Geometric Analysis and Blood Flow Simulation of Basilar Artery

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Aim: The aim of this study was to find a region of low wall shear stress (WSS) in a basilar artery using 3-dimensional (3D) geometric analysis and blood flow simulation.

Methods: A 61-year-old patient who underwent follow-up time-of-flight magnetic resonance angiography (TOF-MRA) of the brain was recruited as the subject of the present study. In the basilar artery, the angle of the directional vector was calculated for the region of low WSS. The subject’s 3D arterial geometry and blood flow velocity from a transcranial Doppler examination were used for a blood flow simulation study. The regions of low WSS identified by both geometric analysis and blood flow simulation were compared, and these methods were repeated for the basilar arteries of various geometries from other patients.

Results: Two distinct arterial angulations along the basilar artery were identified: lateral and anterior angulations on the anteroposterior and lateral TOF-MR views, respectively. A low WSS region was observed in the distal portion along the inner curvatures of both angulations in the basilar artery. The directional vectors of the region of low WSS calculated by geometric analysis and blood flow simulation were very similar (correlation coefficient = 0.996, \( p < 0.001 \)). Follow-up MRA confirmed the progression of plaque in the region of low WSS.

Conclusion: Detailed geometric analysis and blood flow simulation of the basilar artery identified lateral and anterior angulations which determined the low WSS region in the distal portion along the inner curvatures of the angulations.


Key words: Wall shear stress, Basilar artery, Angulations, Geometric analysis, Blood flow simulation

Introduction

Atherothrombotic diseases have become a leading cause of disability and mortality in both industrialized and developing countries. Vascular risk factors such as hypertension, type 2 diabetes mellitus (DM), and hypercholesterolemia are known to be highly prevalent, even in young populations. To correct vascular risk factors, therapeutic interventions, including medications and lifestyle modifications, should be performed appropriately. In addition, atherosclerotic progression in individual patients should be carefully monitored because thromboembolic events could occur on top of atherosclerotic plaque.

Localized atherosclerotic involvements are seen in such regions as the outer walls of branch sites and inner aspects of arterial curvatures. These areas are known to be where wall shear stress (WSS) is chronically low or oscillatory. WSS is a frictional force caused by blood flow acting tangentially on the endothelium. Local arterial geometric features and the characteristics of blood flow (laminar or disturbed) are important determinants of WSS. A region of low WSS with blood flow alterations, combined with vascular risk factors, can activate subsequent inflammatory cascades.

The vertebrobasilar artery is a unique arterial network where two vertebral arteries converge into the
basilar artery, which then divides bilaterally into several arteries. Basilar artery atherothrombosis can lead to infarction of the brainstem (and/or cerebellum), which comprises about 20% of all ischemic strokes. ⁷, ⁸ Although strokes involving the basilar artery and its territories occur frequently, little information has been available on basilar artery geometry and hemodynamics. There have been reports on variations in the configuration of the vertebrobasilar junction and on the curvature of the basilar artery in association with the predominance of the vertebral artery. To improve the understanding of hemodynamics in the posterior circulation vessels, the geometric features of the basilar artery and its mechanical stresses such as WSS should be analyzed in detail. In the present study, the authors aimed to define WSS distribution of the basilar artery using both geometric analysis and blood flow simulation. For this purpose, the authors presented a simple method of geometric analysis of the basilar artery using magnetic resonance (MR) angiography to predict regions of low WSS, performed blood flow simulations using patients’ arterial geometry and blood flow velocity, and compared the results.

