THERAPEUTIC ADVANCES in
Neurological Disorders

Original Research

Endovascular treatment of acute basilar artery occlusion in patients with and without atrial fibrillation: results from the ATTENTION registry

Ther Adv Neurol Disord

2023, Vol. 16: 1–8

DOI: 10.1177/17562864231159438

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Abstract

Background: Previous studies have shown a potential beneficial effect of endovascular therapy (EVT) in patients with acute basilar artery occlusion (BAO). It was unclear that whether atrial fibrillation (AF) can affect the clinical outcomes for BAO patients treated with EVT.

Objectives: To investigate the association between AF and clinical outcomes, and whether AF can modify the efficacy and safety of EVT in patients with BAO.

Design: We conducted a multicenter, nationwide, retrospective analysis to investigate how the presence of AF affects treatment allocation for BAO patients.

Methods: The endovascular treatment for acute basilar artery occlusion (ATTENTION) registry was a multicenter, prospective study in China that included acute BAO patients who underwent EVT or received best medical management (BMM) between 2017 and 2021. The outcomes include the distribution of 3-month modified Rankin scale (mRS) score, functional independence (defined as mRS 0–3), symptomatic intracerebral hemorrhage, and mortality.

Results: 2134 patients were included in the study, of which 619 had AF and 1515 did not have AF. The median age was 65 (interquartile range [IQR]: 56–73) years, and 689 (32.3%) patients were female. Multivariate regression analysis indicated no significant association existed between AF and the distribution of mRS (adjusted common odds ratio, 1.05 [95% CI: 0.88, 1.25]; $p = 0.564$) at 90 days. Similarly, AF was not found to have a significant association with and other measured outcomes, or with the effects of EVT in AF subgroups for at 90 days as measured by ordinal mRS (p for heterogeneity $= 0.247$). Finally, no significant differences were found for symptomatic intracerebral hemorrhage and mortality within 90 days between the EVT and BMM groups across AF subgroups.

Conclusions: Our results illustrated that the effect of EVT did not differ statistically in acute ischemic stroke patients with and without AF. Moreover, no significant association between AF and functional or safety outcomes could be detected at 90 days.

Keywords: atrial fibrillation, basilar artery occlusion, clinical outcomes, endovascular treatment

Received: 3 December 2022; revised manuscript accepted: 31 January 2023.

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Introduction

Basilar artery occlusions (BAOs) constitute about 5%–10% of acute intracranial large vessel occlusions.[1,2] Compared with acute large vessel occlusions in the anterior circulation, the functional independence in patients with BAO decreases significantly and mortality rates increase significantly.[3,4] Previous RCT studies have showed a potential beneficial effect of endovascular therapy (EVT) in BAO patients. Endovascular treatment versus standard medical treatment for vertebrobasilar artery occlusion

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(BEST) study was terminated early on account of the high cross-over rate. However, 'per-protocol' and 'as-treated' population results suggested EVT is a better treatment strategy compared to standard medical therapy. Patients with a National Institutes of Health Stroke Scale (NIHSS) score < 10 were included in the modified protocol due to difficulties of enrolment in the Basilar Artery International Cooperation Study (BASICS), resulting in a negative overall result. However, subgroup analysis of the BASICS trial supported EVT performed better than standard medical treatment in BAO patients with moderate to severe onset symptoms, whereby EVT is often recommended for BAO treatment.

Atrial fibrillation (AF) is an established risk factor for acute ischemic stroke (AIS).[5–8] Compared with atherosclerotic occlusion, embolic occlusion is related to worse outcomes for patients with BAO.[2,9] Several observation trials showed patients with AF have higher hemorrhagic transformation and poorer clinical prognosis compared to those without AF after the implementation of intravenous thrombolysis (IVT) therapy.[10,11] A similar association was found in patients treated with EVT.[12–14] However, it should be noted that these investigations mostly focused on the occlusion of anterior circulation and led to conflicting results.

Here, we aim to evaluate the association between treatment allocation and clinical outcomes in patients with and without AF. Our results should aid recommendations of personalized therapy strategies and lower the risk of disability and mortality.

