Ischemic Stroke due to Acute Basilar Artery Occlusion: Proportion and Outcomes

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ABSTRACT: **Background:** Multiple case series, mostly highly selected, have demonstrated a very high mortality following acute basilar artery occlusion. The more widespread availability and use of non-invasive vascular imaging over recent years has increased the rate of ABAO diagnosis.

Objectives: To estimate the proportion of diagnosed ABAO among all-cause ischemic stroke in an era of increasing use of non-invasive vascular imaging and to compare the characteristics and outcomes between these two groups.

Methods: We compared 27 consecutive cases of ABAO identified in a university hospital between 2003 and 2007 with 311 unselected cases of ischemic stroke from two 4 month surveys.

Results: ABAO diagnosis increased from 0.3% of all-cause ischemic stroke (2003–2004) to 1.1% (2007), reflecting the increased use of non-invasive vascular imaging. In comparison to all-cause ischemic stroke, ABAO patients were younger (mean age 60 vs. 71 years), were more likely to be male (89% vs. 60%), had less atrial fibrillation (7% vs. 26%), more severe strokes (baseline NIHSS over 20: 52% vs. 12%), higher admission white cell count (12,000 vs. 9000 cells/mm^3), lower admission systolic blood pressure (140 ± 24 vs. 153 ± 27 mmHg), higher in-hospital mortality rates (30% vs. 8%) and worse functional outcome (modified Rankin scale ≤ 3, 22% vs. 56%) ($P < 0.05$ for all). Rates of reperfusion therapy for ABAO increased from 0 in 2003–2004 to 60% in 2007.

Conclusions: In this study, ABAO patients represented approximately 1% of all-cause ischemic stroke and were about a decade younger than patients with all-cause ischemic stroke. We report a lower ABAO mortality compared to previous more selected case series; however, most survivors had a poor functional outcome. Given the marked clinical heterogeneity of ABAO, a low threshold for non-invasive vascular imaging with a view to definitive reperfusion treatment is needed.

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KEY WORDS: stroke, reperfusion, basilar artery occlusion, epidemiology

Acute basilar artery occlusion is one of the most feared diagnoses in vascular neurology and is usually associated with a very poor outcome. The need to achieve early recanalization in ABAO is now well appreciated, but there is no consensus yet on the optimal reperfusion strategy or on the therapeutic time window [1]. Early studies based on autopsy material or on highly selected case series of patients noted fatality rates of up to 90%. However, recent prospective case series of patients with ABAO treated conservatively give fatality rates of under 50% [2-4]. Due to the increasing use of non-invasive arterial imaging, it is now recognized that the clinical features of ABAO at presentation may be more heterogeneous than was previously assumed. It was found that about one-fifth of ischemic strokes occur in the territory supplied by the posterior circulation [5]. Few studies have compared the characteristics and outcomes of ABAO versus all-cause ischemic stroke in consecutive unselected patients, and the proportion of all-cause ischemic stroke due to ABAO is not known. The aims of the current study were to estimate the proportion of diagnosed ABAO among all-cause ischemic stroke in this era of increasing use of non-invasive vascular imaging and to compare the characteristics and outcomes between these two groups.

PATIENTS AND METHODS

The study was conducted at a public hospital with an immediate catchment area of about 500,000 people. Consecutive patients with diagnosed ABAO admitted between April 2003 and December 2007 were included. Patients received medical care according to internationally accepted guidelines and the discretion of the treating physician.

During the study period the National Acute Stroke Israeli Survey, a prospective national survey, was performed twice: February-March 2004 and March-April 2007. The NASIS project is a nationwide observational stroke survey with the aim of collecting epidemiologic data on the burden of disease, patient characteristics, management practices, and

ABAO = acute basilar artery occlusion
NIHSS = National Institutes of Health Stroke Scale

NASIS = National Acute Stroke Israeli Survey

clinical outcomes of acute cerebrovascular disease (stroke or transient ischemic attack) across the entire country. We analyzed data from these surveys regarding all patients with acute ischemic stroke admitted to this hospital during the two abovementioned time periods [6]. In addition, a further analysis was performed after excluding patients with lacunar infarcts from the NASIS data.

