Circle of Willis Collateral Flow Investigated by Magnetic Resonance Angiography

Monique J. Hartkamp, MD; Jeroen van der Grond, PhD; Kaspar J. van Everdingen, MD; B. Hillen, MD, PhD; Willem P.T.M. Mali, MD, PhD

Background and Purpose—The circle of Willis (CW) is considered an important collateral pathway in maintaining adequate cerebral blood flow in patients with internal carotid artery (ICA) obstruction. We aimed to investigate the anatomic variation of the CW in patients with severe symptomatic carotid obstructive disease and to analyze diameter changes of its components in relation to varying grades of ICA obstruction and in relation to the presence or absence of (retrograde) collateral flow.

Methods—Seventy-five patients with minor disabling neurological deficits and with ICA stenoses or occlusions were categorized into 4 groups according to the severity of ICA obstruction. This patient population reflected a relatively favorable subgroup of cerebral infarction (considering their minor neurological deficits). All subjects underwent magnetic resonance angiography, including magnetic resonance angiography sensitive to flow direction. CW morphology and the size of its components were determined and compared with those values in control subjects (n=100).

Results—Compared with control subjects, patients demonstrated a significantly higher percentage of entirely complete CW configurations (55% versus 36%, P=0.02), complete anterior configurations (88% versus 68%, P=0.002), and complete posterior CW configurations (63% versus 47%, P=0.04). Patients with severe ICA stenosis did not show significantly increased CW vessel diameters. Patients with ICA occlusion demonstrated a high prevalence of collateral flow through the anterior CW and significantly increased diameters of the communicating channels. Patients with bilateral ICA occlusion relied on collateral flow via the posterior CW and demonstrated a bilateral increase in posterior communicating artery diameters (P<0.05).

Conclusions—The anatomic and functional configuration of the CW reflects the degree of ICA obstruction. (Stroke. 1999;30:2671-2678.)

Key Words: angiography, magnetic resonance ▪ carotid arteries ▪ cerebral circulation ▪ circle of Willis ▪ collateral circulation

The potential of the circle of Willis (CW) to develop collateral flow in case of impaired afferent supply has been known since Sir Thomas Willis first described the collateral function of the arterial anastomosis in 1664.1 In patients with obstruction of the internal carotid arteries (ICAs), adequate cerebral blood flow is maintained by numerous collateral pathways that redistribute blood to the deprived side. The development of such detour routes depends on individual morphological and hemodynamic factors. The anterior communicating artery (ACoA) and (bilateral) posterior communicating arteries (PCoAs) are component vessels of the CW and are designated the primary collateral pathways. Other pathways, known as the secondary collateral pathways, may also be recruited: flow reversal through the ophthalmic arteries, reversed flow through the anterior choroidal artery, and anastomoses between the cortical branches of the intracerebral arteries (leptomeningeal collaterals), which may provide (retrograde) collateral flow to any deprived area. The collateral potential of the CW is believed to be dependent on the presence and size of its component vessels,2–4 which vary among normal individuals.5–9 Recent studies have investigated the role of the CW in the development of collateral flow in ICA obstruction; these studies were based on mathematical models10–12 and used transcranial Doppler ultrasound,13–18 digital contrast–enhanced angiography,2,19 or magnetic resonance angiography (MRA).3,4,13–20–22 The relative importance of the separate components of the CW have thus been assessed, although no clear consensus is found among these reports. MRA has previously been shown to be well suited to investigate the CW, in view of the fact that it is able to provide morphological as well as hemodynamic information concerning blood flow direction in indi-

Received March 30, 1999; final revision received August 20, 1999; accepted September 9, 1999.

From the Department of Radiology (M.J.H., J.v.d.G., K.J.v.E., W.P.T.M.M.) and the Department of Functional Anatomy (B.H.), University Medical Center Utrecht, Utrecht, the Netherlands. Dr Hartkamp is now at the Department of Radiology, University Hospital Nijmegen, Nijmegen, the Netherlands. Reprint requests to Jeroen van der Grond, PhD, Department of Radiology, E01.132, University Hospital Utrecht, AZU, Heidelbergaan 100, 3584 CX Utrecht, Netherlands. E-mail j.vandergrond@azu.umcn.nl

© 1999 American Heart Association, Inc.

Stroke is available at http://www.strokeaha.org

2671
Individual vessels accurately.23,24 The purpose of the present study was 3-fold: (1) to investigate the anatomic variation of the CW in patients with severe carotid obstructive disease, (2) to analyze CW vessel diameter changes in relation to varying grades of ICA obstruction, and (3) to analyze CW vessel diameter changes in relation to the presence or absence of collateral (retrograde) flow.

