Vertebral Artery Dominance Contributes To Basilar Artery Curvature and Peri-vertebrobasilar Junctional Infarcts

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Key words: atherosclerosis, basilar artery, vertebral artery, hemodynamic, ischemic stroke
ABSTRACT

Objectives: The diameters of the vertebral arteries (VAs) are very often unequal. Therefore, we investigated if unequal VA flow contributes to the development of basilar artery (BA) curvature and if it is a link to the laterality of pontine or cerebellar infarcts occurring around the vertebrobasilar junction.

Methods: We analyzed radiological factors (infarct laterality, VA dominance, BA curvature, and their directional relationships) of 91 patients with acute unilateral pontine or posterior inferior cerebellar artery (PICA) territory infarcts. The ‘dominant’ VA side was defined as either that the VA was larger in diameter or the VA was more straightly connected with the BA, if both VAs looked similar in diameter on CT angiography. Multiple regression analysis was performed to predict moderate-to-severe BA curvature.

Results: The dominant VA was more frequent on the left side ($p<0.01$). Most patients had an opposite directional relationship between the dominant VA and BA curvature ($p<0.01$). Pontine infarcts were opposite to the side of BA curvature ($p<0.01$) and PICA infarcts were on the same side as the non-dominant VA side ($p<0.01$). The difference in the VA diameters was the single independent predictor for moderate-to-severe BA curvature (OR per 1-mm, 2.70; 95% CI, 1.22-5.98).

Conclusions: Unequal VA flow is an important hemodynamic contributor of BA curvature and development of peri-vertebrobasilar junctional infarcts.
INTRODUCTION

Atherosclerosis is a chronic, inflammatory, fibroproliferative systemic disease primarily of large and medium-sized conduit arteries. Atherosclerotic plaques tend to develop in focal regions with complicated flow patterns, or with low or oscillatory wall shear stress (WSS) as in regions such as bifurcations, bends, and junctions. Mechanical forces acting on the arterial wall, including the WSS, are thought to be local factors influencing the development of atherosclerosis and regulating vessel caliber and morphology (i.e. vascular remodeling).

The basilar artery (BA), which supplies the brain stem and posterior part of the human brain, arises from the junction of the two vertebral arteries (VAs). Unlike most systemic arteries, which have a treelike branching pattern, the BA is the only large artery in which two arterial flows merge. Few studies have examined the flow dynamics at the vertebrobasilar junction. In addition, the diameters of the VAs are of equal size in only 6–26% patients in angiographic or postmortem studies, and the left VA is often larger than the right VA. Therefore, we postulated that the unequally mechanical forces resulting from asymmetric VA flow might influence the morphological deformation in the vertebrobasilar arterial system (lateral displacement or elongation of the BA, hypoplasia of the VA), and by extension, such deformations might asymmetrically induce the development of infarcts in the areas before or after vertebrobasilar junction.

To test this hypothesis, we investigated the demographics, specific locations of unilateral infarcts around vertebrobasilar junction, radiological findings, and hemodynamic findings. We also analyzed the potential predictors of the moderate-to-severe BA curvature.
PARTICIPANTS AND METHODS

Participants

From January 2005 to June 2007, we retrospectively identified all consecutive acute ischemic stroke patients admitted to two tertiary referral medical centers. We included patients if they had a final diagnosis of acute ischemic stroke with diffusion-weighted imaging (DWI) confirmation of lesions involving the posterior inferior cerebellar artery (PICA) territory unilaterally or pons unilaterally. A detailed history of vascular risk factors was obtained from each patient. To identify the potential mechanism of cerebral infarcts, a set of diagnostic tests was performed that included computed tomographic (CT) angiography, routine blood tests, and a cardiologic workup (electrocardiogram and echocardiogram). MRI was performed in all patients with a 1.5-T scanner (GE Medical, USA) and scanning with conventional T2-weighted MRI and DWI was conducted in the axial plane using 7-mm-thick sections.

