Modeling the circle of Willis to assess the effect of anatomical variations on the development of unilateral internal carotid artery stenosis

Chi Zhang, Ling Wang, Xiaoyun Li, Shuyu Li, Fang Pu, Yubo Fan, and Deyu Li

Abstract. Circle of Willis (CoW) plays a significant role in maintaining the blood supply for the brain. Specifically, when the stenosis occurs in the internal carotid artery (ICA), abnormal structures of CoW would decrease the compensatory capacity, leading to the local insufficiency of cerebral blood supply. The present paper built a series of lumped parameter models for CoW, and simulated the blood redistribution caused by the unilateral ICA stenosis with different severities in cerebral arteries in the normal and abnormal CoW respectively. The results showed that when unilateral ICA stenosis occurred, the collateral circulation was built through the anterior communicating artery and the ipsilateral posterior communicating artery, maintaining the flow in cerebral arteries. The absence of the two communicating arteries would cause an obvious decrease of flow in local cerebral arteries in the anterior circulation. In conclusion, the two arteries play a significant role in maintaining the balance of cerebral blood supply in the development of ICA stenosis.

Keywords: Circle of Willis, internal carotid artery, stenosis, anatomical variation, lumped parameter model

1. Introduction

Circle of Willis (CoW) plays a pivotal role in preventing the stroke caused by cerebral ischemia, because the collateral circulation of CoW can maintain sufficient and stable blood supply for the brain. CoW consists of a network of cerebral arteries, with the function of autoregulation when the inflow of CoW fluctuates or decreases. The blood is delivered to the brain through the two internal carotid arteries (ICAs) and the basilar artery (BA). Each ICA bifurcates into a middle cerebral artery (MCA)

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1 This study was supported by the National Key Technology R & D Program (2012BAI19B04), National Natural Science Foundation of China (No. 61190122) and the grant from the State Key Laboratory of Virtual Reality Technology and Systems, Beihang University.

*Corresponding author: Deyu LI, Email: deyuli@buaa.edu.cn*
and an anterior cerebral artery (ACA) to perfuse the temporal, parietal and frontal regions of the brain (anterior circulation). BA is divided into the left and right posterior cerebral arteries (PCAs), to deliver blood to the regions of the brain stem (posterior circulation). Two ACAs are interconnected by the anterior communicating artery (ACoA). The anterior and posterior circulations are linked by two posterior communicating arteries (PCoAs). The ring-like structure is considered as a safeguard mechanism against cerebral arterial stenosis or occlusion.

Unfortunately, the normal structure of CoW is relatively uncommon. Plenty of clinical studies found that generally only a half of human beings have the normal CoW structures [2, 15]. Though there is no evidence that the variation of CoW structure is correlated with the race and region, it has been proposed that the variation is associated with some vascular diseases [4, 16]. The anatomical variations reduce the collateral availability and increase the risk for stroke and transient ischemia attack (TIA) [12]. The investigation on the morphological variations and the change of the compensatory capacity of CoW has significant implications for understanding the mechanism of stroke and for planning the intracranial neurosurgery or vascular surgery [6, 13].

ICA, as an important pathway for cerebral blood supply, is found a preferred site for stenosis in Chinese people [14, 24]. The ICA stenosis is proved to be closely associated with stroke and TIA [7, 20]. Beyond all doubt, the anatomical variation of CoW plays a significant role in the mechanism of stroke induced by the ICA stenosis. Several mathematical studies have been conducted to investigate the change of compensatory capability of CoW caused by the anatomical variations [5, 11, 21, 23]. They showed that the compensatory ability of the normal CoW could maintain the required efferent flow rates in case of an occlusion of an ICA. Although they also pointed out the worst variation of CoW when an ICA was occluded, the process of blood redistribution in CoW was not fully revealed in the development of ICA stenosis.

Accordingly, the present study focuses on the establishment of collateral circulation in the development of unilateral stenosis based on the lumped parameter model of CoW with anatomical variations. The aim is to investigate how the collateral circulation works in the CoW when the severity of ICA stenosis increases.