Subjects and Methods

Subjects

Seventy-five patients with symptomatic ICA obstruction (including unilateral and bilateral significant stenosis of 70% to 99% or unilateral or bilateral ICA occlusions) were included in the present study. The patient population (mean age 62.1 years, range 35.7 to 79.7 years) consisted of 58 males and 17 females referred to the magnetic resonance (MR) unit by the department of vascular surgery or neurology. Patients were classified according to increasing severity of ICA obstruction: patients with a unilateral or bilateral significant stenosis of 70% to 99% (group S, n = 28), patients with a unilateral ICA occlusion (group O, n = 27), patients with a unilateral ICA occlusion in combination with a contralateral significant ICA stenosis (group OS, n = 11), and patients with bilateral ICA occlusion (group OO, n = 9). Grading of ICA obstruction was performed with intra-arterial digital subtraction angiography measured according to NASCET criteria25 and by Doppler ultrasound. Patients with severe vertebral or basilar artery lesions detected by intra-arterial digital subtraction contrast angiography or those in whom a diagnosis of dissection was made were excluded. Patients were compared with 100 control subjects (group C) aged ≥60 years (46 men and 54 women; age range 60 to 88 years, mean age 70.7 years) as described elsewhere.26

Clinical manifestations of ICA obstruction included transient ischemic attack (n = 25), minor stroke (n = 41), transient monocular blindness (amaurosis fugax, n = 4), and chronic ocular ischemia (n = 5). Patients that had suffered a severely disabling stroke were excluded (Rankin scale 4 or 5). Each side of every circle was designated either the asymptomatic side or the symptomatic side, which corresponded to the side with the most severe ICA obstruction and which was responsible for the (most severe) clinical features. (In patients classified into group OO, the hemisphere causing the severest symptoms was designated the symptomatic side.) Accordingly, vessel segments belonging to the symptomatic side of the CW are indicated by the suffix SS, whereas those on the asymptotic side are indicated by the suffix AS. Signed informed consent was received from all subjects, and approval was obtained from the institution’s commission on scientific research on human subjects. Procedures followed were in accordance with institutional guidelines.

MR Angiography

MRA of the CW was performed on a 1.5-T system (Philips Gyroscan NT, Philips Medical Systems). The MRA imaging protocol consisted of a 2-dimensional phase-contrast (2D PC) sagittal localizer survey through the CW, followed by a 3-dimensional time-of-flight (3D TOF) MRA sequence with the following imaging parameters: repetition time/echo time, 30 ms/6.9 ms; flip angle, 20°; field of view, 100×100 mm; matrix size, 128×128; reconstruction matrix, 256×256; 0.78×0.78-mm pixel resolution (0.61-mm 2 pixel area); number of excitations, 2; slice thickness, 1.2 mm; gap width, −0.6 mm (ie, slices overlapped by 0.6 mm); slice orientation, transverse; number of slices, 50; and stack volume, 30 mm. The direction of blood flow in the A1 segments of both anterior cerebral arteries (ACAs) and in the PCoAs was determined by using two 2D PC sequences, of which one was phase encoded in the anteroposterior direction and another in the left-right direction. The imaging parameters of both 2D PC directional flow acquisitions were as follows: repetition time/echo time, 16 ms/0.1 ms; flip angle, 7.5°; field of view, 250×250 mm; rectangular field of view, 100%; matrix size, 256×256; number of excitations, 8; slice thickness, 13 mm; slice orientation, transverse; single slice; and velocity sensitivity (velocity encoding value), 40 cm/s. Two collateral flow pathways were considered with MRA: (1) collateral flow through the ACA resulting in retrograde flow in the A1 segment on the symptomatic side toward the affected ICA and (2) posterior to anterior (collateral) flow through the ipsilateral PCoA.

Diameter Measurements and Morphology

The presence of CW vessels and measurement of their diameters were determined on the 3D TOF stack by use of a dedicated workstation (Easy vision, Philips Medical Systems; measurement software implemented in the workstation). The anterior and posterior parts of the CW were classified according to the scheme of variant types as demonstrated in Figures 1 and 2. Anterior types a through f (Figure 1) are examples of complete anterior configurations, and size, 256×256; number of excitations, 8; slice thickness, 13 mm; slice orientation, transverse; single slice; and velocity sensitivity (velocity encoding value), 40 cm/s. Two collateral flow pathways were considered with MRA: (1) collateral flow through the ACA resulting in retrograde flow in the A1 segment on the symptomatic side toward the affected ICA and (2) posterior to anterior (collateral) flow through the ipsilateral PCoA.