Methods

Study population

The present data were derived from ATTENTION (Endovascular Treatment for acute Basilar Artery Occlusion) registry study.[15] ATTENTION is a multicenter, nationwide, prospective registry to estimate treatment effects of best medical management (BMM) and EVT for patients with acute BAO sampled from across 48 stroke centers and 22 provinces in China (http://www.chictr.org.cn; ChiCTR2000041117). All patients or their legal representatives provided signed, informed consent.

Consecutive acute BAO patients were recruited in this trial if (1) BAO was confirmed by neurovascular imaging angiography (magnetic resonance angiography, computed tomographic angiography, and digital subtraction angiography) within 24 hours of estimated time; and (2) patients had an independent daily living defined by an mRS $\leqslant 2$ before stroke. Patients with another serious illness, evidences of cerebral hemorrhage on presentation and without records of follow-up information were excluded.

Treatments

According to the treatment received, patients were allocated into the BMM or EVT group. Patients in BMM group received IVT with alteplase, anticoagulation, antiplatelet drugs or a combination of the above therapies. Patients in the EVT group received stent retrievers, thromboaspiration, intra-arterial thrombolysis (rt-PA or urokinase), balloon angioplasty, stent deployment, or various combinations of these approaches as decided by the treating physicians.

Outcomes

The primary outcome was the distribution mRS scores toward a better outcome at 3 months. Secondary efficacy outcomes were the proportions of mRS 0–1, 0–2 and 0–3 at 90 days. Safety outcomes were all cause mortality within 3 months after treatment and symptomatic intracranial hemorrhage (sICH).

Statistical analysis

Data were showed as medians (interquartile ranges [IQRs]) or frequencies (percentages). Univariate analyses of baseline characteristics between non-AF and AF groups were performed using Mann–Whitney U test, χ^2 test. The primary outcome parameter was the common odds ratio to shift toward a better outcome of mRS score, estimated by multivariable ordinal logistic regression. In addition, binary logistic regression was employed for secondary outcomes, presenting as odds ratio. Several variables, including age, sex, history of stroke or transient ischemic attack (TIA), diabetes mellitus, the time of onset to admission, IVT, location of occlusion, baseline NIHSS score, hypertension, coronary heart disease, and baseline Posterior Circulation-Alberta Stroke Program Early CT Score (pc-ASPECTS), were controlled in the multivariable analysis. We estimated interactions between the AF status and treatment allocation in primary, secondary and

Table 1. Baseline characteristics of patients by AF subgroups.

	Non-AF	AF	*p* value
Total	1515	619	
Treatment allocation (EVT), no. (%)	1129 (74.5)	543 (87.7)	<0.001
Age, median (IQR), years	65 (55, 73)	66 (57, 74)	0.015
Male, no. (%)	1031 (68.1)	414 (66.9)	0.600
Medical history, no. (%)			
History of hypertension	1079 (71.2)	417 (67.4)	0.078
History of diabetes mellitus	391 (25.8)	137 (22.1)	0.074
History of hyperlipidemia	509 (33.6)	210 (33.9)	0.884
History of coronary heart disease	191 (12.6)	94 (15.2)	0.112
History of stroke or TIA	343 (22.6)	167 (27.0)	0.033
Systolic blood pressure, median (IQR), mmHg	146 (132, 163)	147 (132, 161)	0.719
Diastolic blood pressure, median (IQR), mmHg	84 (76, 94)	85 (76, 95)	0.414
IVT, no. (%)	348 (23.0)	142 (22.9)	0.988
Baseline NIHSS score, median (IQR)	20 (12, 29)	23 (14, 32)	0.001
Onset to admission, median (IQR), min	324 (214.0, 580.5)	353 (224.5, 609.5)	0.112
Occlusion site, no. (%)			<0.001
Proximal basilar artery	548 (36.2)	166 (26.8)	
Middle basilar artery	452 (29.8)	235 (38.0)	
Distal basilar artery	515 (34.0)	218 (35.2)	
pc-ASPECTS, median (IQR)	10 (9, 10)	10 (10, 10)	0.289

AF, atrial fibrillation; EVT, endovascular treatment; IQR, interquartile range; IVT, intravenous thrombolysis; NIHSS, National Institutes of Health Stroke Scale; pc-ASPECTS, Posterior Circulation-Alberta Stroke Program Early CT Score; TIA, transient ischemic attack.

safety outcomes, and used multivariable multiple imputation with five datasets to impute the missing data. All analyses were performed with *R* (version 4.1.0).