Based on the results of the vascular and cardiologic studies, we divided the patients' stroke mechanisms into six groups: cardioembolism, large-artery atherosclerosis, small artery disease, other determined etiologies (e.g., vasculitis or dissection), undetermined etiology, and coexisting etiologies (>1 cause). We excluded patients 1) if their mechanisms fell into the cardioembolism, other determined cause, or coexisting etiology group, other determined cause, or coexisting etiology, 2) if the VA or BA was not seen on angiographic study, or 3) if the pontine lesion coexisted with the PICA territorial lesion.

To compare the vascular anatomical status (the morphology of the BA and VA) of patients with posterior circulation ischemic stroke with those of the age-matched populations, we evaluated brain CT angiography of above 40-year old patients without stroke history who visited the outpatient clinic of the Department of Neurology, Ajou University Hospital from Jan 2007 to June 2007. This study was approved by the Institutional Review Board at Ajou University Hospital.

Imaging analysis

The topographical determination of acute unilateral cerebellar infarction in the PICA territory was performed using visual correlation between Amarenco’s templates and the locations of high signal intensities from DWI that were more than 2 cm in diameter. Two of the authors (JMH and CSC) came to a topographical consensus. We defined acute unilateral pontine infarction as DWI lesions involving the pons unilaterally. To evaluate the frequency of affected sites in the cerebellum and pons, we made contour maps using MRICro software (C. Rorden, www.mricro.com).

The diameter of each vessel was calculated as the average of the measurements made at three consecutive points, 3-mm apart starting from the vertebrobasilar junction (both VAs and the BA). The ‘dominant’ VA was defined as 1) having the larger diameter within a strict criterion for diameter (i.e. a side to side diameter difference ≥ 0.3mm) or as 2) the VA more straightly connected to the BA if both VAs were visually similar to a criterion of angle on a CT angiography.

The direction of BA curvature was designated as ‘right (R)’ or ‘left (L) side’ according to a course of BA navigation at the vertebrobasilar junction. The degree of BA curvature was evaluated using a previously suggested CT-based method based on the lateral-most position of the BA throughout its course [0, midline; 1 (R or L), medial to lateral margin of the clivus or dorsum sellae; 2 (R or L), lateral to the lateral margin of the clivus or dorsum sellae; 3, in the cerebellopontine angle cistern]. The
moderate-to-severe BA curvature was defined as ≥ 2 of the above criteria. The height of the bifurcation of the BA was scored as: 1, within the suprasellar cistern; 2, at the level of the third ventricle floor; 3, indenting and elevating the floor of the third ventricle.

Transcranial Doppler and wall shear stress analysis

Transcranial Doppler (TCD) was performed with a 2-MHz pulsed Doppler instrument (EME TC-8080; USA) by an experienced technician within 7 days of admission. Patients were asked to relax and breathe normally while in a comfortable supine position in a quiet room. The BA flow was identified by the signal directed away from the probe though the suboccipital window and was evaluated at a depth between 80 and 100 mm through a suboccipital window. After the probe was shifted a few centimeters inferolaterally, it detected the VA flow signals directed away from the probe at depths of 40 to 75 mm.

Based on the assumption of laminar blood flow in the setting of a Poiseuillian parabolic model, we calculated the mean wall shear rate (WSR): 

\[ WSR = 4 \times \text{mean blood flow velocity/internal diameter} \]

The WSR was also calculated for mean shear rate. The whole blood viscosity \( \eta_w \) was estimated from the general plasma viscosity at 37°C \( \eta_0 = 1.5 \, \text{cP} \), and hematocrit \( Ht \) of the patients was determined using Einstein’s equation 

\[ \eta_w = \eta_0 (1 + 2.5 \, Ht) \]

The mean wall shear stresses were calculated using the formula: 

\[ \text{WSS} = \eta_w \times \text{WSR} \]