Figure 1. Scheme of anatomic variations of the anterior part of the CW: types a through f are complete, whereas types g through j are incomplete. a, A single ACoA. The ICA bifurcates (arrow) into the A1 segment of the ACA and the MCA. b, Two (or more) ACoAs. c, A medial artery of the corpus callosum (arrow) arising from the ACoA. d, Fusion of the ACAs over a short distance. e, ACAs forming a common trunk and splitting distally into two A2 segments. f, MCA taking origin from the ICA as 2 separate trunks. g, Hypoplasia or absence of an anterior communication. h, One A1 segment shown as hypoplastic or absent, with the other A1 segment giving rise to both A2 segments. i, Hypoplasia or absence of an anterior communication, with the MCA arising as 2 separate trunks.
TABLE 1. Morphology of Anterior Part of the CW

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>a</th>
<th>b</th>
<th>c</th>
<th>d</th>
<th>e</th>
<th>f</th>
<th>g</th>
<th>h</th>
<th>j</th>
<th>Complete</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>75</td>
<td>56</td>
<td>21</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>7</td>
<td>5</td>
<td>0</td>
<td>88</td>
</tr>
<tr>
<td>Controls</td>
<td>100</td>
<td>57</td>
<td>5</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>20</td>
<td>10</td>
<td>2</td>
<td>68</td>
</tr>
</tbody>
</table>

Types a through j correspond to the schematic representations of anterior variants as shown in Figure 1.

Results

Morphology

Anterior Variant Types
Table 1 lists the prevalence of each of the anterior circle variant types, which correspond to the schematic variant types as illustrated in Figure 1. A significantly higher percentage of complete anterior circle configurations was found in the patient group (88%) than in control subjects (68%, P=0.002). This was predominantly due to an increase in type b, at the expense of types g and h, in the patient group.

Posterior Variant Types
Table 2 lists the prevalence of each of the posterior circle variant types corresponding to the schematic types as illustrated in Figure 2. Patients demonstrated a significantly higher percentage of complete posterior circle configurations on MR angiograms (63%) than did control subjects (47%, P=0.04). The distribution shifted toward an increase in type a at the expense of types b, c, e, and g in the patient group.

General Characteristics of the Circles
Table 3 lists the percentages of circles with an entirely complete configuration and with a partially complete configuration, such as a complete symptomatic side (the presence of the A1 AS, ACoA, A1 SS, PCoA SS, and P1 SS) or a complete asymptomatic side (the presence of the A1 SS, ACoA, A1 AS, PCoA AS, and P1 AS). The percentage of partially complete circles in control subjects was calculated by averaging the percentage of complete “left” and “right” sides. We found that patients with carotid lesions had a significantly (P=0.02) higher percentage of entirely complete circle configurations than did controls. The percentage of complete CW configurations was highest on the symptomatic side (P=0.001). No trend was found in the completeness of the CW with respect to severity of the carotid lesion: an entirely complete CW configuration was found in 54% of group S, 58% of group O, 40% of group OS, and 56% of group OO.

Statistical Analysis
Differences between patients and control subjects in the prevalence of the anatomic variant types of the anterior and posterior parts of the CW and the completeness characteristics of the entire CWs were analyzed with the Fisher exact test (Tables 1 to 3). Analysis of diameter differences between groups C, S, O, OS, and OO (Table 4) and between groups with collateral flow versus those without (Tables 5 and 6) was performed with the nonparametric Wilcoxon rank sum test. A value of P<0.05 was considered statistically significant. All data are expressed as mean±SD. Statistical significance was corrected for repeated measurements (Dunn multiple comparison procedure).

Table 1 and Table 2 provide a detailed analysis of the prevalence of different configurations of the Circle of Willis (CW) in patients and control subjects. The tables list the prevalence of each of the anterior circle variant types, as well as the prevalence of complete and incomplete configurations for both the anterior and posterior parts of the CW. The statistical analysis reveals significant differences in the prevalence of these configurations between patients and control subjects, with patients demonstrating a higher percentage of complete anterior and posterior configurations.