Patients' characteristics, previous medical history, stroke presentation, therapeutic interventions, in-hospital course, complications and clinical outcome were recorded. Similar methods were used to define risk factors, stroke severity, complications and outcome. Stroke severity was assessed by the National Institutes of Health Stroke Scale [7] and functional outcome by the modified Rankin Scale [8]. Good functional outcome was defined as mRS ≤ 3 and poor outcome as mRS > 3. Global outcome was rated: 1 = much worse, 2 = worse, 3 = same, 4 = better, 5 = much better.

ABAO was defined according to accepted criteria and the site of basilar artery occlusion was categorized according to the criteria described by Archer and Horenstein [9]. Collateral supply of the distal basilar artery via posterior communicating arteries and the circle of Willis was graded as "good" if it was visible to the distal basilar artery or "poor" if it was not detectable on computed tomography angiography or was only to one or both posterior cerebral arteries [10]. Length of occlusion was divided into short (one segment only) or long (two or three segments) with each segment being proximal, middle or distal.

Continuous variables were expressed as mean ± SD and were compared using Student's *t*-test, taking the assumption of normal distribution. Ordinal variables were expressed as median (interquartile range) and compared using the Mann-Whitney *U* test. Categorical variables were expressed as number (%) and were compared using Fisher's exact test. All analyses were performed with SAS statistical software version 9.1 (SAS, Inc, Cary, NC, USA).

Table 1. Baseline characteristics, stroke severity and in-hospital course of acute basilar artery occlusion vs. all-cause ischemic stroke patients (NASIS) and non-lacunar ischemic stroke patients (NASIS-NL)

	ABAO (n=27)	NASIS (n=308)	*P* value NASIS compared to ABAO	NASIS–NL (n=210)	*P* value NASIS–NL compared to ABAO
Age (yrs)	60 ± 13	71 ± 14	<0.01	72 ± 13	< 0.01
Men	24 (89%)	185 (60%)	<0.01	129 (61%)	< 0.01
History					
Hypertension	19 (70%)	200 (65%)	0.68	134 (64%)	0.67
Diabetes	11 (41%)	110 (36%)	0.68	76 (36%)	0.67
Dyslipidemia	15 (56%)	196 (64%)	0.41	128 (61%)	0.68
Current smoking	6 (22%)	58 (19%)	0.62	35 (17%)	0.59
Prior stroke	12 (44%)	72 (23%)	0.02	51 (24%)	0.04
Angina or prior MI	5 (19%)	92 (30%)	0.27	68 (33%)	0.18
Prior PCI or CABG	5 (19%)	59 (19%)	1.00	43 (20%)	1.00
Congestive heart failure	1 (4%)	41 (13%)	0.23	28 (14%)	0.22
Atrial fibrillation	2 (7%)	80 (26%)	0.03	57 (28%)	0.02
Chronic use of antiplatelet agents	10 (37%)	158 (53%)	0.16	115 (57%)	0.06
Use of anticoagulation	2 (7%)	37 (12%)	0.76	25 (12%)	0.75
Use of statins	12 (44%)	104 (35%)	0.4	73 (36%)	0.53
Baseline measurements					
Systolic BP (mmHg)	140 ± 24	153 ± 27	0.02	152 ± 26	0.03
Diastolic BP (mmHg)	77 ± 13	81 ± 13	0.15	80 ± 14	0.29
Glucose (mg/dl)	161 ± 66	151 ± 67	0.19	156 ± 73	0.28
Total cholesterol (mg/dl)	168 ± 41	186 ± 44	0.06	182 ± 44	0.14
WBC (1000 cells/mm^3)	12 ± 5	9 ± 3	< 0.01	9 ± 4	< 0.01
Baseline stroke severity (NIH Stroke Scale)					
≤ 5	3 (11%)	147 (48%)		91 (44%)	
6-10	5 (19%)	72 (23%)		42 (20%)	
11-15	3 (11%)	27 (9%)		22 (11%)	
16-20	2 (7%)	23 (7%)		23 (11%)	
20	14 (52%)	38 (12%)	< 0.01	31 (15%)	< 0.01
Complications					
Any	15 (56%)	101 (33%)	0.02	83 (40%)	0.15
Infectious	10 (37%)	71 (23%)	0.11	63 (30%)	0.51
Neurologic	12 (44%)	27 (9%)	< 0.01	25 (12%)	< 0.01
Cardiac	1 (4%)	7 (2%)	0.49	7 (3%)	1.00
Functional outcome at discharge					
mRS 0-3 (good)	6 (22%)	172 (56%)		106 (51%)	
mRS 4-5 (poor)	13 (48%)	109 (36%)		81 (39%)	
mRS 6 (deceased)	8 (30%)	25 (8%)	< 0.01	22 (11%)	< 0.01