Statistical analysis

Differences between groups [patients vs. control, right vs. left, dominant vs. non-dominant VA side, or each tertile according to the diameter difference of the VAs] were analyzed using the Student’s t-test, \( \chi^2 \) test, paired t-test, or analysis of variance (ANOVA), as appropriate for continuous and categorical variables. We performed a multiple regression analysis to determine which variables were independent predictors of moderate-to-severe BA curvature. All potential predictors were entered into a univariate logistic regression model, including demographic variables (i.e. age, sex, and risk factors for stroke) and radiological/hemodynamic variables (i.e. R or L VAs’ diameter, BA diameter, diameter difference of VAs), and WSS (i.e. dominant VA, non-dominant VA, and BA). Potential factors that were not significant (\( p > 0.2 \)) in the univariate analysis were sequentially deleted from the full multivariable model. Results are given as the odds ratio (OR), as estimates of the relative risk with the 95% confidence interval (CI). Statistical significance was considered at \( p < 0.05 \).
RESULTS

General demographics and radiological and hemodynamic findings

Of 133 consecutive patients with an acute unilateral pontine or PICA infarction, 91 were eligible for this study. Forty-one patients were excluded for cardioembolism (n=26), invisible VA or BA (n=11), VA dissection (n=3), coexistence of pontine and PICA infarcts (n=1), and BA dissection (n=1). The mean age of the patients was 63.6±11.6 years, and 55 (60.4%) were male.

Table 1 shows the comparative results of age and sex, and radiological variables between 83 controls and 91 patients. There were no significant differences in their age and sex, the direction of dominant flow VA (predominantly left-sided), and diameter of respective arteries (right and left VA, and BA) between cases and control; however, there were significant differences in the degree of BA dolichosis and BA height between them. The mean viscosity was 3.06 ± 0.17 Cp (centipoise, range: 2.57–3.45 Cp) in the patients. The mean WSS of the VAs was significantly higher on the right side than on the left (10.4 ± 6.8 vs. 8.0 ± 5.2 dyne/cm²; p=0.009), especially on the non-dominant flow VA side (11.3 ± 7.4 vs. 7.1 ± 3.4 dyne/cm²; p<0.001). On the contralateral side, no difference was observed in the mean WSS according to the BA depth between 80 and 90 mm (7.6 ± 4.4 vs. 7.6 ± 4.7 dyne/cm²; p=0.965).
Table 1. Clinical and radiological characteristics of controls (n=83) and patients (n=91) with unilateral pontine or PICA infarcts

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=83)</th>
<th>Patients (n=91)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>General demographic data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, year</td>
<td>62.5±11.7</td>
<td>63.6 ± 11.6</td>
<td>0.526</td>
</tr>
<tr>
<td>Sex, % of male</td>
<td>49 (59.0)</td>
<td>55 (60.0)</td>
<td>0.850</td>
</tr>
<tr>
<td>Risk factors, n (%)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Hypertension</td>
<td>65 (71.4)</td>
<td></td>
<td></td>
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<tr>
<td>Diabetes mellitus</td>
<td>35 (38.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>30 (33.0)</td>
<td></td>
<td></td>
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<tr>
<td>Previous stroke</td>
<td>18 (19.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>22 (24.2)</td>
<td></td>
<td></td>
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<tr>
<td>Direction of vascular deformations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direction of dominant flow VA, n</td>
<td></td>
<td>0.803</td>
<td></td>
</tr>
<tr>
<td>R side</td>
<td>27</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>L side</td>
<td>56</td>
<td>63</td>
<td></td>
</tr>
<tr>
<td>Direction of BA curvature, n</td>
<td></td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>R side</td>
<td>45</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>L side</td>
<td>29</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Visually straight BA</td>
<td>9</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Degree of BA curvature, n</td>
<td></td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Grade 0</td>
<td>9</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>65</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>9</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td>0</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Degree of BA height, n</td>
<td></td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>82</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>Grade 2</td>
<td>1</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Grade 3</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Diameter of arteries</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean diameter of BA, mm</td>
<td>3.17 ± 0.70</td>
<td>3.20 ± 0.56</td>
<td>0.759</td>
</tr>
<tr>
<td>Mean diameter of R VA, mm</td>
<td>2.35 ± 0.82</td>
<td>1.95 ± 0.68</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean diameter of L VA, mm</td>
<td>2.48 ± 0.72</td>
<td>2.48 ± 0.74</td>
<td>0.998</td>
</tr>
</tbody>
</table>