2. Methods

2.1. Mathematical model

The mathematical model is based on the linear, 1D equations of pressure and flow wave propagation in a compliant vessel, which is analogous to an electric component shown in Fig. 1 [12]. The governing equations result from conservation of mass and momentum applied to a 1D impermeable tubular control volume of incompressible and Newtonian fluid, which take the form:

\[ C_i \frac{dP_i}{dt} = Q_i - Q_o \]  \hfill (1)

\[ L \frac{dQ_i}{dt} = P_i - P_o - Q_i R \]  \hfill (2)

where \( Q_i \) and \( Q_o \) are inflow and outflow of the vessel, respectively; \( P_i \) and \( P_o \) are blood pressures upstream and downstream the vessel, respectively. The resistance, inertia of the blood flow, and the
compliance of the vessel are represented as R, L, and C respectively. The value of R, L, and C are calculated using equations based on the geometrical data [3,18]:

\[
R = \frac{8\mu l}{\pi r^4} \quad (3)
\]
\[
L = \frac{9\rho l}{4\pi r^2} \quad (4)
\]
\[
C = \frac{3\pi r^3}{2Eh} \quad (5)
\]

where \(l\), \(r\) and \(h\) represent the length, radius and thickness of the vessel, respectively; \(E\) is the elastic parameter of the vascular; \(\rho\) is the blood density; \(\mu\) is the viscosity of the blood. The values of \(\rho\) and \(\mu\) are set as 1.06 g/ml and 0.004 Pa*s respectively in this study.

In order to investigate the compensatory ability of CoW, 4 lumped parameter models of CoW were constructed based on the governing equations (Fig. 2). Model A was a normal CoW while model B and C were an abnormal CoW with the absence of ACoA or unilateral PCoA respectively. ACoA and one PCoA were absent simultaneously in Model D.

![Fig. 1. Electric circuit analogy of a blood vessel. The flow rate through the vessel was defined as Q (ml/s). The blood pressures in the vessel was defined as P (mmHg). Resistors were denoted by R (mmHg•s/ml), while capacitors and inductances by C (ml/mmHg) and L (mmHg•s²/ml), respectively.](image)

![Fig. 2. The model of CoW. A, a normal case; B, a case without ACoA; C, a case without left PCoA; D, a case without ACoA and left PCoA at the same time.](image)

2.2. Physiological data

The geometric and physiological data of the vessels in CoW were listed in Table 1. The data, aiming at healthy young adults, were referred to the reports by Fahrig et al [9]. To simulate the unilateral stenosis in ICA, the geometric data of ICA was changed according to the severity of the stenosis. The severity of the stenosis (\(\beta\)) was defined as the percentage reduction of cross-section in the obstructed vessels:
\[ \beta = \left(1 - \frac{A_s}{A_0}\right) \times 100\% \]  

(6)

where \(A_s\) and \(A_0\) were the cross-section area of the artery after and before the stenosis respectively. For each model, the collateral circulation in CoW was simulated with the stenosis degree from 0\% to 90\% in the left ICA.

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Table 1

<table>
<thead>
<tr>
<th>Arterial segment</th>
<th>Code*</th>
<th>Length (cm)</th>
<th>Radius (cm)</th>
<th>Thickness (cm)</th>
<th>Elastic modulus (10^6 Pa)</th>
<th>Peripheral resistance (mmHg s/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICA</td>
<td>0102, 1011</td>
<td>17.7</td>
<td>0.200</td>
<td>0.050</td>
<td>0.8</td>
<td>--</td>
</tr>
<tr>
<td>BA</td>
<td>0304</td>
<td>2.9</td>
<td>0.162</td>
<td>0.040</td>
<td>1.6</td>
<td>--</td>
</tr>
<tr>
<td>MCA</td>
<td>0209, 1116</td>
<td>11.9</td>
<td>0.143</td>
<td>0.036</td>
<td>1.6</td>
<td>22.4</td>
</tr>
<tr>
<td>ACA1</td>
<td>0207, 1114</td>
<td>1.2</td>
<td>0.117</td>
<td>0.029</td>
<td>1.6</td>
<td>--</td>
</tr>
<tr>
<td>ACA2</td>
<td>0708, 1415</td>
<td>10.3</td>
<td>0.120</td>
<td>0.030</td>
<td>1.6</td>
<td>43.7</td>
</tr>
<tr>
<td>PCA1</td>
<td>0405, 0412</td>
<td>0.5</td>
<td>0.107</td>
<td>0.027</td>
<td>1.6</td>
<td>--</td>
</tr>
<tr>
<td>PCA2</td>
<td>0506, 1213</td>
<td>8.6</td>
<td>0.105</td>
<td>0.026</td>
<td>1.6</td>
<td>29.1</td>
</tr>
<tr>
<td>ACoA</td>
<td>0714</td>
<td>0.3</td>
<td>0.074</td>
<td>0.019</td>
<td>1.6</td>
<td>--</td>
</tr>
<tr>
<td>PCoA</td>
<td>0502, 1211</td>
<td>1.5</td>
<td>0.073</td>
<td>0.018</td>
<td>1.6</td>
<td>--</td>
</tr>
</tbody>
</table>

* The codes represented the arteries shown in Fig. 2.