Results

Baseline characteristics

A total of 2134 patients constituted the study population (of whom 462 were allocated into BMM group and 1672 were allocated into EVT group), including 619 and 1515 with and without AF, respectively. The baseline characteristics of patients by AF subgroups were presented in Table 1. Patients with AF were older than non-AF patients (66 [57, 74] vs 65 [55, 73]; $p = 0.015$), showed a higher proportion stroke or TIA history (167 [27.0%] vs 343 [22.6%]; $p = 0.033$), had higher baseline NIHSS scores (23 [14, 32] vs 20 [12, 29]; $p = 0.001$), were more frequently treated with EVT (543 [87.7%] vs 1129 [74.5%]) and presented significant differences in occlusion sites (proximal basilar artery 166 [26.8%] vs 548 [36.2%]; middle basilar artery (235 [38.0%] vs 452 [29.8%]; and distal basilar artery (218 [35.2%] vs 515 [34.0%]; $p < 0.001$). No statistical differences were

Table 2. Clinical outcomes by AF subgroups.

	Non-AF	AF	Unadjusted odds ratio (95% CI)	*p* value	Adjusted odds ratio (95% CI)	*p* value
Primary outcome						
mRS at 90 days (IQR)[a]	5 (2, 6)	5 (2, 6)	1.00 (0.85, 1.19)	0.957	1.05 (0.88, 1.25)	0.564
Secondary outcomes[b]						
0–1	321 (21.2)	135 (21.8)	1.04 (0.83, 1.30)	0.751	1.18 (0.92, 1.51)	0.203
0–2	469 (31)	205 (33.1)	1.10 (0.90, 1.35)	0.330	1.21 (0.97, 1.52)	0.088
0–3	565 (37.3)	243 (39.3)	1.09 (0.90, 1.32)	0.396	1.18 (0.95, 1.45)	0.132
Safety outcomes[b]						
sICH	59 (3.9)	30 (4.8)	1.26 (0.80, 1.97)	0.319	1.05 (0.66, 1.66)	0.847
Mortality	594 (39.2)	243 (39.3)	1.00 (0.83, 1.21)	0.983	0.97 (0.79, 1.19)	0.764

AF, atrial fibrillation; CI, confidence interval; IQR, interquartile range; IVT, intravenous thrombolysis; NIHSS, National Institutes of Health Stroke Scale; pc-ASPECTS, Posterior Circulation-Alberta Stroke Program Early CT Score; sICH, symptomatic intracranial hemorrhage; TIA, transient ischemic attack.
Adjusted variables included age, sex, diabetes mellitus, IVT, baseline NIHSS score, location of occlusion, onset-to-admission, history of stroke or TIA, hypertension, baseline pc-ASPECTS, coronary heart disease, treatment allocation.
[a]Indicates common odds ratio results toward a better outcome.
[b]The odds ratio was assessed by logistic regression model.

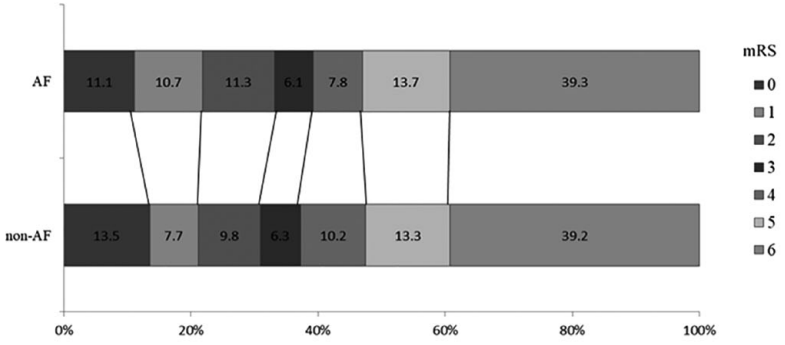

Figure 1. Distribution of 90-day modified Rankin Scale (mRS) by AF subgroups.
AF, atrial fibrillation

detected across remaining baseline characteristics between the two groups.