PICA = posterior inferior cerebellar artery; VA = vertebral artery; BA = basilar artery; R = right; L = left

Directional relationships of the radiological findings

The contour maps of the affected sites in the pons and PICA cerebellum are depicted in Figure 1. We observed 47 pontine infarcts (R: 20 vs. L: 27) and 44 PICA infarcts (R: 26 vs. L: 18). For pontine infarcts, the paramedian region of the left mid-pons was the most affected site, whereas the right inferior medial region in the cerebellum was the most affected site for the PICA infarcts.

The dominant VA side was determined by the diameter criteria in 84 (92.3%) patients, and the rest of the patients by criteria of angle. The dominant VA was more frequent on the left VA side (69.2%; p<0.001). The BA curvature was mainly directed to the right side and the most frequent morphological change in the BA was a C-shaped deformation (n=65), followed by S-shaped (n=17), J-shaped (n=7), and no deformation or straight (n=2). Forty-eight patients had moderate-to-severe curvature of the BA and 18 had elongation of the BA. Eighty-six patients had lateral
displacement of the BA (≥ grade 1) and a directional relationship was detected between the dominant VA side and the BA curvature in the opposite direction in 76 (83.5%) patients (76/91; \( p < 0.001 \)).

Figure 2 shows that pontine infarcts opposite to the side of BA curvature occupied 72.3% (34/47; \( p = 0.002 \)), while PICA infarcts same to the side of the non-dominant VA occupied 72.7% (32/44; \( p = 0.005 \)).

**Relationship between diameter difference of VAs and BA dolichosis**

The patient demographics according to the diameter difference of the VAs are shown in Table 2. The number of patients with hypertension and moderate-to-severe BA curvature was more and more prevalent toward a higher tertile of VA diameter differences. The mean diameter of the right VA gradually decreased into the higher tertile group. The mean WSSs on the right and particularly on the non-dominant VA increased into the higher tertile group of VA diameter differences.
### Table 2. Clinical and hemodynamic characteristics in 91 patients stratified by tertiles according to the diameter difference of VAs

