
Yes	5	10	
Patent PCOMs, No.			
0	2	2	
1	5	9	.38
2	12	8	
Collateral filling top of basilar artery[c]			
No	2	4	.65
Yes	13	12	
Composite collateral score[d]			
0-2 patent collateral vessels	7	11	.19
3-5 patent collateral vessels	12	8	

Abbreviations: PCOM, posterior communicating artery; PICA-SCA, posterior inferior cerebellar artery, superior cerebellar artery; VA, vertebral artery.

[a] Favorable outcome is defined as modified Rankin Scale 0 to 3 at first follow-up.

[b] Six patients were left out because reliable data were lacking.

[c] Retrograde contrast filling of the basilar tip above the SCA by either a PCOM or the PICA-SCA anastomosis. Seven patients were left out because of a normal filling pattern of the basilar artery up to the SCA.

[d] Combined score of the patency of the VA (0, 1, or 2 patent vessels), the PICA-SCA anastomosis (0 or 1 patent vessel), and the PCOM (0, 1, or 2 patent vessels).

Prognostic Factors

There was a significant correlation between favorable outcome and younger age (P = .04 for age <65 years) and lower NIHSS (P = .001 for NIHSS <20), but not for sex, hyperlipidemia, prior treatment with IVT, or time to treatment of more than 4 hours (vs <4 hours) and more than 6 hours (vs <6 hours). eTable 2 in the Supplement provides the full results.

Collateral Circulation Patency and Outcome

No significant influence on outcome was observed for collateral vessel patency, analyzed per vessel category and in various combinations (**Table 3** and eTable 3 in the Supplement). For the presence of at least 1 patent vertebral artery, there was a nonsignificant finding of better outcome: 14 of 23 patients (61%) with 1 or 2 patent vertebral vessels had a favorable outcome, compared with 5 of 15 (33%) without a patent

vertebral artery (P = .10). The relevant results in the subgroups (severe vs mild to moderate) can be found in eTable 3 in the Supplement.

Complications and Postprocedural Imaging Results

Thirty-one patients (82%) underwent follow-up imaging within 36 hours after the intervention, often as a routine procedure before initiation of antiplatelet therapy (**Table 4**). Two symptomatic intracranial hemorrhages were seen (5%), both in patients treated with IA urokinase. In 1 of these cases IVT was also applied, in the other the IA treatment took place approximately 9 hours after onset and additional heparinization was given for 24 hours after the procedure, followed by a second IA procedure. Both patients had TICI scores of less than 2b and an unfavorable outcome. Furthermore, there was 1 case with asymptomatic intracranial hemorrhage after IA combination treatment. When thrombectomy was the only IA treatment modality (n = 15), no intracranial hemorrhage was observed. No other directly procedure-related complications were seen.

The presence of any of the earlier defined abnormalities on the first postprocedural noncontrast CT was negatively correlated with favorable outcome: only 5 of 18 patients (28%) with scan abnormalities had a favorable outcome vs 9 of 13 (69%) without imaging abnormalities (P = .02).

Table 4. Complications and Postprocedural Imaging Characteristics

Characteristic	Patients, No. (N = 38)
Complications during hospitalization	
Symptomatic intracranial hemorrhage	2
Reocclusion	3
Other[a]	4
Imaging characteristics after the intervention (<36 h)	
Intraparenchymal contrast staining	11
Hemorrhage	3[b]
Ischemia	5
No imaging available	7

[a] Other complications: asymptomatic cortical venous thrombosis (detected on computed tomographic angiography 5 days after the procedure) (1), pneumonia (2), pneumothorax (1).

[b] 1 Asymptomatic.

Discussion

This study is one of the largest single-center retrospective analyses of outcome after IA treatment in patients with BAO published in recent years, and only a few studies have examined the influence of collateral circulation in posterior circulation strokes before.

We observed a favorable outcome (mRS, 0-3) in half of the patients. This is substantially better than the rate of 32% in treated patients as reported in the BASICS registry. For severe stroke, the favorable outcome rate was 39%, vs 17% in the IA group of the BASICS registry (note that no IVT was given to these patients and outcome was assessed at 1 month).[2] Compared with our data, embolic stroke was more prevalent in the BASICS registry and large-vessel atherosclerosis occurred less frequently.

In the IA-treated group of the MR CLEAN trial, the first randomized clinical trial that established the effectiveness of thrombectomy in ischemic stroke of the anterior circulation, approximately 50% of the patients had mRS scores of 0 to 3 after 3 months.[12] This percentage of favorable functional outcome is comparable to our results, which is remarkable because mean stroke severity in our group was higher and the prognosis based on the natural history of BAO is generally worse.

No significant correlation between collateral vessel status and outcome could be demonstrated. A recent post hoc analysis of the MR CLEAN study showed that the treatment effect of IA therapy in anterior circulation strokes was greatest in patients with good collateral vessel status at baseline,[13] whereas other authors did not find such correlation.[14] The posterior circulation possesses some distinctive anatomical characteristics, such as multiple collateral vessels from various origins and with different connection sites, plus considerable functional anastomoses. This could lead to less dependency on 1 or 2 large collateral vessels.[4] A functional marker of collateral circulation is perfusion/diffusion magnetic resonance imaging mismatch. This sign of tissue viability could potentially help to identify the patients who can still benefit from treatment despite longer time from BAO onset to treatment, although trial results in anterior circulation strokes have been disappointing thus far.[15]

Symptomatic intracranial hemorrhage occurred in 2 patients (5%); both were treated with local urokinase and received other types of pharmacological therapy as well. The complication percentage is comparable with the rate as reported in the MR CLEAN trial and much lower than was seen in the BASICS registry (14%), probably reflecting the more advanced intervention techniques today. This confirms the overall safety of IA treatment, and in particular the safety of mechanical thrombectomy.

This study has several limitations. The study design is retrospective and the sample size small. We cannot rule out selection bias, although we applied few restrictions for IA treatment and therefore our cohort gives, in our view, a good representation of daily clinical practice. This notion is supported by the broad variation within the group, for example, in terms of time window before treatment and type of treatment. The fact that no significant correlation between outcome and collateral vessel circulation was found should be interpreted with caution because of the small sample size, and more research is needed on this topic.

Our results principally come from the era of modern thrombectomy devices and are more advantageous than the data from the BASICS registry. This corresponds with other recent studies,[16,17] including a meta-analysis by Gory et al[18] of case series of IA-treated patients with BAO. Fifteen studies published between 2010 and 2014 were analyzed, encompassing a total of 312 patients. In this meta-analysis, 42% of the patients had a favorable outcome, defined as mRS 0 to 2 (compared with 37% in our cohort); the recanalization rate was 81%; and serious complications were rare (4%).

However, despite application of the newest techniques, outcome after acute BAO remains poor for many patients. It is still a devastating condition with enormous potential benefit from recanalization therapy, just as is the case for severe ischemic stroke in the anterior circulation.[19,20] Successful recanalization after large-vessel occlusion, including BAO, is associated with better outcome,[6,21,22] and the chance of recanalization is higher with additional IA treatment.[5,23] These findings, together with the improved outcome rates from recent years, can serve as circumstantial evidence for the effectiveness of IA interventions in BAO, even in the absence of a randomized clinical trial.

Conclusions

Outcome in endovascular-treated patients with BAO in the era of modern thrombectomy devices is better than it was before. With all the current evidence for the efficacy of IA treatment in acute large-vessel stroke, we raise the question whether thrombectomy trials in BAO are still mandatory. Alternatively, IA treatment could be regarded as standard of care and thus offered routinely to all eligible patients with an acute BAO.

AUTHOR INFORMATION

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