Association of AF and outcomes at 90 days

Table 2 showed the comparisons of efficacy and safety outcomes between AF patients and non-AF patients. Figure 1 presented the distribution of 90-day mRS scores according to AF status. No significant differences were detected in the distribution of mRS scores at 90 days between the two groups (adjusted common odds ratio [OR]: 1.05 [95% confidence interval [CI]: 0.88, 1.25]). The proportions of mRS 0–1, 0–2, and 0–3 at 90 days were also similar between patients with and without AF. In addition, all secondary efficacy and safety outcomes demonstrated no statistical differences exist between both groups.

Association between AF and treatment allocation on outcomes at 3 months

According to the status of AF and treatment allocation, the distribution of mRS scores was shown

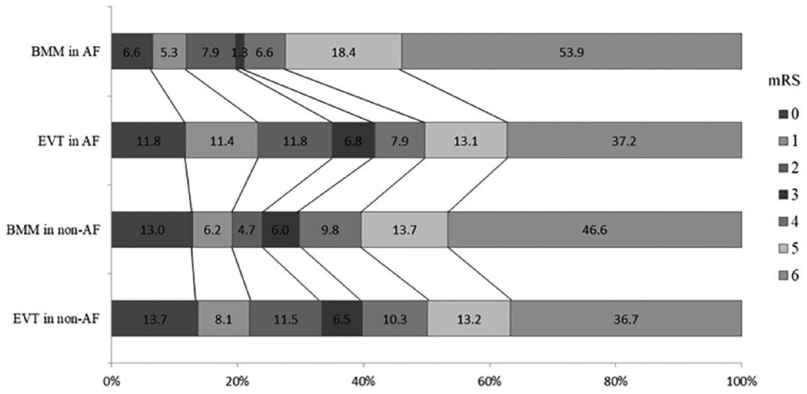

Figure 2. Distribution of 90-day modified Rankin Scale (mRS) by AF subgroups and treatment allocation.

in Figure 2. MRS scores were similar in the two groups and between BMM and EVT (p for interaction = 0.247). We also found that the treatment allocation did not significantly interact with AF in other efficacy outcomes (proportions of mRS 0–1, 0–2, and 0–3 points), and show that AF and treatment allocation do not impact the rate of sICH or the 90-day mortality (sICH: adjusted p for interaction = 0.977; mortality: adjusted p for interaction = 0.393, Table 3).

Discussion

This subgroup analysis of ATTENTION registry showed a similar effect of EVT on functional outcome, and secondary outcomes (mRS 0-1, 0-2 and 0-3 at 90 days, sICH and mortality at 90 days) in AF and non-AF BAO patients. In addition, AF was not related to efficacy and safety outcomes in acute BAO patients.

Patients with BAO caused by AF appeared to be more likely to receive EVT. The incidence of AF in the BEST trial was 27% in patients who received EVT compared to 15% in patients who received BMM.[16] In BASIC trial, the proportion of AF patients in the EVT group (24%) was also higher than those in the BMM group (15%).[17] The underlying reason for the higher use of EVT among BAO patients with concurrent AF remains unclear but may be related to a more abrupt onset and rapid diagnosis of this condition. However, we observed no significant changes associated with EVT effect of AF and non-AF BAO patients in our trial, suggesting that EVT should be performed regardless of the patients had AF or not.

A subgroup analysis of the MR CLEAN trial which mostly enrolled patients with occlusion of anterior circulation found worse clinical outcomes for AF-caused AIS patients after EVT compared to non-AF patients.[18] However, the sample size of AF patients was small and the interpretation of the results should be made cautious. A subsequent meta-analysis from the HERMES collaboration and the ANGEL-ACT registry trials supported no significant interaction effect between AF and functional outcomes at 90 days after EVT.[14,19] Here, our study showed that EVT had similar effects on AF and non-AF patients, whereby AF status should not influence clinical decision to conduct thrombectomy for acute BAO patients.