<table>
<thead>
<tr>
<th>Diameter difference of VAs, mm</th>
<th>Low 1/3 (range, 0.04 ~ 0.70)</th>
<th>Middle 1/3 (range, 0.71 ~ 1.17)</th>
<th>High 1/3 (range, 1.19 ~ 2.67)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases</td>
<td>30</td>
<td>30</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Age, year</td>
<td>62.7 ± 13.0</td>
<td>62.5 ± 11.0</td>
<td>66.2 ± 10.4</td>
<td>0.390</td>
</tr>
<tr>
<td>Risk factors, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>17 (56.7)</td>
<td>21 (70.0)</td>
<td>27 (87.1)</td>
<td>0.031*</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>11 (36.7)</td>
<td>14 (46.7)</td>
<td>10 (32.3)</td>
<td>0.497</td>
</tr>
<tr>
<td>Smoking</td>
<td>10 (33.3)</td>
<td>8 (26.7)</td>
<td>12 (40.0)</td>
<td>0.547</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>8 (26.7)</td>
<td>5 (16.7)</td>
<td>5 (16.1)</td>
<td>0.512</td>
</tr>
<tr>
<td>Initial laboratory findings</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>14.3 ± 1.6</td>
<td>13.6 ± 1.5</td>
<td>14.4 ± 1.8</td>
<td>0.166</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>137.7 ± 48.0</td>
<td>171.0 ± 74.1</td>
<td>151.7 ± 67.1</td>
<td>0.138</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>176.0 ± 36.4</td>
<td>171.8 ± 45.8</td>
<td>180.4 ± 41.7</td>
<td>0.984</td>
</tr>
<tr>
<td>C-reactive protein, mg/dL</td>
<td>0.36 ± 0.51</td>
<td>0.80 ± 2.18</td>
<td>0.69 ± 1.49</td>
<td>0.512</td>
</tr>
<tr>
<td>Fibrinogen, mg/dL</td>
<td>314.3 ± 72.6</td>
<td>357.4 ± 88.3</td>
<td>324.9 ± 74.2</td>
<td>0.112</td>
</tr>
<tr>
<td>Radiological findings</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M-to-S BA curvature, n (%)</td>
<td>10 (33.3)</td>
<td>15 (50.0)</td>
<td>23 (74.2)</td>
<td>0.006*</td>
</tr>
<tr>
<td>M-to-S BA elongation, n (%)</td>
<td>4 (13.3)</td>
<td>9 (30.0)</td>
<td>5 (16.1)</td>
<td>0.221</td>
</tr>
<tr>
<td>Mean diameter of BA, mm</td>
<td>3.15 ± 0.58</td>
<td>3.16 ± 0.56</td>
<td>3.27 ± 0.55</td>
<td>0.660</td>
</tr>
<tr>
<td>Mean diameter of R VA, mm</td>
<td>2.29 ± 0.38</td>
<td>1.98 ± 0.56</td>
<td>1.58 ± 0.86</td>
<td>0.001*</td>
</tr>
<tr>
<td>Mean diameter of L VA, mm</td>
<td>2.35 ± 0.60</td>
<td>2.52 ± 0.57</td>
<td>2.53 ± 0.97</td>
<td>0.589</td>
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<tr>
<td>WSS, (dyne/cm²)</td>
<td></td>
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<td></td>
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<tr>
<td>Mean WSS in R VA</td>
<td>7.1 ± 2.0</td>
<td>11.2 ± 7.7</td>
<td>14.0 ± 8.2</td>
<td>0.004*</td>
</tr>
<tr>
<td>Mean WSS in L VA</td>
<td>6.9 ± 2.8</td>
<td>9.1 ± 8.2</td>
<td>8.5 ± 4.4</td>
<td>0.407</td>
</tr>
<tr>
<td>Mean WSS in BA at 80 mm</td>
<td>6.6 ± 4.0</td>
<td>8.3 ± 5.5</td>
<td>8.2 ± 4.0</td>
<td>0.429</td>
</tr>
<tr>
<td>Mean WSS in BA at 90 mm</td>
<td>6.4 ± 5.1</td>
<td>8.5 ± 4.8</td>
<td>8.4 ± 3.8</td>
<td>0.308</td>
</tr>
<tr>
<td>Mean WSS in dominant VA</td>
<td>6.6 ± 2.4</td>
<td>8.1 ± 5.3</td>
<td>6.9 ± 2.6</td>
<td>0.449</td>
</tr>
<tr>
<td>Mean WSS in non-dominant</td>
<td>7.4 ± 2.5</td>
<td>12.3 ± 9.5</td>
<td>15.6 ± 7.5</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

M-to-S = moderate-to-severe; BA = basilar artery; VA = vertebral artery; R = right; L = left; WSS = wall shear stress

*: p < 0.05

Hypertension, older age, and the diameter difference of the VAs were associated with the moderate-to-severe BA curvature in the univariate analysis. After adjusting for all potential variables, only the diameter difference of the VAs remained as an independent predictor of the moderate-to-severe BA curvature in the full multivariate model (OR per 1-mm increase: 2.70, 95% CI: 1.22–5.98; p=0.015). Other hemodynamic variables, such as viscosity, other vessel diameters, WSR, and WSS of vessels, were not significantly associated with the moderate-to-severe BA curvature.
DISCUSSION

We found that pontine infarcts more frequently occurred opposite to the side of BA curvature, and PICA infarcts, more frequent on the non-dominant VA side, and that the difference in the diameters of the right and left VA was the only independent predictor for moderate-to-severe BA curvature. Hence, the present study suggested that the asymmetrical flow pattern of VAs around the vertebrobilar junction might be an important mechanical force of the origin of BA curvature as well as a causing factor of peri-vertebrobasilar junctional infarcts (i.e. pontine and PICA infarcts).