NL = non-lacunar, MI = myocardial infarction, PCI = percutaneous coronary intervention, CABG = coronary artery bypass graft, BP = blood pressure, WBC = white blood cell count, NIH = National Institute of Health.

RESULTS

ABAO was diagnosed in 27 patients over the 4.5 years of the study. During the 2004 and 2007 NASIS surveys (4 months in total), 308 unselected patients with "all-cause" ischemic stroke were admitted to our center, one with ABAO [12]. The estimated proportion of diagnosed ABAO during the study period increased nearly fourfold, from 0.3% in 2003–2004 to 1.1% in 2007, largely reflecting the increased use of non-invasive vascular imaging during this period. Indeed, based on data from the NASIS project, the percentage of patients with TIA or ischemic stroke who underwent inpatient CT or magnetic resonance angiography at our center rose from 7% in 2004 to 15% in 2007. The baseline characteristics, stroke severity and in-hospital course of patients with ABAO versus all ischemic strokes are presented in Table 1. Twenty-five patients were diagnosed with ABAO according to vascular

mRS = modified Rankin Scale
TIA = transient ischemic attack

imaging findings (CT angiography alone or combined with transcranial Doppler), 7 of whom also underwent four-vessel cerebral angiography. In addition, two patients with clinical and brain CT findings diagnostic of ABAO, but without vascular imaging, were included.

Patients with ABAO were about a decade younger (mean age 60 ± 13 vs. 71 ± 14 years, $P < 0.01$). They were more often males (89% vs. 60%, $P < 0.01$), were less likely to have atrial fibrillation (7% vs. 26%, $P = 0.03$), more likely to have had a previous stroke (44% vs. 23%, $P = 0.02$) and had a lower mean serum cholesterol on admission (168 ± 41 vs. 186 ± 44 mg/dl, $P = 0.06$). Systolic blood pressure on presentation was lower (140 ± 24 vs. 153 ± 27 mmHg, $P = 0.02$) and the white cell count was higher (12,000 vs. 9000 cells/mm^3, $P < 0.01$).

Patients with ABAO had a much higher baseline stroke severity score (52% vs. 12% had a NIHSS score > 20, $P < 0.01$) and a higher in-hospital complication rate, particularly of neurologic etiology (44% vs. 9%, $P < 0.01$). Overall, ABAO patients were, as expected, less likely to have a favorable outcome (mRS ≤ 3 discharge, 22% vs. 57%, $P < 0.01$), and in-hospital mortality rates were higher (30% vs. 8% respectively, $P < 0.01$).

Stroke presentation, radiologic features and subsequent in-hospital course of ABAO patients are presented in Table 2. The sample was markedly heterogeneous with respect to time course and severity of clinical presentation. Over 40% had a recent cerebrovascular prodrome of at least one TIA or a minor stroke in the same vascular territory. Two-thirds of the patients presented with tetraplegia, coma or a locked-in state, 15% arrived at the hospital already intubated and over half were intubated during admission. The presenting course was gradually progressive in 66%, fluctuating in 7% and maximal from onset in 22%.