Subjects and Methods

Case Study

A 61-year-old male patient with a recurrent history of non-spinning dizziness and mild headache diagnosed as vertebrobasilar insufficiency (VBI) was chosen for the present hemodynamic and geometric study. The patient underwent follow-up brain magnetic resonance imaging (MRI) and time-of-flight (TOF)-MR angiography at Chonbuk National University Hospital. The imaging parameters for the TOF-MR angiographic scan were: repetition time (TR)/echo time (TE)=25/3.45 ms; flip angle=20°; field of view (FOV)=197×249 mm; matrix size=416×208; sensitivity encoding (SENSE) factor=2.5; slice thickness=0.50 mm; and number of average (NEX)=1. The TOF-MR angiography scan time was 4 min. Follow-up brain TOF-MR angiography was performed 1622 days after the initial examination. The follow-up MR angiography of the basilar artery was overlaid on the initial angiography after the registration of spots such as the points of arterial branching for analysis of geometric changes. The patient had no acute ischemic lesions along the brainstem when both MR angiographies were examined. He had hypertension, type 2 diabetes mellitus (DM), and hypercholesterolemia, and was receiving medications for these risk factors. This study was performed with the approval of the institutional ethics committee, and all participating patients gave written informed consent for participation in this study at the time of transcranial Doppler (TCD) examination.

Geometric Analysis to Determine the Region of Low WSS in a Basilar Artery (Using MR Angiography)

Two-dimensional axial images of the vertebrobasilar artery obtained by MR angiography were used to reconstruct 3D arterial geometry with our own inhouse code of a modified marching-cube algorithm. The directional vectors of the proximal and distal portions of the basilar artery from the center of angulation were defined as follows (Fig. 1A and C):

Proximal segment of the basilar artery:

\[ n_p = a_p \cdot \sin(\theta) + b_p \cdot \cos(\theta) + c_p \cdot \tan(\theta) \] ①

Distal segment of the basilar artery:

\[ n_d = a_d \cdot \sin(\theta) + b_d \cdot \cos(\theta) + c_d \cdot \tan(\theta) \] ②

Subscript \( p \) represents the proximal portion of the basilar artery from the angulation point, and subscript \( d \) represents the distal portion of the artery.

To obtain the coefficients of directional vectors for the basilar artery, the arterial angulations were designated as follows: from the antero-posterior (AP) view, the lateral proximal angulation \( \theta_{Lat,p} \) and the lateral distal angulation \( \theta_{Lat,d} \) and from the lateral view, the anterior proximal angulation \( \theta_{Ant,p} \) and the anterior distal angulation \( \theta_{Ant,d} \) (shown in Fig. 1B and D). Subscript \( Lat \) represents the lateral angulation from the AP view, and \( Ant \) represents the anterior angulation from the lateral view.

The relationships between the angulations and the coefficients of directional vectors in the basilar artery can be described using the tangent functions as follows:

Proximal segment:

\[ \theta_{Lat,p} = \tan^{-1}(a_p/c_p), \quad \theta_{Ant,p} = \tan^{-1}(b_p/c_p) \] ③

Distal segment:

\[ \theta_{Lat,d} = \tan^{-1}(a_d/c_d), \quad \theta_{Ant,d} = \tan^{-1}(b_d/c_d) \] ④

From Equation (3), the directional vector for the proximal segment of the basilar artery can be calculated using the definitions of the arterial angulations:

\[ a_p = c_p \cdot \tan(\theta_{Lat,p}), \quad b_p = c_p \cdot \tan(\theta_{Ant,p}), \quad c_p = \frac{1}{\sqrt{\tan^2(\theta_{Lat,p}) + \tan^2(\theta_{Ant,p}) + 1}} \] ⑤

By the inertial effect of blood passing through the angulated portion of basilar artery, the region of low WSS was assumed to be located in the distal portion of the inner curvatures of both angulations. With
where, $u$ denotes the velocity vector in Cartesian coordinates, $p$ denotes pressure, $\rho$ denotes density, $\mu$ denotes dynamic viscosity, and $g$ denotes the gravity vector. The properties of blood for this present simulation were set as follows: density $\rho = 1,004$ kg/m$^3$ and dynamic viscosity $\mu = 3.5$ cP. Computational meshes for basilar arterial geometry were generated on 3D reconstructed data from 2D MR angiographic images\(^1\).

