

# Prevalence of basilar artery dolichoectasia in patients with acute ischemic stroke or transient ischemic attack in a single center of Spain

Aldo F. Costa, Alejandro Peral, Francisco Bravo, Francisco Fernández, Roberto Valverde

**Introduction.** Basilar artery dolichoectasia (BADE) refers to abnormal enlargement or displacement of the basilar artery (BA). The previously reported prevalence of BADE among patients with stroke is 0.3 to 33.1%, however, it might vary among studied populations. We aim is to determine the prevalence of BADE in patients presenting with acute ischemic stroke (AIS) or transient ischemic attack (TIA) in a Stroke Unit in a single center in Spain.

**Patients and methods.** Patients 50 years old or older presenting with AIS or TIA were eligible for inclusion. Demographic and clinical data were prospectively collected. Two neuroradiologists, blind to each other, assessed BA morphology.

**Results.** Among 126 patients, 34.1% fulfilled the criteria for BADE (ectasia or dolichosis). BADE was associated with advanced age ( $p = 0.04$ ). Patients with fetal-type circle of Willis presented smaller BA diameters ( $2.9 \pm 0.1$  vs.  $3.5 \pm 0.1$ ;  $p < 0.001$ ), whereas patients with lacunar strokes presented a greater diameter than other stroke subtypes ( $3.8 \pm 0.3$  mm vs.  $3.3 \pm 0.1$  mm;  $p = 0.04$ ).

**Discussion and conclusions.** In this single-center study of patients presenting with AIS or TIA, the prevalence of BADE (ectasia or dolichosis) is high. Further studies focusing on Spaniards should confirm our results.

**Key words.** Basilar artery. Basilar artery dolichoectasia. Dilatative arteriopathy. Ischemic stroke. Spain. Transient ischemic attack.

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## Introduction

Dolichoectasia refers to tortuosity or dilatation of an artery that is often referred to as dilatative arteriopathy [1]. The term intracranial artery dolichoectasia (IADE) describes the dolichoectasia of one or more intracranial arteries, of which, the basilar artery (BA) is involved in 80% of cases [2,3]. Patients with basilar artery dolichoectasia (BADE) present an increased risk of acute ischemic strokes (AIS) and AIS recurrence, predominately in the vertebrobasilar territory [4-6].

Previous studies have shown that the prevalence of BADE varies among populations. This heterogeneity might be explained by the lack of generally accepted quantitative criteria for the BADE definition as well as the variability of the selected populations. For instance, BADE can be found in 0.8 to 13.6% of the general population [7-11], while in patients with stroke, the prevalence of BADE ranges from 0.3 to as high as 33.1% [12-17].

This study aimed to determine the prevalence of BADE in patients presenting with AIS or transient

ischemic attack (TIA) in a stroke unit. Secondly, we analyzed subgroups of patients with characteristics of special interest for BADE such as the fetal-type circle of Willis, posterior circulation strokes, and lacunar strokes. Previous studies have reported an inverse relationship between the BA diameter and the presence of fetal-type circle of Willis [18,19], a strong relationship between BADE and posterior circulation strokes [20-23], and a significant association between BADE and lacunar strokes [24]. To the best of our knowledge, this is the first prospective study on evaluating BADE in stroke patients from Spain.

## Patients and methods

### Participants and demographics

We consecutively included patients  $\geq 50$ -year-old patients presenting with AIS or TIA admitted to the stroke unit of the Hospital Universitario Reina Sofía (Córdoba, Spain), who underwent magnetic resonance angiography or computed tomography



**Table I.** Smoker et al criteria for the assignment of basilar artery dolichosis.

	Height of bifurcation	Position
Grade 0	At or below dorsum sellae	Midline throughout
Grade 1	Within suprasellar cistern (one cut above dorsum)	Medial to the lateral margin of clivus or dorsum sellae
Grade 2	At the level of the third ventricle floor (one cut above the suprasellar cistern)	Lateral to the lateral margin of clivus or dorsum sellae
Grade 3	Indenting and elevating the third ventricle floor (two or more cuts above the suprasellar cistern)	In cerebellopontine angle cistern

angiography for two months. Approximately 1,000 patients are admitted to our stroke unit per year. Hospital Universitario Reina Sofía is the referring center for mechanical thrombectomy in the Córdoba province (13,771 km<sup>2</sup>; 781,451 inhabitants) and for the neighboring province of Jaén (14,496 km<sup>2</sup>; 627,190 inhabitants).

Demographics and cardiovascular risk factors stroke, coronary heart disease, smoking status, and medications were obtained from medical records and confirmed by a patient's representative when possible. Patients with missing data, ethnic/race origins other than Caucasians Spaniards, final diagnosis other than AIS/TIA (stroke mimics) or, without brain magnetic resonance imaging (MRI) stroke confirmation in the setting of absence of large vessel occlusion were excluded from the study. The patients underwent were prospectively collected in each patient by 2 neurology residents (A.C. and A.P.). The history of hypertension, diabetes, dyslipidemia, atrial fibrillation (AF), ischemic electrocardiographic monitoring in the first 24 hours of admission. Additional extended electrocardiographic monitoring, transthoracic echocardiogram, and transcranial Doppler to detect right-to-left shunt were done on a case-by-case basis.

All patients (or a legal representative in cases of incapability) signed informed consent. The protocol was approved by the Ethics Committee of the Córdoba Province (Reference 4929, N.319).

### Basilar artery assessment

Computed tomography angiographies were performed using a multidetector CT scanner (Gener-

al Electric, Fairfield, CT, USA) with a slice thickness of 0.625 mm in patients that fulfill the criteria for the 'stroke code' based on the stroke protocol for Andalusian hospitals. Gadolinium-enhanced magnetic resonance angiography was performed on a 1.5-Tesla MRI machine (Siemens Healthineers, MAGNETOM Vida, Germany) in patients without initial computed tomography angiography that required further vascular assessment for etiologic diagnosis of the vascular event.

Two experienced neuroradiologists (F.B. and F.F.) separately assessed BADE on computed tomography angiography and magnetic resonance angiography studies using the Carestream Health Software (Onex Corporation, Rochester, NY, USA) and blinded to patients' characteristics. BA diameter was evaluated at three different points of the artery length (at the proximal, middle, and top segments) and a mean of the three values was calculated. We use this triple measurement approach instead of a single measurement at mid-pons because, in the setting of dolichosis of the vertebral arteries, the BA is pushed up causing variability of the measured segment. When stenosis was present in the BA, the remaining non-stenotic segment was selected for measurements. In cases of any vertebral artery terminating in a posterior inferior cerebellar artery, only measurements at the top and the middle segment were obtained.

For the evaluation of BADE, we follow Smoker et al criteria (Table I) [25]. Ectasia was defined as the BA diameter > 4.5 mm. The height of bifurcation as well as the lateral displacement of BA was graded from 0 to 3, as explained in table I. A classification of two or more, in either bifurcation height or laterality, was considered dolichosis. BADE was defined as the presence of ectasia or dolichosis (Figure). Discrepancies were solved by a stroke neurologist (R.V.) as a third reader.

The prevalence of embryonic derivation of the posterior cerebral artery (PCA) from the internal carotid artery (ICA), the so-called fetal-type circle of Willis, was evaluated using a definition by Horikoshi et al [26]. Patients with AIS were divided according to the stroke subtype in lacunar strokes and non-lacunar strokes to assess differences regarding BA diameter in both groups. Lacunar stroke was defined as subcortical ischemic lesions of < 15 mm with a congruent neurological deficit in which no other causes of stroke were identified [27].

### Statistical analysis

Continuous variables were recorded as means ± standard deviations and compared between groups

using Student’s *t*-test or Mann–Whitney U test, as appropriate. Categorical data were presented as percentages and compared between groups by  $\chi^2$  or the Fisher exact test. Inter-reader reliability for BA diameter measurements as well as dolichosis classification was evaluated with Lin’s concordance correlation coefficient and Cohen’s weighted kappa coefficient, respectively. All statistical analyses were carried out using STATA version 16 (College Station, TX, USA) and a *p*-value of < 0.05 was considered statistically significant.

**Results**

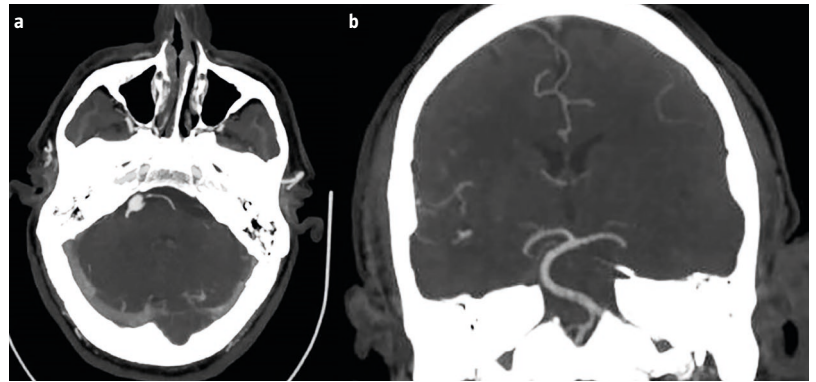
A total of 151 patients were admitted to the stroke unit during the study period. Of this, 142 patients fulfilled the inclusion criteria. Among the 142 patients that were initially screened, we excluded 13 patients for the following reasons: in 11 patients the final diagnosis was other than AIS/TIA, and two patients with no large vessel occlusion did not undergo MRI for stroke confirmation. Three additional patients were excluded due to a low-quality computed tomography angiography in two patients, and a complex anatomical variant of the vertebrbasilar system in one subject.

A total of 126 patients (93.7% computed tomography angiography and 6.4% magnetic resonance angiography) were included in the final analysis. The final diagnosis was AIS in 90.5% and TIA in 9.5%. Among patients with AIS, 10 (8.8%) were considered lacunar strokes.

Of the total sample, 69 (54.8%) were men and the mean age was 73 ± 11 years. Hypertension was the most common risk factor present in 95 patients (75.4%), followed by dyslipidemia in 68 (54%), and diabetes in 42 (33.3%) (Table II). It was not possible to assess the height of bifurcation due to a lack of visualization of both PCAs in one patient that presented an occlusion at the top of the BA. This patient had a BA diameter of 3.0 mm and had a 0 on the lateralization grading.

The mean BA diameter of our sample was 3.4 ± 0.7 mm. Forty-three patients fulfilled the criteria for BADE (34.1%) including 4 (3.2%) subjects with ectasia (BA diameter > 4.5 mm), and 48 (38.1%) with dolichosis. Patients with both conditions were those who presented ectasia (*n* = 4, 3.2%). In terms of the height of bifurcation, 19 patients (15.2%) presented grade 0, 65 (52.0%) grade 1, 32 (25.6 %) grade 2 and 9 (7.2%) grade 3. Also, in terms of laterality, 53 (42.1%) patients presented grade 0, 50 (39.7%) grade 1, 18 (14.3%) grade 2, and 5 (4.0%)

**Figure.** Computed tomography angiography of a patient showing: a) a dilated basilar artery lateralized to the right pontocerebellar angle in an axial view and b) abnormally high bifurcation indenting the floor of the third ventricle in a coronal view.



**Table II.** Characteristics of the included patients according to their basilar artery dolichoectasia status.

	All patients (N = 126)	BADE (+) (n = 43)	BADE (-) (n = 83)	<i>p</i> -value
Age	73 ± 11	75 ± 10	72 ± 10	0.04
Male sex	69 (54.8%)	25 (54.8%)	44 (53%)	0.71
Hypertension	95 (75.4%)	33 (76.8%)	62 (74.7%)	1
Diabetes	42 (33.3%)	12 (28%)	30 (36.1%)	0.43
Dyslipidemia	68 (54%)	19 (44.2%)	49 (59%)	0.13
Coronary heart disease	14 (11.1%)	3 (7%)	11 (13.3%)	0.38
Previous ischemic stroke	27 (21.4%)	4 (9.3%)	23 (27.7%)	0.02
Active smoking	28 (22.2%)	9 (20.9%)	19 (22.9%)	1
Past smoking habit	20 (15.9%)	5 (11.6%)	15 (18.1%)	0.44
Atrial fibrillation	26 (20.6%)	10 (23.4%)	16 (19.3%)	0.65
Statins use	57 (45.2%)	21 (48.8%)	36 (43.4%)	0.58
Anti-hypertension medication	95 (75.4%)	34 (79.1%)	61 (73.5%)	0.52
Oral anti-diabetics	34 (27%)	10 (23.3%)	24 (28.9%)	0.53
Insulin treatment	10 (7.9%)	1 (2.3%)	9 (10.8%)	0.16
Anti-platelet medication	39 (31%)	15 (34.9%)	24 (28.9%)	0.54
Oral anticoagulation	20 (15.9%)	7 (16.3%)	13 (15.7%)	1
Fetal-type circle of Willis	29 (23%)	10 (23.3%)	19 (22.9%)	1

BADE: basilar artery dolichoectasia.

**Table III.** Distributions of the two conditions that defines dolichosis according with Smoker et al criteria.

	Height of bifurcation (n = 125)	Laterality (n = 126)
0	19 (15.2%)	53 (42.1%)
1	65 (52%)	50 (39.7%)
2	32 (25.6%)	18 (14.3%)
3	9 (7.2%)	5 (4%)

**Table IV.** Distribution of 125 patients according to the basilar artery elongation and lateral migration status using the criteria proposed by Smoker et al.

Laterality	Height of bifurcation			
	Grade 0	Grade 1	Grade 2	Grade 3
Grade 0	12 (9.6%)	33 (26.4%)	5 (4%)	2 (1.6%)
Grade 1	7 (5.6%)	25 (20%)	16 (12.8%)	2 (1.6%)
Grade 2	0	7 (5.6%)	7 (5.6%)	4 (3.2%)
Grade 3	0	0	4 (3.2%)	5 (4%)

grade 3 (Table III). The most common combination of dolichosis status was grade 1 for height of bifurcation and grade 0 for lateralization in 33 (26.4%) followed by grade 1 for both height of bifurcation and laterality in 25 patients (20.0%) (Table IV). Kappa coefficients were 0.85 for laterality and 0.77 for the height of bifurcation. The concordance coefficient was 0.87 for BA diameter measurements between both readers.

Patients with BADE were significantly older ( $75 \pm 10$  vs.  $72 \pm 10$ ;  $p = 0.04$ ). Other traditional cardiovascular risk factors such as hypertension, diabetes, or dyslipidemia did not show a significant association with BADE as shown in table II. Regarding stroke subtype, patients with lacunar stroke had significantly greater diameter of the BA ( $3.8 \pm 0.3$  mm vs.  $3.3 \pm 0.1$  mm;  $p = 0.04$ ). Other factors associated with lacunar strokes were younger age ( $p = 0.01$ ), active smoking ( $p = 0.03$ ), and posterior circulation strokes ( $p = 0.01$ ). However, lacunar stroke was not associated with the presence of ectasia, dolichosis, individual components of dolichosis, or BADE.

The stroke localization was available in 110 (96.5%) patients with AIS. Posterior circulation stroke was present in 19 patients (17.3%). There

was no difference between patients with BADE and their counterparts regarding posterior compared with anterior circulation strokes (18.4% vs. 16.7%; respectively,  $p = 0.82$ ). Besides, the presence of posterior circulation stroke was not associated with the BADE, BA diameter, ectasia, dolichosis, or individual components of dolichosis.

The fetal-type circle of Willis was present in 29 patients (23.0%), affecting the right PCA in 13 cases, the left PCA in 12 cases, and both PCAs in 4 cases. Patients with fetal-type circle of Willis presented a smaller diameter of the BA ( $2.9 \pm 0.1$  vs.  $3.5 \pm 0.1$ ;  $p < 0.001$ ).

## Discussion and conclusion

The current study reports a BADE prevalence (ectasia or dolichosis) of 34.1% among Spaniards with AIS or TIA. To our knowledge, this is the highest BADE prevalence reported in the literature and the first report among Spaniards (Table V).

Two retrospective studies based on visual impressions of the BA morphology have shown conflicting results in terms of BADE prevalence and its association with cardiovascular risk factors. Ince et al (1998), included 387 stroke patients from the United States. Twelve patients had IADE (3.1%) and the prevalence of BADE was 2.1% in the total sample [13]. The authors did not find significant associations of BADE with traditional cardiovascular risk factors, but patients with BADE were more likely to have lacunar stroke. Instead, in the Étude du Profil Génétique de l'Infarctus Cerebral (GENIC) study, IADE was present in 12% of 510 stroke patients of 12 French neurologic centers [28]. BADE represented 78% of the patients with IADE and stroke. IADE was significantly associated with cardiovascular risk factors and with lacunar stroke. Different methodologies and imaging modalities might explain the difference between these two studies. Nevertheless, the association of IADE and the presence of lacunar stroke was documented in both. The underlying pathophysiology of the BADE and small vessel disease is still unknown. However, it is well known that both conditions are diseases of the tunica media and extracellular matrix dysfunction [29]. These conformational changes increase the vascular permeability and the deposition of extracellular matrix macromolecules in the white matter [30]. The blood-brain barrier damage favors perivascular edema and neuronal damage of penetrating small arteries [31]. Furthermore, in a more recent prospective study including 200 stroke pa-

**Table V.** Description of studies of basilar artery dolichoectasia in stroke patients.

	Study design	Country	Number of patients	Study population	Mean age (± SD)	Mean BA diameter (mm) (± SD)	Cutoff value for BA ectasia (mm)	Dolichosis definition	BADE definition	BADE prevalence
Cao, 2021	Prospective	China	113	Pontine infarcts	64 (56-73) <sup>a</sup>	2.9 ± 0.6	>4.5 at any location	Quantitative method	Ectasia and dolichosis	1.8%
Del Brutto, 2021	Prospective	United States	200	AIS	67 ± 14	3.4 ± 0.8 (proximal); 2.8 ± 0.7 (distal)	≥5.0 (proximal); ≥ 4.1 (distal)	Semiquantitative method	Ectasia and dolichosis	11%
Chen, 2019	Prospective	China	115	AIS (cardioembolic stroke excluded)	63 ± 11	4.3 ± 1.1	≥ 4.6 at midpons	Smoker's	–	14.8% <sup>b</sup>
Zhou, 2022	Prospective	China	534	Posterior circulation stroke	–	–	≥4.6	Smokers' s and quantitative	Ectasia and dolichosis	29.8%
Nakamura, 2012	Prospective	Japan	481	Ischemic and hemorrhagic stroke	69 ± 12	5.0 ± 0.4 (AIS)	≥ 4.6 at midpons	Smoker's	–	7.7% (6.4% in AIS)
Kwon, 2009	Prospective	South Korea	96	Pontine infarction	67 ± 11 (PPI); 66 ± 11 (LPI)	–	≥ 4.6 at midpons	Smoker's	–	Ectasia, in 31.4% of PPI and 11.5 % in LPI; dolichosis 20.8%
Pico, 2003	Prospective	France	510	AIS	–	3.9 ± 1.8 (VBD); 2.6 ± 0.6 (non-VBD)	≥ 4.6 at midpons	Smoker's	Consensus method	12.4%
Yin, 2021	Prospective	China	469	AIS (cardioembolic stroke excluded)	60 ± 11	3.3 (1-8.5) <sup>c</sup>	≥ 4.6 at any location	Smoker's	–	13%
Ince, 1998	Retrospective	United States	387	All	–	–	–	Smoker's	Neuroradiologist reports, visual assessment	2.1%
Present study	Prospective	Spain	126	AIS and TIA	73 ± 11	3.4 ± 0.7	> 4.5 (mean of 3 segments)	Smoker's	Ectasia or dolichosis	34.1%

BA: basilar artery; BADE: basilar artery dolichoectasia; IS: ischemic stroke; LPI: lacunar pontine infarction; PPI: paramedian pontine infarction; TIA: transient ischemic attack; VBD: vertebral-basilar dolichoectasia. <sup>a</sup> Median (interquartile range). <sup>b</sup> The prevalence was calculated in base on an initial number of 778 eligible patients with stroke. <sup>c</sup> Median (range).

tients in a US center, IADE was present in 24% and BADE was present in 11% of the patients [32]. Similar to our results, advanced age was the only cardiovascular risk factor associated with IADE and IADE was more prevalent in patients with lacunar strokes. These findings support the non-atherosclerotic nature of IADE and its role in the developing of small vessel disease.

The prevalence of BADE is higher in patients with posterior circulation stroke (~18%) [33]. In the present study, we found no significant differences in posterior circulation stroke among patients with or without BADE. This might be attributable to the lack of power as the number of posterior circulation stroke patients was low ( $n = 19$ ).

Determination of the fetal-type circle of Willis prevalence could be of special interest for the reporting of BADE prevalence. However, only a few studies have addressed this issue. In the Northern Manhattan Study (NOMAS) fetal-type circle of Willis was present in 13.4% of the stroke-free individuals (6.8% on the right, 6.1% on the left, and 0.5% both) [18]. In community-dwelling older adults from Ecuador 28% had fetal-type circle of Willis [19]. In the Osaka Follow-up Study for Carotid Atherosclerosis, part 2 (OSACA2) the prevalence of fetal-type circle of Willis was only present in 4.1%. In all three studies, BAs were significantly thinner in patients with fetal-type circle of Willis. Our results are consistent with the mentioned studies.

It is noteworthy that in our study ectasia was present in only four patients (3.2%) while the majority of the BADE was defined by the presence of dolichosis. Similar findings have been pointed out by Cao et al in a Chinese population in which dolichosis is the predominant component of BADE [34]. In Chinese patients with posterior circulation stroke dolichosis is an independent risk factor for stroke recurrence [35], whereas in large longitudinal studies in other populations, ectasia was considered the most important component of BADE for incident cardiovascular outcomes [36,37]. Whether dolichosis alone represents an independent risk factor for stroke in the Spaniard population is yet to be determined.

The major limitation of this study is the relatively small sample of a single center. Also, we studied dolichoectasia only among stroke patients with computed tomography angiography or magnetic resonance angiography. Minor strokes without a vascular imaging study were excluded.

We used Smoker et al criteria for the BADE definition because of its accuracy, simplicity, and reproducibility. Some authors have argued that intracranial arteries' diameters should be adjusted to the total cranial volume, however, this methodology has poorer accuracy and is more time-consuming compared with Smoker et al criteria [7].

In conclusion, in Spaniard patients admitted with AIS or AIT in a stroke unit the prevalence of BADE (ectasia or dolichosis) is high. The presence of BADE is associated with advanced age but not with other traditional cardiovascular risk factors. The patients with lacunar strokes had a greater BA diameter than patients with non-lacunar strokes while patients with fetal-type circle of Willis presented significantly lower BA diameters when compared with their counterparts. We were not able to find differences regarding stroke localizations (posterior circulation stroke vs. anterior circulation stroke) in our patients. Finally, the majority of BADE patients were classified as it because of the sole presence of dolichosis, whereas ectasia (>4.5 mm) was markedly less frequent. Further longitudinal studies with larger sample size should confirm our results.

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### Prevalencia de la dolichoectasia de la arteria basilar en pacientes con ictus isquémico agudo o ataque isquémico transitorio en un centro español

**Introducción.** La dolichoectasia de la arteria basilar (DEAB) es un término que se refiere a la dilatación o elongación anormal de la arteria basilar (AB). La prevalencia de DEAB notificada hasta la fecha en pacientes con ictus es del 0,3 al 33,1%; sin embargo, puede variar entre poblaciones. Se propuso determinar la prevalencia de DEAB en pacientes con ictus isquémico agudo (IIA) o ataque isquémico transitorio (AIT) en una unidad de ictus de España.

**Pacientes y métodos.** Se consideró a pacientes de 50 años o más con IIA o AIT para ser incluidos. La información demográfica y clínica se obtuvo de forma prospectiva. Dos neurorradiólogos evaluaron la morfología de la AB de forma independiente.

**Resultados.** De 126 pacientes, el 34,1% cumplió los criterios de DEAB (ectasia o dolicosis). La DEAB se asoció a mayor edad ( $p = 0,04$ ). Los pacientes con la variante fetal del polígono de Willis presentaron menor diámetro de la AB ( $2,9 \pm 0,1$  frente a  $3,5 \pm 0,1$ ;  $p < 0,001$ ), mientras que pacientes con ictus lacunar presentaron diámetros mayores de la AB que otros subtipos de ictus ( $3,8 \pm 0,3$  mm frente a  $3,3 \pm 0,1$  mm;  $p = 0,04$ ).

**Discusión y conclusiones.** En este estudio de centro único de pacientes con IIA o AIT, la prevalencia de DEAB (ectasia o dolicosis) fue alta. Estudios futuros enfocados en población española podrían confirmar nuestros resultados.

**Palabras clave.** Arteriopatía dilatante. Arteria basilar. Ataque isquémico transitorio. Dolichoectasia de la arteria basilar. España. Ictus isquémico.