Basilar Artery Diameter and 5-Year Mortality in Patients With Stroke

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Background and Purpose—Few and conflicting data exist on the case fatality rate in stroke patients with basilar artery dolichoectasia. We analyzed basilar artery characteristics (diameter, height of bifurcation, transverse position) and 5-year mortality (all-cause, nonstroke vascular, and stroke) in patients with brain infarction.

Methods—The basilar artery diameter was measured with a 16-diopter lens in 466 consecutively recruited patients with brain infarction confirmed by magnetic resonance imaging. The height of the bifurcation and the transverse position of the basilar artery were assessed on semiquantitative scales. Patients were followed up for a median of 5.3 years (range, 1.5 to 6.6) and were classified as having had stroke, nonstroke vascular, and nonvascular death according to the French national registry of death certificates.

Results—Of the 157 deaths, 88 were vascular (including 54 stroke deaths). Basilar artery diameter was associated with an increased 5-year stroke mortality rate but not with all-cause or nonstroke vascular mortality. The adjusted hazard ratio (HR) of stroke mortality per 1-mm increase in basilar artery diameter was 1.23 (95% confidence interval [CI], 1.07 to 1.41). A higher risk of stroke death was associated with basilar artery diameter at the 95th percentile (diameter >4.3 mm; adjusted HR 3.69; 95% CI, 1.63 to 8.38) and the height of bifurcation (adjusted HR for score >1, 2.08; 95% CI, 0.93 to 4.68) but not with transverse position.

Conclusions—Basilar artery diameter was independently associated with cerebrovascular mortality. A diameter >4.3 mm may be a marker for a high risk of fatal stroke. (Stroke. 2006;37:2342-2347.)

Key Words: basilar artery ■ mortality ■ stroke

Intracranial dilatative arteriopathy (ie, dolichoectasia) is identified in 12% of patients with brain infarction.1,2 The basilar artery is the most commonly affected of the intracranial arteries: in 1 study, the basilar artery was dolichoectatic in 78% of cases.1 Autopsy studies have shown that one third of patients with dolichoectasia have an abdominal aortic aneurysm (AAA).3 Predictors of rupture and mortality in patients with an AAA are initial and 1-year increases in the diameter of the abdominal aorta.4 Life-threatening complications of basilar artery dolichoectasia (BADE) are rupture, brain infarction, and brainstem compression.5,6 Other than in case series,5,7-6 the prognosis for patients with BADE has been investigated in only 2 case-control studies.10,11 An increase in mortality was reported in 1 study, whereas the other found a protective effect. Neither of these studies investigated the prognosis according to basilar artery diameter as a continuous variable, by analogy to AAA.

The aim of this study was to investigate trends in 5-year mortality (all-cause, nonstroke vascular, and stroke) according to basilar artery diameter. We also assessed the prognosis of basilar artery elongation, assessed indirectly by the height of the bifurcation and the transverse position of the basilar artery.

Subjects and Methods

The GENIC Study: Inclusion Criteria and Data Collection

In the GENIC study (étude du profil GENétique de l’Infarctus Cérébral), consecutive patients were recruited in 12 French neurological centers when they fulfilled the following criteria: clinical symptoms suggestive of stroke; no brain hemorrhage on computed tomography scan; infarct proven by magnetic resonance imaging (MRI); age 18 to 85 years; and both parents of white origin. Patients were enrolled into the study in the 1-week interval after the event. Those reporting previous cardiovascular or cerebrovascular history were eligible for inclusion.

Patients’ demographic characteristics, risk factors, and definitions have been reported previously.1 Electrocardiographic, extracranial duplex, transcranial Doppler, and carotid ultrasonography studies were performed in all patients.
Basilar Artery Characteristics on MRI Scan
Details of the methods have been reported previously. In brief, we measured the diameter of the basilar artery at the midpons with a 16-diopter achromatic hand-held graduated (1/10 mm) lens on hard copies of the axial MRI scan. An intrareader reproducibility study, based on 50 random MRI scans, was performed at the end of the study; the intraclass correlation coefficient of measurement of the basilar arteries with the graduated lens was 0.92.