### Table 1: Morphology of Anterior Part of the CW

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>a</th>
<th>b</th>
<th>c</th>
<th>d</th>
<th>e</th>
<th>f</th>
<th>g</th>
<th>h</th>
<th>j</th>
<th>Complete</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>75</td>
<td>56</td>
<td>21</td>
<td>3</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td>7</td>
<td>5</td>
<td>0</td>
<td>88</td>
</tr>
<tr>
<td>Controls</td>
<td>100</td>
<td>57</td>
<td>5</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>20</td>
<td>10</td>
<td>2</td>
<td>68</td>
</tr>
</tbody>
</table>

Types a through j correspond to the schematic representations of anterior variants as shown in Figure 1.

### Table 2: Morphology of Posterior Part of the CW

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>a</th>
<th>b</th>
<th>c</th>
<th>d</th>
<th>e</th>
<th>f</th>
<th>g</th>
<th>h</th>
<th>i</th>
<th>j</th>
<th>Complete</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>75</td>
<td>54</td>
<td>8</td>
<td>1</td>
<td>27</td>
<td>7</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>63</td>
<td></td>
</tr>
<tr>
<td>Controls</td>
<td>100</td>
<td>25</td>
<td>14</td>
<td>8</td>
<td>30</td>
<td>12</td>
<td>2</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>47</td>
<td></td>
</tr>
</tbody>
</table>

Types a through j correspond to the schematic representations of posterior variants as shown in Figure 2.
group OO compared with 36% of control subjects. The configuration of the CW on the symptomatic side (the A1 AS, ACoA, A1 SS, PCoA SS, and P1 SS) was complete in 68% of group S, 78% of group O, 64% of group OS, and 67% of group OO compared with 42% of control subjects.

Figure 3 demonstrates a typical example of a complete CW configuration.

Diameter Measurements

Table 4 demonstrates the mean diameters for control subjects and for each of the patient groups. This table shows that patients with severe stenosis of the ICA (group S) do not have significantly increased vessel diameters of the CW. Seven percent of these patients showed collateral flow through the A1 segment of the ACA on the symptomatic side, whereas collateral flow via the PCoA on the symptomatic side was found in 21% of these (group S) patients.

All patients with unilateral ICA occlusion (groups O and OS) demonstrated a statistically significant increase in ACoA and A1 AS diameters. Collateral flow via the anterior CW was present in 70% (group O) and 46% (group OS). Furthermore, we found a statistically significant increase in diameter of the PCoA on the symptomatic side and of the P1 segments on both sides. Collateral flow through the PCoA on the symptomatic side was found in 41% (group O) and 36% (group OS).

Patients with bilateral ICA occlusions (group OO) demonstrated a statistically significant increase in ACoA diameter but no significant increase in the diameter of the A1 AS. Eleven percent (n=1) of these patients demonstrated collateral flow via the anterior CW. Group OO patients also demonstrated a statistically significant increase in the diameter of the PCoA and P1 segments on both sides. Seventy-eight percent of group OO demonstrated collateral flow via the PCoA on the symptomatic side, and 89% of group OO demonstrated collateral flow via the asymptomatic PCoA.

Tables 5 and 6 show mean vessel diameter values according to the presence or absence of collateral flow via the ACoA and A1 SS or via the PCoA SS, respectively. Table 5 demonstrates that the diameters of the ACoA and A1 AS are significantly increased in the presence of collateral flow via the anterior circle. Without collateral flow, these vessel diameters are within normal limits. When collateral flow is present in the PCoA on the symptomatic side, the diameter of this artery is significantly increased. The diameter of the P1 SS is significantly increased irrespective of the presence of collateral flow via the PCoA.

Discussion

Morphology

The most important finding of the present study is the presence of a higher percentage of complete CW configurations in patients with ICA obstruction compared with control subjects. Several factors may explain this finding, including population selection, adaptation of CW morphology (also known as remodeling), and improved detection of vessels with increased flow on MR angiograms (increased sensitivity of MRA).

An inevitable prerequisite for inclusion into this in vivo study was that patients had survived ICA obstruction. Possession of an arterial circle with collateral potential (favoring a “relatively complete” configuration) is inherent to this prerequisite and results in population selection. Therefore, it is fair to conclude that this patient population represents a subgroup of the entire population with a higher prevalence of favorable circle configurations. Whether the configurations of these circles represented preexistent morphological variants as opposed to acquired morphology secondary to hemodynamic adaptation elicited by progressive ICA obstruction over time cannot be differentiated retrospectively. However, the general trend toward increasing diameters of the communicating channels indicates that remodeling of CW morphology does occur.
TABLE 4. Mean Vessel Diameters According to Severity of ICA Lesion