In this study, the VA diameter was significantly larger on the left than the right side which was consistent with numerous previous reports.\textsuperscript{7, 13, 14} Traditionally, most physicians have regarded an asymmetric VA as a congenital variant or a clinically meaningless finding, unless vertebrobasilar insufficiency occurs.\textsuperscript{15, 16} However, recent studies have regarded VA hypoplasia as a risk factor for posterior circulation stroke, and that its directional association with a stroke had an ipsilateral tendency to VA hypoplasia.\textsuperscript{13, 17-19} Interestingly, we found that a specific stroke (i.e. pontine infarction) had a tendency to the opposite side to the lateral displacement of the BA as well. Also, the curvature of the BA was directionally opposite to the dominant VA.

Vertebrobasilar dolichoectasia is anatomically well-known and appears to be postulated as a risk factor for posterior circulation stroke.\textsuperscript{20-22} Currently, a study reported on the directional relationship between vertebrobasilar dolichoectasia and the specific locations of infarcts in the vertebrobasilar system, that is, 58% of the patients (11/19) had pontine or cerebellar lesions (superior and anterior cerebellar lesions) contralateral to the lateral displacement of the BA versus ipsilateral in 26% of the patients (5/19).\textsuperscript{20} A recent study on consecutive series of cerebellar infarcts showed that cerebellar infarcts at the post-vertebrobasilar-junction (AICA and SCA territory) were more common in the left side. This study also indicated that there was the right predilection involvement at the pre-vertebrobasilar junction (PICA territory) and the left predilection at the post-vertebrobasilar junction (SCA territory) even in patients with combined involvements of cerebellar arterial territories.\textsuperscript{23} For this reasons, our findings may provide more evidence that the specific location of infarcts is closely connected to the BA curvature or VA hypoplasia.

Such directional relationships can be explained by several hemodynamic mechanisms. First, the inner wall of BA curvature may be more thrombogenic because of a low WSS \textsuperscript{4, 24} and traction of the pontine perforators caused by the BA curvature may lead to infarction.\textsuperscript{20} Second, a hypoplastic VA can cause ipsilateral PICA infarction by directly decreasing the blood flow in the smaller intracranial VA.\textsuperscript{24} This can occur due to the easy collapsibility of a narrowed vessel because of Bernoulli’s effect under the decreased VA remodeling capacity.\textsuperscript{25} Our theory is outlined in Figure 3. The vector of BA flow merging from unequal VAs makes the BA flow curve to the side of the weaker VA, and the chronic processes caused by asymmetric VA flow can induce greater curving the BA wall. Subsequently, such deformation of the BA can cause atherogenesis, leading to ischemic stroke in the vertebrobasilar system. A hypoplastic VA can also result in the ipsilateral occlusion of this vessel due to a direct decrease in the blood flow, and easy collapse of the vessel caused by the smaller intracranial VA caliber.

The diameter difference of the VAs was the only independent predictor for the moderate-to-severe BA dolichosis even after adjusting for confounding variables (demographics, radiological variables, and hemodynamic variables). In general, the
flow rate is proportional to the fourth power of the vessel radius according to Poiseuille's law. Therefore, the radius of the vessel is the most essential determinant of blood flow even in the vertebrobasilar system. Pressure, blood flow, or both factors are widely recognized as potential stimuli for morphological change or the functional adaptation of vessels. Numerous studies have examined flow-dependent remodeling, and if such hemodynamic forces are altered chronically, a subsequent morphological or structural adaptation of the artery can occur to minimize the effect of the altered hemodynamic forces on the vascular wall, including changes in caliber and wall thickness.