In addition to basilar artery diameter, we assessed the height bifurcation and transverse position of the basilar artery according to Smoker’s criteria, with a semiquantitative 4-point scale for both. These 2 parameters allow indirect evaluation of the basilar artery length, and therefore its elongation and tortuosity, based on brain axial imaging. The scale for assignment of basilar artery height of bifurcation was as follows: 0 (at or below the dorsum sellae); 1 (within the suprasellar cistern); 2 (at the level of the third ventricle floor); and 3 (indenting and elevating the floor of the third ventricle).

The diameters of 6 other intracranial arteries were measured: the 2 vertebral arteries at the V4 segment, the 2 intracavernous internal carotid arteries, and the middle cerebral artery at the M1 segment. We focused on the basilar artery because it is the most commonly affected by the dolichoectatic process. The corresponding percentages for the other arteries were 57%, 48%, and 30% for the vertebral, internal carotid, and middle cerebral arteries, respectively. The basilar artery was measured in 91% of the MRI scans compared with 74% for the intracranial arteries.

In addition to quantitative parameters, 2 neurologists determined whether at least 1 dolichoectatic intracranial artery could be identified on visual examination. Patients with dolichoectasia corresponded to strokes with at least 1 dolichoectatic artery based on consensus. This variable is of clinical significance because it is based on consensus between the 2 physicians and could be assessed in all patients.

Follow-Up
Follow-up examinations were scheduled as follows: 10-day visits were performed during hospitalization or at discharge (median, 11 days; range, 0 to 40); 6-month visits consisted of a neurological consultation with a local investigator (median delay, 193 days; range, 29 to 587); and the last visit was performed by a research nurse who visited patients at their homes (median delay, 2.7 years; range, 1.4 to 4.0).

To assess the mortality rate, a phone call to patients or their families was scheduled after 5 years (median delay, 5.3 years; range, 4.0 to 6.6). If there was no answer, information was obtained from primary care records or from the Registrar for Births, Marriages, and Deaths from the city of birth (or from the city of Nantes for births outside France), with a “dead” or “alive” answer. We then used the French national registry of death certificates (INSERM) to classify cases into stroke and nonstroke vascular deaths. French death certificates are completed by a certified practitioner who diagnoses the death and specifies 4 items: immediate cause of death, underlying disease, complication of the underlying disease, and other diseases that could have contributed to death. The underlying causes of death were coded according to the International Classification of Disease (ICD), 9th revision, for the period 1995 to 1999, and 10th revision, for the period 2000 to 2001. Deaths attributed to vascular disease were identified as ICD-9 codes 390 to 459 and ICD-10 codes I00 to I99, and deaths attributed to stroke, as ICD-9 codes 430 to 438 and ICD-10 codes I60 to I69. Deaths attributed to nonstroke vascular death included all ICD codes from vascular disease other than stroke. Because there is good comparability of statistical classification for mortality from vascular disease between the 2 ICD versions (ICD-10/ICD-9 comparability ratio = 1.0), no adjustments were needed for changes in the coding system.13,14 The ethics committee of Cochin Hospital approved the research protocol, and all subjects signed an informed consent form before enrollment into the study.

Statistical Analysis
Statistical analysis was based on data for 466 patients with stroke for whom a measurement of the basilar artery diameter was available. We studied the association between several risk factors and basilar artery diameter (introduced as a continuous variable) by simple linear regression. Risk factors associated with basilar artery diameter were used subsequently to adjust the relation between basilar artery characteristics and mortality. We estimated and compared the all-cause, nonstroke vascular, and stroke death rates according to tertiles of basilar artery diameter by the Kaplan-Meier method and log-rank test. For nonstroke vascular and stroke-free survival analyses, patients who died from causes other than nonstroke vascular and cerebrovascular diseases were censored at the time of death. A Cox proportional-hazards model was used to estimate the relative risk of all-cause, nonstroke vascular, and stroke death. The proportional-hazards assumption was examined with the use of log-log survival plots. We also reported survival analyses according to the height of bifurcation (score >1) and transverse position (score >1) of the basilar artery. Finally, in post hoc analysis, we compared the Kaplan-Meier survival curves according to basilar artery diameter dichotomized to the 95th percentile threshold (4.3 mm) and to groups with dolichoectasia or not. Statistical testing was done with a 2-tailed α level of 0.05. Data were analyzed with the SAS package (SAS Institute).