<table>
<thead>
<tr>
<th>Diameter, mm</th>
<th>C (n=100)</th>
<th>S (n=28)</th>
<th>O (n=27)</th>
<th>OS (n=11)</th>
<th>OO (n=9)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACoA</td>
<td>1.13±0.28</td>
<td>1.20±0.33</td>
<td>1.33±0.38</td>
<td>1.34±0.36*</td>
<td>1.50±0.25†</td>
</tr>
<tr>
<td>A1 SS</td>
<td>1.78±0.41</td>
<td>1.63±0.51</td>
<td>1.90±0.42</td>
<td>1.84±0.67</td>
<td>2.02±0.60</td>
</tr>
<tr>
<td>A1 AS</td>
<td>1.78±0.41</td>
<td>1.86±0.37</td>
<td>2.82±0.60†</td>
<td>2.58±0.79*</td>
<td>1.78±0.33</td>
</tr>
<tr>
<td>PCoA SS</td>
<td>1.29±0.42</td>
<td>1.40±0.44</td>
<td>1.55±0.45*</td>
<td>1.60±0.42*</td>
<td>1.76±0.41*</td>
</tr>
<tr>
<td>PCoA AS</td>
<td>1.29±0.42</td>
<td>1.25±0.32</td>
<td>1.45±0.66</td>
<td>1.39±0.64</td>
<td>1.95±0.32*</td>
</tr>
<tr>
<td>P1 SS</td>
<td>1.79±0.45</td>
<td>1.91±0.43</td>
<td>2.79±0.44†</td>
<td>2.63±0.61†</td>
<td>2.63±0.42†</td>
</tr>
<tr>
<td>P1 AS</td>
<td>1.79±0.45</td>
<td>1.92±0.49</td>
<td>2.41±0.59†</td>
<td>2.62±0.58†</td>
<td>2.66±0.39†</td>
</tr>
</tbody>
</table>

Values are mean±SD.

*P<0.05 patients vs control subjects; †P<0.01 patients vs control subjects.

Limitations

The results of the present study were influenced by at least 2 factors. First, the patients and control subjects were not age- and sex-matched (control group, mean age 70.7 years and 46% male; patients, mean age 62.1 years and 77% male). Second, 3D TOF MRA is known to have lower sensitivity for detecting low or turbulent flow.

The results of our previous study, in which only control subjects were described, demonstrated that the MR angiographic diameters of CW components tended to decrease with age and that these diameters also tended to be larger in males. Although both the age and sex mismatches between the patients and control population will likely have contributed to the finding of increased CW vessel diameters in our patient population, this effect is expected to be small. Only a relatively small (<0.1 mm) age effect was found over a range of 48 years in the control group. Considering that the mean age difference between patients and control subjects in this study was only 8.6 years, the large differences in mean vessel diameters between patients and control subjects found in the present study cannot be accounted for by a mismatch in mean age of these populations only. Similar differences in vessel diameter were found between males and females in the control study. Although the percentage of males was higher in our patient population than in the control group, it is expected that this mismatch contributes only slightly to the increased CW vessel diameter in patients.

Furthermore, it should be noted that the control group was recruited from a population-based study, as described previously. The medical histories of our control group subjects (n=100) included cerebrovascular accident (n=2), myocardial infarction (n=4), diabetes mellitus (n=8), transient ischemic attack (n=3), hypertension (n=32), and viral meningitis (n=2). It should be realized that our control group, therefore, does not reflect a healthy control group but rather a cross section of the normal Dutch population at this age. Although we did not find a relation between the medical history of subjects and vessel diameter or CW configuration in our control group, the remote possibility that the history of these 51 control subjects may indeed have affected the “normal control” values used in the present study cannot be excluded.

A second important limitation of the present study is related to the use of 3D TOF MRA in evaluating the presence of small intracranial arteries. It is well known that the sensitivity of 3D TOF MRA decreases when blood flow velocity decreases. As was mentioned above, age- and sex-related differences in blood flow velocity between controls and ICA-obstructed patients are expected to have had little or no influence on the diameters found in the present study. However, hemodynamic adaptations (resulting in increased flow through the collateral channels) does result in improved sensitivity of MRA in detecting these vessels. As flow increases through small vessels, visibility on TOF MR angiograms improves and consequently, fewer vessel segments are classified as hypoplastic or absent. Thus, as the functionality of the CW vessels improves, their visibility on TOF MR angiograms also improves relative to the normal control subjects. Because the primary collateral pathways may carry slow or negligible flow in the absence of ICA obstruction, it is expected that these effects are less significant in the control group.