We observed a dramatic rise in the rates of reperfusion therapy (intraarterial and/or intravenous thrombolysis and/or endovascular mechanical clot retrieval): nil during 2003–4, 25% during 2005–6 and 60% during 2007. As compared to ABAO patients with poor outcome, those with good outcome were nearly a decade younger (mean age 54 ± 10 vs. 62 ± 13 years, $P = 0.15$), and tended to have lower admission glucose levels (122 ± 34 vs. 176 ± 70 mg/dl, $P = 0.04$) and a lower median NIHSS score on admission (9, interquartile range 5–36 vs. 26, IQR 10–40, $P = 0.14$).

With regard to collateral flow, patients with good collateral flow had a better functional outcome on discharge than patients with poor collateral flow (median mRS 5, IQR 2–5 vs. 5, IQR 5–6, $P = 0.06$). Baseline NIHSS and global outcome scores were not significantly different between the two groups. Regarding length of occlusion, occlusion of two or more segments versus only one segment did not have a significant effect on outcome as measured by median mRS at discharge (5, IQR 4–5 vs. 5.5, IQR 4–6, $P = 0.32$) or by median global outcome score (4, IQR 3–5 vs. 3, IQR 1–4, $P = 0.29$).

Further analysis comparing the ABAO cohort with the NASIS cohort of non-lacunar strokes revealed similar results to the first analysis.

IQR = interquartile range

Table 2. Clinical presentation, radiologic features and treatment of acute basilar artery occlusion

Clinical characteristics	
Prodrome	
Single TIA	1 (4%)
Multiple TIAs	7 (26%)
Recent stroke	3 (11%)
Any of the above	11 (41%)
Onset on awakening	6 (22%)
Presenting course	
Gradually progressive	18 (66%)
Maximal deficit from onset	6 (22%)
Fluctuating symptoms	2 (7%)
Unknown	1 (4%)
Worst clinical state	
Coma	12 (44%)
Tetraparesis or locked-in	6 (22%)
Other neurologic deficit	9 (33%)
Required intubation	15 (56%)
Radiologic features	
Hyperdense basilar artery sign	12 (44%)
Evidence of acute posterior circulation hypodensity*	9 (33%)
Basilar artery part**	
Proximal	7 (28%)
Mid	7 (28%)
Distal	6 (24%)
More than one segment	5 (20%)
Including vertebral artery occlusion **	2 (8%)
Collateral flow **	
Good	19 (76%)
Poor	6 (24%)
Treatment	
None or antiplatelet only	3 (11%)
Anticoagulation + aspirin	14 (52%)
Attempted reperfusion therapy	10 (37%)
Intravenous thrombolysis	2 (20%)
Endovascular	7 (70%)
Combined intravenous and endovascular	1 (10%)

*Cerebellar, brainstem, thalamic or PCA territory hypodensity by CT scan of brain
**Based on 25 patients with radiologically proven basilar artery occlusion

DISCUSSION

Previous data on ABAO have been derived mainly from multiple case series, while more detailed epidemiologic data are scarce. During the period of the study, the estimated proportion of ischemic stroke due to diagnosed ABAO increased

nearly fourfold. This likely reflects the considerably improved availability and use of non-invasive vascular imaging. Indeed, the study period was characterized at our center by an increasing use of non-invasive vascular imaging (in particular CT angiography) and recanalization interventions [11].

CT angiography has been shown to be a reliable diagnostic modality for suspected ABAO [12] and it served as the principal diagnostic test in the current study. Towards the end of our study period, the rate of ABAO diagnosis (at 1%) was comparable with recent data from a cohort of patients with acute cerebrovascular ischemia (1.2% among those who underwent complete cerebrovascular workup) [2].