The input boundary condition for CoW models was set as the blood pressure at the beginning of ICA and VA shown in Fig. 3, when ICA was not constricted [8]. The cardiac cycle was set as 0.8s. The blood flow through the contralateral ICA and BA was assumed to be constant when the stenosis occurred in left ICA. The fourth-order Runge-Kutta algorithm was used to solve the differential equations of the CoW models. The calculation was performed for 5 cycles. The data of the last cycle was considered as the simulation results to make sure the convergence of the calculation. The blood flow in each artery simulated by Model A without stenosis was compared with the data measured by Transcranial Doppler (TCD), to validate the accuracy of the model. The TCD measurement was performed on a healthy adult female. Since TCD could only provide the velocity information of flow, the data was integrated over the area of the artery to calculate the flow rate.

Fig. 3. The input pressure wave at ICA and BA.
3. Results

The results for the blood pressure and flow pulses in the arterials of CoW in Model A without any stenosis were shown in Fig. 4, comparable to the published reports [21]. The results were compared with the data from TCD measurement shown in Fig. 5, indicating that the simulation results were consistent with the clinical data.

Fig. 4. The blood pressure (right side) and flow rate (left side) in the arteries of CoW in Model A. The results in only half arteries were shown, since the model was symmetric. The abscissa ranged from \( t=0 \) to \( t=0.8 \text{s} \) (one full cardiac cycle). The ordinate ranged from 60 to 120 mmHg (for blood pressure) or from 0 to 8 ml/s (for flow rate).

Fig. 5. The comparance between the simulation results and the clinical data measured by TCD in left ACA, MCA, and PCA. Left: the flow rate of simulation results in arteries. Right: the flow rate calculated with the clinical data from TCD measurement.

Since the model was validated, the compensatory capacity were evaluated between the 4 models with the different stenosis degrees in ICA (Fig. 6). For each model, the flow rate in the left ICA decreased gradually to 1% of that in the normal case (without stenosis), as the stenosis degree increased to 90%. In Model A, the decrease of the flow rate in the ipsilateral ACA, MCA, and PCA was slow, because that the collateral circulation was built through ACoA and PCoAs. The flow rate in the ipsilateral PCoA and ACoA increased significantly, as the stenosis degree increased, indicating that they played a significant role in the establishment of collateral circulation (Figure 7).
Fig. 6. The decrease of the flow rate in ACA, MCA, and PCA with the stenosis degree increasing from 0% to 90% in ICA. The flow rate in the ipsilateral ACA, MCA, and PCA was shown in the left column (a, c, and e respectively); while the contralateral arteries was in the right (b, d, and f respectively).

Fig. 7. The change of flow rate in communicating arteries.
In Model B and C, the decrease of flow rate became faster, because the ipsilateral PCoA or ACoA was absent in the model, which diminished the compensatory ability of CoW. In Model D, the flow rate in the ipsilateral ACA and MCA decreased dramatically, because of the simultaneous absence of the ipsilateral PCoA and ACoA. The flow rate decreased to nearly 0 when ICA stenosis degree increased to 90%, implying that the cerebral blood supply was severely insufficient, and the risk for stroke was extremely elevated.

4. Discussion and Conclusion

Lumped parameter models of CoW were developed in the present study to simulate how ICA stenosis affected the blood flow in the normal or abnormal CoW. The model of the normal case was validated by the clinical data from TCD measurement. The simulation results from Model A were also compared with the published reports, and showed a good agreement with them. Based on Model A, the CoW without one PCoA or/and ACoA was also simulated by Model B to D. Therefore, the results in the study were convincing and capable to reveal the difference in the compensatory ability caused by the structural variation of CoW in the development of ICA stenosis.