Results
Patients’ Baseline Characteristics
Among the 510 patients with stroke enrolled in the GENIC study, 466 (91%) had basilar artery diameter measurements available. There were no significant differences in terms of age, sex, history of hypertension or diabetes, smoking, lipid profile levels, blood pressure values, and personal history of myocardial infarction and stroke between patients included in the study and those who were excluded (data not shown). Patients with missing measurements for the basilar artery had a higher body mass index than those with measurements (mean ± SD, 26.9 ± 4.7 versus 25.3 ± 4.4; Student t test, P = 0.03).

The baseline characteristics of the population according to tertiles of basilar artery diameter are presented in Table 1. In univariable analysis, older age, male sex, hypertension, admission systolic blood pressure, and history of myocardial infarction were associated with an increased basilar artery diameter (P < 0.05). After the initial brain infarction, the patients were followed up for a median of 5.3 years (range, 1.5 to 6.6); 157 patients died, and 22 were lost to follow-up after the third examination. There were 88 vascular deaths (including 54 strokes), 20 cancer deaths, 35 other nonvascular deaths, and 14 deaths of unknown cause.

Basilar Artery Diameter and 5-Year Mortality
No significant difference was found in overall survival for patients with stroke according to tertiles of basilar artery diameter (log-rank test, P = 0.26). The Kaplan-Meier estimates of 5-year death for the basilar artery diameter tertiles were 35.1% (95% confidence interval [CI], 28.1 to 43.1), 32.5% (95% CI, 25.2 to 41.1), and 41.1% (95% CI, 32.6 to 50.9), respectively (Table 2). Similar results were found when the analysis was restricted to nonstroke vascular mortality (log-rank test, P = 0.24). As shown by the Kaplan-Meier curves in Figure 1, there was also no significant difference...
Survival analyses performed according to the 95th percentiles of basilar artery diameter distribution (4.3 mm) showed a significant difference in survival without fatal stroke (Figure 2). Stroke patients with a basilar artery diameter >4.3 mm had a higher risk of stroke death (35.1%; 95% CI, 18.2 to 60.5) than those with a basilar artery diameter ≤4.3 mm (12.4%; 95% CI, 9.4 to 16.3). The adjusted HR of stroke death associated with a basilar artery diameter ≤4.3 mm was 3.69 (95% CI, 1.63 to 8.38). As shown in Figure 2, a trend toward a higher risk of overall death for stroke patients with a basilar artery diameter >4.3 mm was found compared with those with a smaller artery diameter (47.4% versus 35.2%, P<0.11). The adjusted HR of overall death for basilar artery diameter >4.3 mm was 1.43 (95% CI, 0.77 to 2.66). Only 1 patient with a basilar artery diameter >4.3 mm died of a nonstroke vascular disease.

### TABLE 1. Baseline Characteristics of Study Subjects According to Tertiles of Basilar Artery Diameter

<table>
<thead>
<tr>
<th>Basilar Artery Diameter, mm</th>
<th>&lt;2.6 (n=195)</th>
<th>2.6–3.1 (n=141)</th>
<th>&gt;3.1 (n=130)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>63.0 (15.0)</td>
<td>67.0 (12.2)</td>
<td>70.0 (10.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male sex, % (n)</td>
<td>55.4 (108)</td>
<td>62.4 (88)</td>
<td>70.8 (92)</td>
<td>0.004</td>
</tr>
<tr>
<td>Body mass index, kg/m², mean (SD)</td>
<td>24.9 (4.3)</td>
<td>25.2 (4.2)</td>
<td>26.1 (4.7)</td>
<td>0.11</td>
</tr>
<tr>
<td>Hypertension, % (n)</td>
<td>58.0 (113)</td>
<td>63.8 (90)</td>
<td>74.6 (97)</td>
<td>0.009</td>
</tr>
<tr>
<td>History of diabetes, % (n)</td>
<td>18.6 (36)</td>
<td>19.9 (28)</td>
<td>15.5 (20)</td>
<td>0.66</td>
</tr>
<tr>
<td>Current smokers, % (n)</td>
<td>30.8 (60)</td>
<td>31.2 (44)</td>
<td>24.2 (31)</td>
<td>0.10</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL, mean (SD)</td>
<td>204 (44)</td>
<td>199 (41)</td>
<td>197 (44)</td>
<td>0.11</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL, mean (SD)</td>
<td>127 (34)</td>
<td>122 (34)</td>
<td>122 (37)</td>
<td>0.15</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL, mean (SD)</td>
<td>46 (17)</td>
<td>48 (15)</td>
<td>45 (13)</td>
<td>0.32</td>
</tr>
<tr>
<td>Systolic BP, mm Hg, mean (SD)</td>
<td>146 (23)</td>
<td>149 (21)</td>
<td>151 (19)</td>
<td>0.03</td>
</tr>
<tr>
<td>History of myocardial infarction, % (n)</td>
<td>9.8 (19)</td>
<td>7.9 (11)</td>
<td>16.3 (21)</td>
<td>0.04</td>
</tr>
<tr>
<td>History of stroke, % (n)</td>
<td>20.5 (40)</td>
<td>22.0 (31)</td>
<td>25.4 (33)</td>
<td>0.35</td>
</tr>
</tbody>
</table>

BP indicates blood pressure. Simple linear regression of several risk factors on basilar artery diameter (as continuous variable) was performed.

### TABLE 2. Five-Year Rates and Relative Risk of All-Cause, Nonstroke Vascular, and Stroke Mortality According to Basilar Artery Characteristics

<table>
<thead>
<tr>
<th>Diameter, mm</th>
<th>All-Cause Death</th>
<th>Nonstroke Vascular Death</th>
<th>Stroke Death</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rates %*</td>
<td>HR (95% CI)†</td>
<td>P</td>
</tr>
<tr>
<td>&lt;2.6 (n=195)</td>
<td>35.1</td>
<td>1.00 (reference)</td>
<td>...</td>
</tr>
<tr>
<td>2.6–3.1 (n=141)</td>
<td>32.5</td>
<td>0.97 (0.66–1.43)</td>
<td>0.89</td>
</tr>
<tr>
<td>&gt;3.1 (n=130)</td>
<td>41.1</td>
<td>1.30 (0.90–1.89)</td>
<td>0.16</td>
</tr>
<tr>
<td>Height of bifurcation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score ≥1 (n=379)</td>
<td>33.2</td>
<td>1.00 (reference)</td>
<td>0.01</td>
</tr>
<tr>
<td>Score &gt;1 (n=43)</td>
<td>50.2</td>
<td>1.80 (1.13–2.86)</td>
<td>0.01</td>
</tr>
<tr>
<td>Transverse of position</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Score ≥1 (n=414)</td>
<td>35.6</td>
<td>1.00 (reference)</td>
<td>0.01</td>
</tr>
<tr>
<td>Score &gt;1 (n=51)</td>
<td>39.0</td>
<td>1.13 (0.70–1.83)</td>
<td>0.62</td>
</tr>
</tbody>
</table>

*Estimated by the Kaplan-Meier method; †Crude HRs computed from the Cox proportional-hazards model.
Height of Bifurcation and Transverse Position of the Basilar Artery and 5-Year Mortality

The transverse position of the basilar artery was not associated with 5-year all-cause, nonstroke vascular, or stroke mortality. Patients with a bifurcation height \( \leq 1 \) had higher all-cause and stroke death rates compared with the other group (Table 2; log-rank tests, \( P = 0.01 \), \( P = 0.05 \), respectively). In multivariable analysis, the associations between height of the basilar artery bifurcation and 5-year all-cause or stroke mortality were no longer significant, but the HRs were of similar magnitude. The adjusted HR for all-cause, nonstroke vascular, and stroke deaths were 1.60 (95% CI, 0.99 to 2.60), 1.55 (95% CI, 0.52 to 4.65), and 2.08 (95% CI, 0.93 to 4.68), respectively.

Dolichoectasia and 5-Year Mortality

During the follow-up period, 23 of the 61 patients (13.5%) with dolichoectasia in the posterior or anterior circulation died (including 12 vascular deaths; 6 from cerebrovascular disease). In a post hoc analysis, we found no significant difference in patients’ survival between groups with dolichoectasia regarding all-cause, nonstroke vascular, and stroke deaths (log-rank tests, \( P > 0.39 \)).

Discussion

In this cohort of 466 consecutively enrolled patients with brain infarction, increasing basilar artery diameter was associated with an increased risk of stroke death at 5 years. Basilar artery diameter \( \geq 4.3 \) mm was a predictor of fatal stroke.

The discrepancy in the literature regarding fatal outcome in patients with BADE is likely explained by the different types of analysis used in these studies. Intracranial artery diameters were not considered as continuous variables, causes of death (all-cause, nonstroke vascular, stroke deaths) were not always assessed, and some studies either failed to include a control group or had an inadequate control group. The characteristics and main findings from studies that assessed the prognosis of patients with dolichoectasia, including BADE, are summarized in Table 3. In clinical series, the poor short-term survival (ranging from 40% to 63%) was likely attributable to retrospective inclusion of very severe cases (mean diameter, 7 mm) selected on the basis of medical or radiological records.

In the Rochester Epidemiology Project, long-term survival was better in 12 stroke patients with dolichoectasia compared with 375 patients without (\( P = 0.04 \)). Among these patients, dolichoectasia affected the posterior circulation in 10 instances. The higher frequency of lacunar brain infarction in patients with dolichoectasia relative to those without could account for an apparent protective effect (\( P = 0.02 \)). However, the severity of intracranial arterial dolichoectasia was not detailed. On the contrary, a retrospective review of 45 patients with dolichoectasia (mean diameters unknown) found a 4-fold risk of death compared with 45 age- and sex-matched controls. However, most of the patients had no previous symptoms of stroke, and the results may have been confounded by more frequent coronary artery disease in those with dolichoectasia.

In the present study, patients with or without dolichoectasia had the same prognosis. However, when the severity of dolichoectasia (assessed by basilar artery diameter) was taken into account, patients with a basilar artery diameter \( > 4.3 \) mm had a poorer prognosis than those with a smaller diameter. In a series of 159 patients with mean basilar artery diameters equal to 8 mm, a higher risk of rupture was observed for an
risk factor for basilar artery rupture. We previously reported that basilar artery diameter was associated with the number and severity of small-vessel-disease parenchymal abnormalities (ie, multilacunar state, leukoaraoisis, état crible). Acknowledging that stroke patients with lacunar infarct have a lower risk of stroke death, the association between small-vessel disease and basilar artery diameters has likely decreased the strength of the association between basilar artery diameters and cerebrovascular mortality. We have 2 hypotheses with which to reconcile a higher case fatality in patients with enlarged basilar artery diameters and a lower death rate in patients with small-vessel disease. The first is that basilar artery diameters, particularly when >4.3 mm, could discriminate stroke patients with small-vessel disease at high risk of stroke death. The second is that, for an equal size of stroke, patients with enlargement of the basilar artery have more cerebral lesions and therefore more fragile brain tissue, which could lead to a higher stroke case fatality. Overall, because we had only 1 patient with a basilar artery >10 mm, enlarged basilar artery diameters seem to be a marker rather than a cause of fatal stroke in this study. If confirmed, further studies should investigate the biological mechanisms underlying this association. Prognosis studies in stroke have focused on cerebral and intracranial artery atherosclerosis, an arteriopathy involving the intima. Dolichoectasia is a dilatative arteriopathy affecting the media, which has been overlooked. Being associated with stroke and ageing, it is not a rare arterial disease.

**Strengths and Limitations**

Compared with previous reports, our study has several strengths, including the low percentage of patients (4.5%) who were lost to follow-up; clinical factors were defined initially by a structured questionnaire; and multivariable analysis was performed after adjusting for age, sex, arterial hypertension, and coronary artery disease. Furthermore, we included basilar artery diameter as a continuous variable in the analyses.

Our study was limited by the lack of information on the presence of abdominal aorta diameter or AAA. We previously reported an association between basilar artery dolichoectasia and a history of myocardial infarction in the case-control portion of the GENIC study. However, we were limited by the low number of nonstroke vascular deaths, so this study was underpowered to determine whether basilar artery diameter is a predictor of cardiac death.

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Disclosures
None.

References
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The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/37/9/2342