TABLE 5. Mean Vessel Diameters According to Presence or Absence of Collateral Flow via the ACoA

<table>
<thead>
<tr>
<th>Diameter, mm</th>
<th>Control Subjects</th>
<th>Collateral Flow via ACoA and A1 SS</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACoA</td>
<td>1.13±0.28</td>
<td>1.22±0.31</td>
</tr>
<tr>
<td>A1 SS</td>
<td>1.78±0.41</td>
<td>1.75±0.57</td>
</tr>
<tr>
<td>A1 AS</td>
<td>1.78±0.41</td>
<td>1.74±0.57</td>
</tr>
</tbody>
</table>

Values are mean±SD.

*Includes cases of antegrade flow and nondetected collateral flow.
†P<0.05 patients vs control subjects; †P<0.01 patients vs control subjects; and §P<0.05 patients with collateral flow vs patients without collateral flow.

TABLE 6. Mean Vessel Diameters According to Presence or Absence of Collateral Flow via the PCoA

<table>
<thead>
<tr>
<th>Diameter, mm</th>
<th>Control Subjects</th>
<th>Collateral Flow via PCoA</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCoA SS</td>
<td>1.29±0.42</td>
<td>1.41±0.41</td>
</tr>
<tr>
<td>P1 SS</td>
<td>1.79±0.45</td>
<td>2.31±0.67†</td>
</tr>
</tbody>
</table>

Values are mean±SD.

*Includes cases of antegrade flow and nondetected collateral flow.
†P<0.05 and †P<0.01 patients vs control subjects.
is likely that the prevalence of complete CW configurations in control subjects may have been underestimated because of impaired visualization of nonfunctional communicating vessels. Conversely, transcranial ultrasound studies have indicated that the primary collateral pathways and their parent arteries, A1 SS and P1 SS, develop severe turbulence when used as CW collaterals. It is known that turbulence may lead to loss of signal intensity on TOF MRA and, thus, to underestimation of vessel diameters. Therefore, it remains unclear whether collateral cross flow leads to either an overestimation or to an underestimation of the vessel diameters on MR angiograms.

**Hemodynamics**

**Collateral Flow in the A1 SS**

Collateral (reversed) flow through the symptomatic A1 was not accompanied by any statistically significant mean diameter increase in this vessel. However, when flow was collateral in the symptomatic A1, we did find statistically significant diameter increases in the asymptomatic A1 and ACoA. This reflects additional blood flow through the asymptomatic A1, which is needed to supply collateral flow to its counterpart. Collateral flow in the anterior CW develops as a result of a blood pressure gradient across the ACoA, and this concept forms the basis of hemodynamic adaptation. The pressure gradient results from the blood pressure difference between the poststenotic or postocclusional ICA branches compared with the blood pressure in the contralateral ICA branches, which may be normal (or reduced because of stenosis or occlusion). In group S, only very few patients developed collateral flow through the anterior or posterior circle, indicating that stenosed ICAs are able to provide an adequate contribution. In patients with a unilateral ICA occlusion (group O), an evident asymmetry of perfusion pressure between the 2 ICAs, in combination with increased demand on the occluded side, results in collateral flow in the majority of anterior circles (70%). As the severity of ICA obstruction on the asymptomatic side increases (group OS), asymmetry in arterial pressure across the anterior circle becomes less evident than in group O, but in combination with increased demand on the occluded side of the brain, it still brings about flow reversal through the A1 on the symptomatic side in 46% of cases. In patients with bilateral occlusion, asymmetry in arterial pressure between the symptomatic and asymptomatic ICA does not apply or is negligible. Although flow reversal in the anterior circle is therefore uncommon in group OO, we did find a statistically significant increase in the ACoA diameter in this patient group. An explanation might be that patients with bilateral ICA occlusion first develop a unilateral stenosis or occlusion of the ICA with cross flow through the ACoA and a corresponding diameter increase of this vessel. Later, when the contralateral ICA becomes increasingly obstructed, this cross flow through the ACoA disappears, and the ACoA returns only partially to its original diameter. Consequently, in patients with bilateral ICA occlusions, a large diameter of the ACoA does not guarantee the presence of collateral flow.