For the condition of the inlet, curve-fitted pulse waveforms were applied to the right and left vertebral arteries using values from the transcranial Doppler examination. The arterial wall was assumed to be rigid without compliance. A grid density sensitivity test was performed using various grid base sizes ranging from 0.08 to 0.16 mm, because the numerical results depended on the computational grid density. For analysis, a computational grid with a base size of 0.10 mm was adopted for all the computations in this study. The total numbers of computational grids were about 300,000. The time to perform blood flow simulation over 5 cardiac cycles, using 1 CPU of a Linux server with a 2.4 GHz AMD Opteron 64-bit processor, was about 3 days.

The WSS ($\tau_w$) could be calculated as follows:
metric analysis, using lateral and anterior angulations of the artery from AP and the lateral view of MR angiography, respectively and 2) blood flow simulation, using the patients’ own arterial geometry and blood flow velocity. To see whether the results of geometric analysis coincided well with those of blood flow simulation, four more subjects who showed no ischemic lesions in the brainstem were studied. Information was obtained, including the past medical history, vascular risk factors, and medications.

**Statistical Analysis**

Peak-systolic velocities (cm/sec) in both vertebral arteries are presented. The correlation between the results of geometric analysis and blood flow simulation for the region of low WSS was calculated using Spearman’s rank correlation test. The values of TAWSS were compared using Wilcoxon’s rank sum test. Statistical significance was set at $p < 0.05$.

**Results**

**Case Study for the Region of Low WSS in the Basilar Artery**

The patient had right lateral (9°) and anterior (16°) angulations in the basilar artery, as shown in Fig. 1. Geometric analysis using the directional vectors

$$\tau_w = \mu (\nabla u + \nabla u^T) \cdot n_w - \mu |(\nabla u + \nabla u^T) \cdot n_w| \cdot n_w \quad (10)$$

where $n_w$ represents the normal vector of a blood vessel. The time-averaged wall shear stress (TAWSS, $\tau_{aw}$) was obtained by averaging the WSS during the cardiac cycle as follows:

$$\tau_{aw} = \frac{1}{T} \int_0^T |\tau_w| dt \quad (11)$$

where $T$ represents the duration of time of the cardiac cycle.

**Transcranial Doppler (TCD) Examination**

The blood flow velocities of both the right and left vertebral arteries and the basilar artery were measured using a SONARA/tek 5.18B with a 2 MHz probe, as reported previously. Blood flow velocities, such as the peak-systolic velocity and end-diastolic velocity, were measured in both vertebral arteries along entire segments, as recommended. For this simulation study, the velocities and pulse wave forms at the nearest point from the inlet conditions were selected and used.

**Case Series Study**

As described above, the region of low WSS in the basilar artery was defined with two methods: 1) geometric analysis, using lateral and anterior angulations of the artery from AP and the lateral view of MR angiography, respectively and 2) blood flow simulation, using the patients’ own arterial geometry and blood flow velocity. To see whether the results of geometric analysis coincided well with those of blood flow simulation, four more subjects who showed no ischemic lesions in the brainstem were studied. Information was obtained, including the past medical history, vascular risk factors, and medications.
401

Geometric Analysis and Simulation of Basilar Artery

62° of the directional vector from the equatorial line as predicted in the initial MR angiography (Fig.3B-D).

Case Series Study

The arterial angulations for the proximal and distal segments of the basilar artery and the peak systolic velocity in the right and left vertebral arteries are presented in Table 1. Two subjects (I and II) had right lateral angulations and the others (III and IV) had left lateral angulations, and all had anterior angulations of varying degrees. The directional vectors of the regions of low WSS from both geometric analyses and blood flow simulations, and the exact values of TAWSS in the representative locations are presented in Fig.4.

Differences in the directional vectors for the regions of low WSS between the two methods used in the of both the anterior and lateral angulations estimated that the region of low WSS was approximately 61.7° from the equatorial line of the left lateral axis in the distal segment of the basilar artery (Fig.2A). Blood flow simulation analysis indicated that low TAWSS (TAWSSlow, 3.40 dyne/cm²) was located at 62.0° (Fig.2B), which is very similar to the estimation by geometric analysis. Higher TAWSS values were obtained from the opposite side in the distal segment of the basilar artery (TAWSA, 45.5 dyne/cm²) and the inner curvature before the angulation (TAWSSb, 97.55 dyne/cm²).