Many cases of vertebrobasilar disease in general may remain undiagnosed or may be initially incorrectly diagnosed, particularly if assessed by non-neurologists [13]. Vague symptoms of nausea and dizziness when associated with additional focal neurologic symptoms or signs may be the premonitory manifestation of a severe stroke. Studies by Flossman and Rothwell [14] and Gulli et al. [15] suggest that posterior circulation TIAs may have a higher risk of subsequent stroke than anterior circulation TIAs. The most challenging cases are those with a progressive or stepwise presenting course, where the presenting clinical features may be mild and non-specific and the potential for deterioration may initially not be fully appreciated. This presenting pattern represented about two-thirds of patients in this series. Basilar ischemia may present with recurrent events before the major occlusive event, thus providing an opportunity for risk-lowering interventions and observing acute deterioration. In the current series over 40% had a recent cerebrovascular prodrome of at least one TIA or a minor stroke in the same vascular territory (38% in a recent multicenter study) [16]. A potentially misleading presenting feature is seizure-like contractions or posturing that may be interpreted as being epileptic in nature rather than a sign of brain-stem ischemia.

In this series, patients with ABAO are on average nearly a decade younger and there is a greater male preponderance in comparison to patients with all-cause ischemic stroke. The age distribution of our ABAO cohort is comparable to previous case series. Forty percent of patients were under 60 years old, as compared to 43% in the series by Schonewille et al. [3] and the mean age (60 years) is comparable to the mean age (ranging from 52 to 62 years) reported in other studies both of conventional and of reperfusion treatment [9,17-19]. ABAO patients had similar rates of vascular risk factors, but lower rates of atrial fibrillation. This is consistent with studies that show an association between atrial fibrillation and large anterior circulation infarcts [20] and is partly explained by in vitro studies showing a tendency for larger embolic-like particles to enter the wider vessel in a bifurcation (the carotid arteries being wider than the vertebral arteries [21].

Two-thirds of the patients presented with tetraplegia, coma or a locked-in state, which is comparable to that reported in a recent multicenter study (59%) [13]. The in-hospital mortality rate among ABAO patients in the current series was 30%, while the rate of poor outcome was just below 80%. These mortality rates are lower than the up to 90% mortality rates reported in early studies based on autopsy material or on highly selected case series of patients, but are comparable to more recent less selected series [2-4]. Schonewille and co-workers [3] found a mortality of 40% and a poor outcome rate of 80% among patients with ABAO treated conventionally, and Weimar et al. [2] reported a 3 month mortality rate of 45% and a rate of residual disability (Barthel Index < 95) of 86%.

Outcome of ABAO depends on the age and clinical state at presentation, the length and location of the occlusion, the extent of collateral circulation, and the degree and timing of recanalization achieved [1,18]. We found a trend towards better outcome with better collateral circulation and a shorter length of occlusion but this did not reach statistical significance.

The immediate therapeutic goal in ABAO is to achieve early recanalization. In a recent systematic analysis comparing intraarterial and intravenous thrombolysis, no significant difference in the likelihood of good outcome between the two treatment modalities was found [22]. Further strategies to achieve effective and early recanalization are being tested, but the optimal strategy and effective time window have not yet been established. A key challenge to timely treatment, whether intravenous or intraarterial, is the establishment of an improved and comprehensive infrastructure. [11]

LIMITATIONS

Firstly, since intracranial arterial imaging was not performed systematically for all patients with a suspected acute cerebrovascular event, minor strokes or TIAs due to ABAO may not have been diagnosed. However, since our data toward the end of the study were comparable to that obtained among patients who underwent complete cerebrovascular workup, this bias is likely to be minimal [2]. Secondly, characteristics and estimates of all-cause ischemic stroke were based on two separate 2 month long evaluations within the study period rather than on an ongoing registry. However, these data, derived from triennial prospective national surveys, are a representative sample of the general acute stroke population. Larger studies with unselected cohorts and systematic use of non-invasive vascular imaging need to be performed.

CONCLUSIONS AND IMPLICATIONS

Patients afflicted with ABAO represent approximately 1% of ischemic stroke and are nearly a decade younger than patients with all-cause ischemic stroke. Mortality rates in this study are not as high as reported in earlier case series with highly selected patient populations; however, most survivors had a poor functional outcome. Given the marked heterogeneity of

ABAO presentation and early clinical course, a low threshold for using non-invasive vascular imaging is required.

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