To consistent with previous reports on EVT in anterior circulation, we found no association between AF and 90-day functional outcomes for patients with acute BAO. Accumulating evidence in patients with anterior circulation occlusions supported the neutral association between AF and long-term functional outcomes after EVT,[14,19] and limiting evidence from studies focused on BAO patients also supported this neutral association.[20–24]

For death at 90 days and symptomatic ICH, the differences between the EVT and BMM versus BMM alone groups were similar between the AF subgroups. No determined association between AF and hemorrhage transformation could be drawn in AIS patients after reperfusion therapy.[19,18,25–27] However, the absolute risk of sICH after EVT due to BAO remains low.[16,17,28] The ATTENTION registry trial suggests that EVT

Table 3. Clinical outcomes by AF subgroups and treatment allocation.

	Non-AF				AF				*p* value for treatment interaction
	BMM	**EVT**	**Adjusted value (95% CI)**	***p* value**	**BMM**	**EVT**	**Adjusted value (95% CI)**	***p* value**	
Primary outcome									
Median mRS at 90 days (IQR)[a]	5 (3, 6)	4 (2, 6)	1.51 (1.21, 1.89)	<0.001	6 (4, 6)	5 (2, 6)	1.90 (1.20, 3.06)	0.007	0.247
Secondary efficacy outcomes[b]									
0–1	74 (19.2)	247 (21.9)	1.28 (0.93, 1.76)	0.127	9 (11.8)	126 (23.2)	2.14 (1.00, 4.62)	0.051	0.165
0–2	92 (23.8)	377 (33.4)	1.77 (1.32, 2.37)	<0.001	15 (19.7)	190 (35.0)	2.15 (1.13, 4.10)	0.020	0.460
0–3	115 (29.8)	450 (39.9)	1.66 (1.26, 2.18)	<0.001	16 (21.1)	227 (41.8)	2.74 (1.46, 5.12)	0.002	0.119
Safety outcomes[b]									
sICH	4 (1)	55 (4.9)	4.93 (1.76, 13.85)	0.002	0 (0)	30 (5.5)			0.977
Mortality	180 (46.6)	414 (36.7)	0.63 (0.49, 0.81)	<0.001	41 (53.9)	202 (37.2)	0.51 (0.30, 0.87)	0.014	0.393

AF, atrial fibrillation; BMM, best medical management; CI, confidence interval; EVT, endovascular treatment; IQR, interquartile range; IVT, intravenous thrombolysis; NIHSS, National Institutes of Health Stroke Scale; pc-ASPECTS, Posterior Circulation-Alberta Stroke Program Early CT Score; sICH, symptomatic intracranial hemorrhage; TIA, transient ischemic attack.
Adjusted variables include: age, sex, diabetes mellitus, IVT, baseline NIHSS score, location of occlusion, onset-to-admission, history of stroke or TIA, hypertension, baseline pc-ASPECTS, coronary heart disease.
[a]The common odds ratio was assessed by ordinal logistic regression model.
[b]The odds ratio was assessed by binary logistic regression model.

should not be abandoned for fears of post-treatment hemorrhagic transformation regardless of AF status.

Our analysis contains remarkable statistical power by including 2134 patients with BAO from 48 centers nationwide. The study does have limitations, including the fact that Asians have high rates of intracranial atherosclerotic diseases, which might hamper extending this to other populations. However, we note that the proportion of AF observed in the ATTENTION registry was similar to those of the BASICS trial; in addition, most patients did not receive a 24-hour electrocardiogram after admission, whereby it is possible that patients with paroxysmal AF were not included in the AF group.

The subgroup analysis of the ATTENTION registry demonstrates that the efficacy and safety of EVT does not differ significantly between AF and non-AF BAO patients, and that no significant associations exist between AF and functional outcomes at 90 days in patients with acute BAO.

Declarations

Ethical approval and consent to participate

The registry study was approved by the ethical committee of the First Affiliated Hospital of the University of Science and Technology of China (USTC) with the approval code 2020-KY202. All patients or their legal representatives provided signed, informed consent. ATTENTION is a multicenter, nationwide, prospective registry to

estimate treatment effects of best medical management (BMM) and EVT for patients with acute BAO sampled from across 48 stroke centers and 22 provinces in China (http://www.chictr.org.cn; ChiCTR2000041117).

Consent for publication
Not applicable.

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Acknowledgements
Not applicable.

Funding
The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Anhui Province Stroke Association, Program for Innovative Research Team of the First Affiliated Hospital of USTC and National Natural Science Foundation of China (No. U20A20357).

Competing interests
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Availability of data and materials
Not applicable.

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