Follow-up brain MR angiography performed 1622 days after the initial examination revealed atherosclerotic progression in the distal segment of the basilar artery (Fig.3A). The progression of atherosclerotic plaque along the basilar artery was seen around

Table 1. Arterial geometry and blood flow velocity

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Arterial angulations (°)</th>
<th>TAMFV (cm/s)</th>
<th>Major risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>θ_{Lat,p}</td>
<td>θ_{Lat,d}</td>
<td>θ_{Ant,p}</td>
</tr>
<tr>
<td>Case I</td>
<td>62</td>
<td>M</td>
<td>170</td>
<td>1</td>
</tr>
<tr>
<td>Case series (Fig.4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>60</td>
<td>F</td>
<td>177</td>
<td>1</td>
</tr>
<tr>
<td>III</td>
<td>59</td>
<td>F</td>
<td>155</td>
<td>3</td>
</tr>
<tr>
<td>IV</td>
<td>63</td>
<td>M</td>
<td>177</td>
<td>8</td>
</tr>
<tr>
<td>V</td>
<td>49</td>
<td>M</td>
<td>198</td>
<td>17</td>
</tr>
</tbody>
</table>

TAMFV, time-averaged mean flow velocity; VA, vertebral artery; HTN, hypertension; DM, diabetes mellitus; HChol, hypercholesterolemia.
Fig. 4. Blood flow simulations of basilar arteries for the case series study. The angles of the region of low WSS determined by geometric analyses and blood flow simulations are shown below the figure, along with representative TAWSS values.
five subjects ranged from 0.1 (Fig. 4B) to 3.1 (Fig. 4D), resulting in a correlation coefficient of 0.996 ($p < 0.001$). The TAWSS values were significantly lower in the regions of low WSS (median, 3.49 dynes/cm$^2$; range, 2.34-6.88 dynes/cm$^2$) than the two other regions (opposite side of the distal segment, TAWSS; median, 22.46 dynes/cm$^2$; range, 17.24-45.5 dynes/cm$^2$; $p = 0.043$; and the inner curvature before the angulation, TAWSS; median, 27.48 dynes/cm$^2$; range, 21.81-97.55 dynes/cm$^2$; $p = 0.043$).

**Discussion**

In the present study, we identified two distinct arterial angulations along the basilar artery: lateral and anterior angulations seen on the antero-posterior and lateral views, respectively. The region of low WSS could be localized precisely in the distal segment of the inner curvatures of the basilar artery using both the lateral and anterior angulations. The exact localization of the region of low WSS was confirmed by blood flow simulation using the subjects’ arterial geometry and hemodynamic information. In the follow-up MR angiography, atherosclerotic progression was observed in the region of low WSS, which was defined in the former examination.

The regions of low WSS in the distal segment from the angulated portion of the basilar artery were reported for the first time in the present study, although the vertebrobasilar junction and the lateral angulation of the basilar artery have been reported previously. Brainstem infarction occurred significantly more on the side of the lesser curvature of the lateral angulation of the basilar artery, suggesting the higher propensity of atherothrombosis. When the basilar artery was largely angulated laterally, the angle of the directional vector for the region of low WSS might be close to 0° or 180° (along the lesser curvature of the lateral angulation), which might be a good explanation for the association between the low WSS region and the higher occurrence of brainstem infarction affecting that side; however, when the basilar artery was angulated anteriorly, as shown in Fig. 1 and 4A, C, and D, the angle of the directional vector for the low WSS was displaced to around 90°. This might explain the occurrence of brainstem infarction around the fourth ventricle where there was no direct arterial supply, except the penetrating artery from the basilar artery.