**Collateral Flow in the PCoA SS**

The PCoAs demonstrated a trend toward increased mean diameter when flow through this vessel was collateral. A statistically significant increase in mean diameter for the P1 segments on both the symptomatic and asymptomatic side was found in groups O, OS, and OO, irrespective of flow direction through the arterial circle. This indicates that when at least one ICA is occluded, the blood flow in the posterior circulation increases. Surprisingly, our results show that flow in both P1 segments increases when only one ICA is occluded. It might be that because of the drop in arterial pressure in the (ipsilateral) anterior system and the subsequent use of the ACoA as a collateral pathway, the perfusion pressure in symptomatic middle cerebral artery (MCA) territory as well as in the asymptomatic MCA territory is reduced, leading to an increased flow territory of both PCAs and therefore to increased P1 diameters bilaterally. This is in agreement with the finding that blood flow through the basilar artery is increased in these patients. This phenomenon cannot be ascribed to collateral flow through the ipsilateral PCoA only, because in patients without collateral PCoA flow, basilar artery flow is also increased.

Considering the collateral contribution of the PCoAs, it is noted that 21% of group S demonstrated collateral PCoA flow, although the mean diameter increase in these cases was negligible. A minimal diameter increase indicates that the collateral contribution of the PCoA in group S is small, because it does not induce remodeling to accommodate increased volume flow. An interesting observation is that the prevalence of collateral ACoA flow was higher in group O than it was in group OS, although the prevalence of collateral PCoA flow was similar in groups O and OS. Apparently, as the asymptomatic ICA becomes increasingly obstructed, the option of recruiting collateral flow via the anterior circle gradually decreases because of a decreasing pressure gradient over the ACoA (decreased supply from the asymptomatic ICA). We expected that this would be accompanied by a significant increase in the relative contribution of PCoA collateral flow in group OS; however, this occurred only in patients with bilateral ICA occlusions. This implies that the anterior circle is the preferential mode of collateral supply for patients with unilateral ICA occlusion. As the contralateral ICA becomes completely occluded, resulting in bilateral ICA occlusion, the option of supplying collateral flow through the anterior circle is lost, and alternative collateral flow pathways such as the PCoAs become the most important route in bilateral ICA occlusions. One might question why the PCoA is not the preferred route of supply in cases of unilateral occlusion. An explanation might be that resistance to flow across the PCoA is greater than across the ACoA, because the PCoA is usually a longer vessel. Longer vessels result in an increased resistance to flow that is due to the larger area of endoluminal vessel wall available for friction.

The observations in the present study demonstrate that the development of collateral flow through the CW is governed by morphological factors, such as an individual’s anatomic configuration of the circle, as well as related hemodynamic factors, such as increased flow through the primary pathways, flow reversal, and vasodilatation. Although preexistent mor-
phological characteristics are a precondition determining the patterns of hemodynamic adaptations that are able occur, the subsequent hemodynamic changes themselves may induce remodeling of CW morphology. This is reflected in the significant increases in ACoA and PCoA diameters on the symptomatic side, for all grades of ICA obstruction, as collateral flow increases through these vessels.

**Comparison Between Authors**

The results of the present study show that patients with severe ICA lesions have a much higher percentage of complete circle configurations (55%) than would have been expected on the basis of autopsy studies. Alpers and Berry\(^2\) reported that only 33% of autopsy brains with cerebral softening demonstrated a normal configuration of the CW. Riggs and Rupp\(^2\) investigated autopsy brains taken from adults with evidence of neurological dysfunction and classified only 21% of the arterial circles as normal. Miralles et al\(^3\) investigated the circles of 38 patients with carotid artery occlusion in vivo and found high percentages of complete anterior circles (60%) and complete posterior circles (74%), in agreement with the results of the present study (88% and 63%, respectively). A higher percentage of complete circles in living patients with ICA obstruction compared with the autopsy populations as described by Alpers and Berry and Riggs and Rupp is likely due to (1) the use of 3D TOF MRA and (2) differences in the patient populations studied. As was discussed earlier, the effect of increased (collateral) flow in the CW on the sensitivity of 3D TOF MRA remains unclear. However, our previous study,\(^4\) in which MRA results were compared with autopsy results from a study of Hillen\(^6\) based on 100 normal adult brains, demonstrated that 3D TOF MRA might slightly overestimate vessel diameters. This may also partially account for the higher number of complete circle configurations found in the present study compared with autopsy studies. Another explanation for the higher percentage of complete circles found in the present study could be that Alpers and Berry performed autopsy studies, whereas our patient population consisted of a relative favorable subgroup of cerebral infarction survivors (Rankin scale <4). The differences in CW configurations found in these study populations may therefore indicate the protective role of the CW in survivors of ICA occlusive disease.