Our study has several limitations. We investigated the values of WSSs using the pulsed-Doppler sonography. Although it is a simple, easy, and non-invasive way for the assessment of WSS, it can be technically limited as it is unable to visualize the vessel and also has angle correction problem. Additionally, it is necessary to assume a linear velocity distribution of the flow with the central peak velocity to measure the wall shear rate. In future studies, an accurate and timely measurement of WSS with the good spatial resolution should be utilized. Further research involving vessel remodeling mediators, such as matrix metalloproteinases (MMPs) and nitric oxide (NO), suggesting a role for vascular adaptation, is needed to assess the regulatory aspects of the vessel in response to the flow-related mechanical forces.

In conclusion, this study suggests that unequal blood flow from bilateral VAs is a significant hemodynamic contributor to BA curvature. Moreover, it is a potential determinant for the development of acute infarcts around the vertebrobasilar junction.
Acknowledgements

Completing Interests
   All authors declare that they have nothing to declare.

Funding
   None

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Legends of figures

**Figure 1.** Overlapping contour maps of peri-vertebrobasilar junctional infarcts. Paramedian region of the left mid-pons was the most affected site for post-vertebrobasilar junctional infarcts (*i.e.* pontine infarcts), whereas the right inferior medial region in the cerebellum was the most affected site for the ischemic infarcts around pre-vertebrobasilar junction (*i.e.* PICA infarcts).

BA=basilar artery, VA=vertebral artery.

**Figure 2.** Directional relationships according to BA angulation, VA dominancy, and peri-vertebral junctional infarcts (*i.e.* pontine and PICA infarcts).

BA=basilar artery, VA=vertebral artery, PICA=posterior inferior cerebellar artery

**Figure 3.** Schematic illustrations of the pathophysiologic process of peri-vertebral junctional infarcts: possible changes of vetebrobasilar vessels under the condition of an unequal VA flow.
REFERENCES


A 46-year-old male with the left lateral medullary infarction caused by cardioembolic mechanism was admitted in 1998. The BA is shown as a straight nature on MRA (A). Nine years later, the BA is curved to the left side (B).
• **BA angulation**
  - BA curvature of grade ≥ 1; (n=89, 97.8%)
  - BA curvature of grade ≥ 2; (n=48, 52.7%)
  - BA elongation of grade ≥ 2; (n=18, 19.8%)

• **PICA infarcts**
  - 72.7% is located in non-dominant VA side (32/44; \( p=0.005 \))

• **Pontine infarcts**
  - 72.3% is located in the opposite side of BA curvature (34/47; \( p=0.002 \))

• **Dominant VA**
  - 69.2% is located in the left VA side (63/91; \( p<0.001 \))
  - Patients having dominant VA is opposite to BA curvature are 83.5% (76/91; \( p<0.001 \))
Stage 1
- Congenitally asymmetric flow of VAs with straight BA

Stage 2
- Curving or elongation of BA caused by asymmetric wall tension
- Non-dominant VA can lead to be narrower due to direct decrease of flow or easy collapse by Bernoulli’s effect under the condition of decreased vascular remodeling capacity

Stage 3
- Eventually, pre-junctional infarctions in non-dominant VA side, and post-junctional infarctions frequently occur in opposite site to the BA curvature (eq. more thrombogenic at the inner bending portion of BA or traction of pontine perforators)
Vertebral Artery Dominance Contributes To Basilar Artery Curvature and Peri-vertebrobasilar Junctional Infarcts
Ji Man Hong, Chin-Sang Chung, Oh Young Bang, In Soo Joo and Kyoon Huh

*J Neurol Neurosurg Psychiatry* published online May 3, 2009

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