Our results showed that, in spite of the anatomical variations of CoW, the influence of ICA stenosis was mainly focused on the anterior circulation. Because the blood in posterior circulation was mainly supplied by BA, the flow rate in PCA was less affected by the ICA stenosis, even when ICA was occluded. BA, rather than ICA, was therefore considered as an important artery for the posterior circulation. On the other hand, in the anterior circulation, the effect of ICA stenosis was much more obvious. In Model A, which simulated the normal CoW, the ICA stenosis caused an obvious decrease of flow rate in ACA and MCA. When the stenosis degree increased from 0% to 90%, the flow rate in the ipsilateral ACA and MCA decreased 31.5% and 32.8% respectively. The flow rate in contralateral arteries also decreased, but in a smaller extent, since the blood redistributed through the collateral circulation. If ACoA was absent in CoW (Model B), the decrease was more obvious in the ipsilateral arteries (both 41.9% in ACA and MCA). The decrease was also enlarged by the absence of the ipsilateral PCoA (34.4% and 36.6% in ACA and MCA respectively in Model C). In Model D, the flow rate in the ipsilateral ACA and MCA decreased dramatically (both 99.0% in ACA and MCA), because the absence of the ipsilateral PCoA and ACoA invalidated the collateral circulation.

Our results also showed that the ACA and the ipsilateral PCoA played a significant role in the establishment of the collateral circulation of CoW. Cassot firstly pointed out the importance of ACoA in cerebral hemodynamics with ICA diseases [5]. Aalstuey et al. systematically analyzed the effects of ACoA and PCoA diameters on cerebral flows, and revealed the association between the diameters of communicating arteries and the compensatory ability of CoW [1]. In the present study, although the effect of communicating arteries diameters was not considered in the models, the effect of the absence of communicating arteries on the cerebral flows were simulated during the development of ICA stenosis. The decrease of blood flows in the ipsilateral ACA, MCA, and PCA caused by the absence of the ACoA and ipsilateral PCoA were enlarged when the severity of ICA stenosis increased, indicating that the effect of the absence of ACoA and PCoA on the compensatory ability was larger in the patient with severe ICA stenosis.

Our study indicated that the abnormality of CoW aggravated the effect of ICA stenosis on the cerebral blood supply. Actually, the abnormality of CoW is quite common clinically. Cassot et al. found that PCoA was absent in 9% people while only 1% have no ACoA [20]. Raghavendra investigated the morphological variation in Indian, and found that the absence of ACoA accounted for
9.1% of the cases with variations while PCoA accounted for 18.2% [22]. Li et al. also statistically analyzed the variation of CoW in Chinese [19]. He classified the abnormality of CoW into 2 classes, partly complete and incomplete CoW. The incomplete CoW was defined as the CoW with the absence of arteries in both anterior and posterior circulation, which accounted for 5.9% in Chinese [17]. The value was even higher (18.0%) in the patients with cerebrovascular diseases. The present study indicated that, for the people with incomplete CoW, ICA stenosis would be very dangerous, since the blood flow in anterior circulation were easily affected by ICA stenosis.

The findings in the present study were based on the computations for the CoW of a healthy adult without concomitant cardiac or other arterial diseases. However, the physiological situation might be complicated, as the stenosis in carotid arteries might also be associated with coronary heart disease or other vascular diseases. In addition, although the simulation results were comparable with the experimental data, the quantitative comparison was difficult to achieve because of the measurement errors of TCD and the individual variations. Regarding the gap to the complexities of realistic cases, our results have limitations, which point to the future study, but do not challenge our fundamental findings concerning the influence of ICA stenosis on the blood flow in CoW. Further efforts should be focused on the effect of the whole cardiovascular system on the establishment of collateral circulation in CoW.

In conclusion, the effect of unilateral ICA stenosis with different degrees on normal and abnormal CoW has been assessed with the lumped parameter models. The results show that the ipsilateral PCoA and ACoA play a significant role in maintaining the cerebral blood supply, especially in anterior circulation. The absence of the ipsilateral PCoA or ACA would aggravate the decrease of flow rate in the ipsilateral ACA and MCA caused by ICA stenosis. The simultaneous absence of the ipsilateral PCoA and ACA would be very dangerous for the patients with ICA stenosis, whose blood flow decreases dramatically in anterior circulation. Therefore, the abnormality of CoW should be an important screening factor for the precaution of ICA stenosis and stroke.

5. Acknowledgement

This study was supported by the National Key Technology R & D Program (2012BAI19B04), National Natural Science Foundation of China (No. 61190122) and the grant from the State Key Laboratory of Virtual Reality Technology and Systems, Beihang University. The author would like to acknowledge Lihong Yang and Feiyan Chang for their contributions.

Reference