Other studies have investigated collateral pathways in the CW in patients with ICA occlusion, although the role of the primary pathways in relation to differing grades of ICA obstruction has not been investigated extensively before. Two such studies focused on the relative importance of the anterior or posterior circle as separate entities in preventing hypoperfusion infarction (watershed/low-flow/ischemic infarction). The study by Miralles et al\(^3\) concluded that the relative risk of hypoperfusion infarctions was significantly higher in cases with a nonfunctioning ACoA. Schomer et al\(^4\) however, concluded that the presence of a large ipsilateral PCoA was the only feature that correlated significantly with the absence of a watershed infarct. CW hemodynamics are influenced by the presence of retrograde flow through the ophthalmic artery, the prevalence of which differed greatly among the aforementioned study populations: 92%\(^3\) versus 37%\(^4\). This may well explain the differences in their observations. Moreover, whereas the population studied by Miralles et al included only unilateral occlusions, the population investigated by Schomer et al included 3 patients with bilateral ICA occlusions, affecting 6 hemispheres of the 32 studied (19%). In light of our results, which demonstrate that the PCoA is more important in cases of bilateral ICA occlusions than it is in cases of unilateral ICA occlusion, we may safely presume that in the study of Schomer et al, the inclusion of bilateral ICA occlusion patients in the population affected the results. Consequently, the role of PCoA appeared to be of more importance in preventing cerebral ischemia in the report of Schomer et al. In the present study, 7 (78%) of 9 patients with bilateral occlusions showed retrograde flow through the ipsilateral ophthalmic artery. Therefore, it is likely that in patients with bilateral ICA occlusion, collateral flow via both the PCoA and ophthalmic artery is important. Our results indicate that although this is true for bilateral ICA occlusion patients, the ACoA is the preferred collateral route in unilateral ICA occlusion.

A recent transcranial color-coded duplex ultrasonography (TCCS) study by Baumgartner et al\(^30\) investigated 93 patients with severe stenoses or occlusions (n=2) of the ICA and showed an even higher prevalence of functionally complete configurations. That study detected collateral flow through the ACoA in 98% of patients with obstructive carotid artery disease. In the present study, 88% of patients demonstrated a patent anterior circle. In the study of Baumgartner et al, collateral flow through the PCoA was detected in 84% of the study population, which compares with 63% in the present study. The results of Baumgartner et al are in agreement with those of Muller and Schimrigk,\(^31\) who reported a 95% sensitivity for transcranial Doppler ultrasound detecting a functional PCoA and 87% sensitivity for detecting a functional PCoA. In contrast, another TCCS study showed much lower values: Martin et al\(^32\) demonstrated the presence of the ACoA in at least 66% and a functioning PCoA in 34% of patients with an ICA occlusion. For patients with ICA stenosis of >80%, these percentages were 51% and 29%, respectively. These differences between MRA and TCCS are likely to be caused by differences in technical approach between the 2 techniques.

Cross flow to the MCA via the anterior circle is reported in 93%\(^3\) and 62%\(^4\) of ICA occlusion patients, and anteriorly directed flow in the PCoA is reported in 68%\(^3\). Similar observations were made in the present study: in corresponding patients (group O plus OS) collateral flow was seen most frequently through the anterior circle (63% demonstrated collateral flow) and less frequently through the PCoA on the symptomatic side (39%). (Schomer et al\(^4\) report the presence of the PCoA in 59% and note anteriorly directed flow in the larger of these, i.e., diameter >1 mm, but do not provide flow directional data for the remaining smaller vessels.)

**Conclusion**

Patients with ICA obstruction with minor disabling neurological deficits demonstrate a higher prevalence of complete arterial configurations, and those with at least one ICA occlusion demonstrate statistically significant mean diameter
increases of the CW collateral vessel segments compared with diameter increases in controls. Patients without occlusion (but with significant stenosis) of the ICA do not have significantly altered vessel diameters, although the ipsilateral configuration of the CW is more often complete in this stenosis patient group as well. Patients with unilateral ICA occlusion, with and without a significant contralateral ICA stenosis, have a higher prevalence of collateral flow via the anterior CW than via the posterior CW, indicating that the anterior circle is the preferred route of supply in unilateral ICA occlusion. Patients with bilateral ICA occlusions, however, fully rely on collateral flow via the posterior circulation. Ultimately, therefore, the anatomic and functional configuration of the CW reflects the severity of ICA obstruction.

Acknowledgments

This study was supported by The Netherlands’ Organization for Scientific Research, