

# Outcome in patients with basilar artery occlusion treated conventionally

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**Background:** Most data on the outcome of basilar artery occlusion are from recent case series of patients treated with intra-arterial thrombolysis. The limited knowledge on the outcome after a conventional treatment approach comes from a few small case series of highly selected patients.

**Objective:** To provide more data on the outcome of conventional treatment.

**Methods:** Data were analysed on patients from three centres with symptomatic basilar artery occlusion treated conventionally. Conventional therapy was defined as treatment with antiplatelets, anticoagulation, or both.

**Results:** Data were available on 82 patients. The case fatality was 40%. Among survivors, 65% remained dependent (Rankin score 4–5). Patients younger than 60 years (odds ratio = 3.1 (95% confidence interval, 1.0 to 9.5)) and those with a minor stroke (OR = 3.1 (1.0 to 9.6)) were more likely to have a good outcome (Rankin score 0–3). Patients with a progressive stroke were less likely to have a good outcome (OR = 0.3 (0.08 to 1.2)) than patients with a maximum deficit at onset or fluctuating symptoms at presentation.

**Conclusions:** Conventional treatment of symptomatic basilar artery occlusion is associated with a poor outcome in almost 80% of patients, which emphasises the importance of the search for a more effective treatment approach.

Unlike the anterior circulation, the posterior circulation depends on one main artery. The basilar artery supplies the occipital lobes, part of the temporal lobes, the thalami, the cerebellum, and most importantly the brain stem. Acute occlusion of the basilar artery has been associated with a high case fatality rate and morbidity, although reliable data about the natural history are lacking. Studies on the outcome of basilar artery occlusion using a conventional treatment approach have been small and have described the outcome of highly selected patients or used very broad definitions, including vertebral and branch artery occlusions.<sup>1–10</sup> Hacke *et al*, in the largest study to date with detailed individual angiographic data (n = 22), found a case fatality of 86% in patients treated conventionally.<sup>11, 12</sup> Recently several uncontrolled larger case series of patients treated with intra-arterial thrombolysis have found case fatality rates ranging between 20% and 70%.<sup>11–25</sup> More data are needed on the outcome of conventional treatment to validate these results.

## METHODS

Three centres participated in our database search: the University Medical Centre Utrecht, Netherlands; Hospital Universitari Doctor Josep Trueta in Girona, Spain; and Hospital Vall d'Hebron in Barcelona, Spain. All are academic hospitals with a special interest in stroke. The databases used in the three centres were constructed in similar fashion, with comparable definitions and outcome measures. Patients' records were reviewed for details of clinical presentation. Patients were included in the study if they fulfilled at least one of the following diagnostic criteria:

- (A) acute neurological deficit attributable to the posterior circulation and basilar artery occlusion on angiography, magnetic resonance angiography (MRA), computed tomography angiography (CTA), or necropsy;

- (B) acute "classic" symptoms of basilar artery occlusion including alternating hemiplegia/tetraplegia with brain stem deficits, leading to a locked-in state, coma, or death;
- (C) coma or loss of consciousness and acute posterior circulation infarction on computed tomography (CT) or magnetic resonance imaging (MRI).

Patients were considered to have been treated conventionally if they had not received any specified treatment, or if they had been treated with antiplatelets, anticoagulation, or a combination of the two. During the time period studied, thrombolytic treatment was not a standard option in these three centres. Most studies of intravenous or intra-arterial thrombolysis in acute stroke have used a modified Rankin score of 0–1 or 0–2 to define good outcome. Because of the poor natural history of basilar artery occlusion we used a modified Rankin score of 0–3 as a measure of independence and good outcome. Outcome was assessed at the time of discharge or in-hospital death, without knowledge of baseline characteristics pertinent to the outcome. Stroke severity at the time of presentation was considered minor if a patient was non-comatose and was not tetraplegic, intubated, or locked-in.

We distinguished three different types of clinical presentation: fluctuating symptoms with alternating periods of neurological worsening (at least one) and improvement, without full recovery; progressive stroke with a progressive worsening of deficit, stepwise or gradual, but without intermittent periods of improvement; and maximum deficit from onset with or without subsequent improvement or fluctuating symptoms.

## Data analysis

We assessed the relation between potential prognostic factors and outcome by univariate logistic regression. The strength of a relation was expressed as an odds ratio (OR) with corresponding 95% confidence interval (CI) to describe its precision.

**Table 1** Patient characteristics and outcome: three centre database search (n = 82)

Patient characteristics	n	%	Rankin score		
			0–3 (n (%))	4–5 (n (%))	Death (n (%))
All	82		17 (21)	32 (39)	33 (40)
Age <60 years	35	43	11 (31)	18 (51)	6 (17)
Male sex	44	54	12 (27)	15 (34)	17 (39)
Fluctuating symptoms	13	16	3 (23)	7 (54)	3 (23)
Progressive stroke	29	35	3 (10)	10 (35)	16 (55)
Maximum from onset	40	49	11 (28)	15 (38)	14 (35)
Coma	28	34	6 (21)	7 (25)	15 (54)
Locked-in/tetraplegia	18	22	0	10 (56)	8 (44)
Intubated	18	22	3 (17)	4 (22)	11 (61)
Minor stroke	35	43	11 (31)	15 (43)	9 (26)
Previous TIAs*	16	20	4 (25)	9 (56)	3 (19)
Previous stroke*	16	20	1 (6)	8 (50)	7 (44)
Use of antiplatelet agents	55	67	10 (18)	22 (40)	23 (42)
Use of anticoagulation	27	33	7 (26)	10 (37)	10 (37)
Diagnostic category A†	25	30	9 (36)	6 (24)	10 (40)
Diagnostic category B‡	26	32	0	13 (50)	13 (50)
Diagnostic category C§	31	38	8 (26)	13 (42)	10 (32)

\*Posterior circulation.

†Diagnostic criteria A, B, and C are defined in the text.

## RESULTS

On our database search we found 82 patients with the clinical diagnosis of symptomatic basilar artery occlusion, treated conventionally, over a period of 20 database years (11 years for Utrecht, 5 years for Girona, and 4 years for Barcelona), ending in 2002 (table 1). Eleven patients with basilar artery occlusion treated with intravenous (n = 2, from two centres) or intra-arterial thrombolysis (n = 9, three in each centre) where excluded from the study. These were all treated within the first three hours in cases of intravenous treatment or within 12 hours in cases of intra-arterial thrombolysis. Fifty three patients were treated in Utrecht, 20 in Girona, and nine in Barcelona. Of these 82 patients, 25 were categorised in diagnostic group A, 26 in group B, and 31 in group C. All patients in group B had a poor outcome (Rankin score 4–6), 74% had a poor outcome in group C, and 64% in group A. The small number of patients who had necropsy (n = 2) did not cause a bias towards a worse outcome in group A.

The poor outcome in patients with basilar artery occlusion did not improve in more recent years (82% in 1997 to 2002 v 74% in 1991 to 1996), despite more patients being diagnosed with a minor stroke (47% v 35%). The mean time to assessment was 28 days (range 1 to 280) for all patients. Twenty nine per cent of the deaths occurred within the first 48 hours and 53% within the first week, with a mean time to death of 12 days (range 1 to 76). Discharge of the 42 survivors was after a mean of 40 days (range 3 to 280); 61% were discharged within a month, 84% within two months, and 91% within three months. There was a clear trend

towards a better outcome in patients younger than 60 years (odds ratio (OR) = 3.1 (95% confidence interval, 1.0 to 9.5)) and patients with a minor stroke (OR = 3.1 (1.0 to 9.6)). Patients who presented with a progressive stroke were less likely to have a good outcome than patients presenting with fluctuating symptoms or a maximum deficit from onset (OR = 0.3 (0.08 to 1.2) (table 2).

## DISCUSSION

Basilar artery occlusion has generally been associated with a high mortality and morbidity. Among the patients from our database search—the largest series to date on patients treated conventionally—almost 80% had a poor outcome, with a case fatality of 40% and the presence of a severe residual deficit in more than 65% of survivors.

The results of our study should be interpreted with caution. Outcome in our study was assessed after a mean of 28 days. This information, however, is lacking in the previous case series, possibly explaining the different findings among studies, because outcome tends to be better after a longer follow up. The three diagnostic groups recognised in the database search by no means represent the whole range of patients with basilar artery occlusion. However, we believe that with a combination of strict clinical and simple frequently used imaging techniques as inclusion criteria for our database search, our patient group is more representative of the conventional treatment approach than most previously published series in which individual patient data were described (table 3). These series included cases confirmed

**Table 2** Predictors of good outcome: three centre database search (n = 82)

Characteristic	Good outcome		OR (95% CI)
	Present	Absent	
Age <60 years	31% (11/35)	13% (6/47)	3.1 (1.0 to 9.5)
Male sex	27% (12/44)	13% (5/38)	2.5 (0.8 to 7.8)
Fluctuating stroke	23% (3/13)	20% (14/69)	1.2 (0.3 to 4.9)
Progressive stroke	10% (3/29)	26% (14/53)	0.3 (0.08 to 1.2)
Maximum from onset	28% (11/40)	14% (6/42)	2.3 (0.8 to 6.9)
Coma	21% (6/28)	20% (11/54)	1.1 (0.3 to 3.3)
Minor stroke	31% (11/35)	13% (6/47)	3.1 (1.0 to 9.6)
Previous TIAs*	25% (4/16)	20% (13/66)	1.4 (0.4 to 4.9)
Previous stroke*	6% (1/16)	24% (16/66)	0.2 (0.03 to 1.7)

\*Posterior circulation.

CI, confidence interval; OR, odds ratio; TIA, transient ischaemic attack.

by MRA or conventional angiography. It is unlikely that, in a disorder for which no specific treatment other than anti-thrombotic agents was available, all consecutive patients with the possible clinical diagnosis of basilar artery occlusion had radiological confirmation of their occlusion, while a few would have been imaged within the first 24 hours, causing an important selection bias. This is especially true for the older case series done at a time when non-invasive vascular imaging was not an option.<sup>8-11</sup> In our database review, basilar artery occlusion was only confirmed by radiological imaging in 30% of patients (group A). Interestingly these patients had the best outcome, despite having similar stroke severity at onset. One possible explanation for the better outcome in patients who had radiological confirmation of their occlusion is that most were imaged more than 24 hours after the time of occlusion and had already survived the most critical phase. Our patient groups B and C, presenting with a severe progressive deficit or an acute loss of consciousness, are probably most representative of the way most physicians would think of a typical patient with basilar artery occlusion. However, this latter group excludes an important subgroup of patients with a minor stroke, causing a bias towards the inclusion of patients with a more severe deficit.

The more frequent use of non-invasive vascular imaging in the two most recent studies could have caused an increase in the number of patients diagnosed with basilar artery occlusion with a minor deficit.<sup>9-10</sup> Voetsch *et al*<sup>10</sup> described the outcome of 87 patients with occlusive basilar artery disease including patients with basilar artery stenosis and 32 patients with basilar artery occlusion documented by transcranial Doppler, MRA, or conventional angiography. They found an overall case fatality of only 2.3%. No individual patient data were described concerning stroke severity, treatment, or time to radiological confirmation. Most patients had a minor stroke, and only five had tetraparesis or tetraplegia; one patient was locked-in and 16 had a decreased level of consciousness. The only data available on the subgroup of patients with basilar artery occlusion described a poor outcome (death or major disability) in 40% of patients with an atherosclerotic occlusion.

The severity of deficit in the 20 patients described by Archer and Horenstein<sup>8</sup> seems comparable to our patient group. In contrast to our results, they found coma to be an important predictor of poor outcome. This difference might reflect improved monitoring and treatment options in comatose patients, as on average our patients were treated 25 years later. The mayor difference in outcome with the study of Hacke *et al* is more difficult to explain, as all their patients had minimal symptoms (n = 2) or a stable moderate brain stem stroke (n = 20).<sup>11-12</sup>

The numbers of patients described by Moscow and Newton<sup>7</sup> and Devuyt *et al*<sup>9</sup> are too small for a meaningful comparison, but interestingly both studies describe the same

possible positive influence on outcome of previous TIAs as found in our study.

The emphasis in our study was on the outcome in relation with the clinical presentation; because of the low rate of vascular imaging the aetiology could not reliably be assessed. We identified three potentially important predictors of good outcome in patients treated conventionally: young age, limited stroke severity, and a presentation with fluctuating symptoms or a maximum deficit from onset (table 2). Age could influence both the spontaneous recanalisation rate and the quality of collateral flow, as the rate of atherothrombotic disease increases with age. Initial stroke severity could be an indicator of the quality of collateral flow at the time of occlusion, and progression of deficit could represent failure of augmentation of collateral flow or growth of the thrombus.

In conclusion, the outcome of patients with basilar artery occlusion treated conventionally varies considerably among case series. Considering our limited knowledge on the outcome of patients treated conventionally, future studies on the outcome of basilar artery occlusion should not be limited to patients receiving more aggressive treatment.

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**Table 3** Case series on the outcome of basilar artery occlusion treated conventionally

Study	Year	n	Rankin score		
			0–3	4–5	6
Moscow <sup>7</sup>	1973	9	44	22	33
Archer <sup>8</sup>	1977	20	5	25	70
Hacke <sup>11</sup>	1988	22	14		86
Devuyt <sup>9</sup>	2002	9	66	22	11
Present study	2004	82	21	39	40
Total		142	21	28	49

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## HISTORICAL NOTE

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### Marshall Hall and “Romberg’s sign”

Marshall Hall is famous, *inter alia*, for his concept of the spinal reflex arc<sup>1</sup> when he demonstrated reflex function—an “excito-motory system”<sup>2</sup>—of the spinal cord and nerves in animals after removal of the brain. This ended the misconceptions that the soul and psychic functions resided in the cord as well as in the brain. Often overlooked, in his *Lectures on the nervous system and its diseases* (1836)<sup>3</sup>, he predated Romberg’s account of sensory ataxia, in *tabes dorsalis*. Hall plainly described the loss of postural control in the dark of a patient with proprioceptive loss:

“I have this day seen a patient with a slight degree of paralysis of feeling and of voluntary motion of the lower limbs. He walks safely while his eyes are fixed upon the ground, but stumbles immediately if he attempts to walk in the dark. His own words are ‘my feet are numb; I cannot tell in the dark where they are, and I cannot poise myself.’ The voluntary motions are regulated by the sense of touch, when this is unimpaired; or by that of sight, when the touch is paralyzed.”

Hall failed to consider fully its anatomical substrate and its implications for cord physiology. Surprisingly, he did not advocate the sign in clinical practice, but the importance of his description is undeniable.

Romberg published his *Lehrbuch der Nervenkrankheiten* in sections between 1840 and 1846. The depiction<sup>4</sup> of that most misspelled of all eponyms<sup>5</sup> lies in his account of sensory ataxia in *tabes dorsalis*<sup>6</sup> (Romberg’s sign, named “locomotor ataxia” by Duchenne in 1858/9). Romberg reported:

“... The feet feel numbed in standing, walking or lying down, and the patient has the sensation as if they were covered in fur; the resistance of the ground is not felt... The gait begins to be insecure... he puts down his feet with greater force... The individual keeps his eyes on his feet to prevent his movements from becoming still more unsteady. If he is ordered to close his eyes while in the erect posture, he at once commences to totter and swing from side to side; the insecurity of his gait also exhibits itself more in the dark.”

He gave a full description of the tabetic gait, urinary frequency, retention, incontinence, and the classical lighting and girdle pains.

But Marshall Hall was not alone in anticipating Romberg’s sign for in 1840 Bernardus Brach<sup>7</sup> had given an earlier account. And Romberg’s teacher, Ernst Horn (1774–1848), had shown dorsal cord atrophy in a tabetic at autopsy.<sup>8</sup> Moreover, five of Horn’s students wrote their doctoral theses on the same subject, published between 1817 and 1827.

Robert Bentley Todd, however, like Romberg, gave an exemplary detailed account of *tabes* in 1847<sup>9</sup>, of which Gowers said:

“The credit of the discovery of the disease belongs, if to anyone, unquestionably to Todd.”

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