The basilar artery seems to have two angulations naturally between the confluence of the vertebral arteries proximally and the division of the basilar artery distally. The lateral angulation (from the AP view) of the basilar artery has been reported to be associated with the asymmetries of the diameters and flow volumes of the vertebral arteries, and the asymmetry of vertebral artery has been also known to be associated with increased rates of brainstem stroke on the side of the hypoplastic artery. The anterior angulation of the basilar artery, when viewed laterally, could be found easily: the two vertebral arteries extend anteriorly in the intracranial portion, wrapping laterally around the distal portion of the brainstem and merge as the basilar artery, usually anterior to the pons. The basilar artery then divides into two posterior cerebral arteries, which extend posteriorly, wrapping around the midbrain. All of the subjects in the present study showed anterior angulations of the basilar artery with varying degrees, as shown in Fig. 4.

Along the arterial tree, regions of low WSS have been seen at certain specific sites, such as the outer walls of branches and portions of the bulb where blood flow is affected by inertial forces and blood flow stasis develops. Using detailed arterial geometric analysis of the carotid artery, a previous study showed that tortuosity of the carotid bifurcation could be a surrogate marker of low or oscillatory WSS. In this study, as proposed by Equation 7, there were two essential geometric components in the basilar artery, the lateral and anterior angulations that predicted a region of low WSS. As an emerging biomarker of atherosclerosis and its evolution (plaque growth, rupture, and thrombosis), WSS is a very important blood flow parameter. A mechanosensory complex, composed of platelet endothelial cell adhesion molecule (PECAM-1 or CD31), vascular endothelial cell cadherin, and vascular endothelial growth factor receptor 2 (VEGFR-2), has been reported to confer responsiveness to shear stress and activate integrins. With disturbed blood flow, where the magnitude of flow is very low or the direction is continually changing, the pathways function in a sustained manner to activate NF-κB. If the region of low WSS is affected by combined vascular risk factors, inflammatory molecules such as adhesion molecules, E-selectin, and platelet-derived growth factor (PDGF) may be expressed.

As part of translational research on arterial hemodynamics, blood flow simulation can provide detailed hemodynamic information, such as WSS, as well as on the effects of various interventions. For this simulation study of vertebrobasilar arteries, information on the arterial geometry (MR angiography) of each subject and flow-dynamic data (transcranial Doppler) were used to develop a more realistic hemodynamic simulation study than has been previously performed. The region of low WSS in the basilar artery corre-
sponded to the subsequent plaque growth seen in follow-up MR angiography, supporting the hypothesis that the region of low WSS is prone to atherosclerotic evolution.

To obtain blood flow velocities and pulse wave forms, transcranial Doppler was used in this study. Transcranial Doppler has been used as an application of computational fluid dynamics because it can provide a detailed pulse wave form and blood flow velocity for each heart beat. Although the pulse wave form and flow velocity can differ among individuals, there have been very few studies using patient-specific flow data. For more precise calculation of the TAWSS value, the pulse wave form of each patient should be used in addition to the subject’s own arterial geometry.

The present study has some limitations. First, it did not demonstrate a direct association between plaque growth in the region of low WSS in the basilar artery and brainstem infarction, although atherosclerotic plaque burden is known to be associated with increased long-term mortality. Plaque progression can also lead to increased flow disturbance, resulting in plaque rupture or erosion. Second, the geometric analysis in this study could not provide information on how far distally the region of low WSS was located from the center of the angulations, but only indicated the angle of the directional vectors from the equatorial line of the left axis. Finally, blood was assumed to have Newtonian features of viscosity as a constant value (3.5 cP). In the low WSS region, the values of WSS might be lower with a constant value of blood viscosity than with non-Newtonian characteristics of blood viscosity.

Conclusion

The present study demonstrated that the basilar artery had anterior and lateral angulations that determined the low WSS region in the distal portion along the inner curvatures of the angulations. Follow-up brain MR angiography in the subject confirmed that atherosclerotic plaque in the basilar artery had progressed in the region of low WSS.

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Author Contributions

SHL performed numerical analyses and reviewed the manuscript. NH participated in numerical analyses and reviewed the manuscript. SKJ performed numerical analyses, drafted, and reviewed the manuscript. All authors read and approved the final manuscript.

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Conflicts of Interest

None declared.

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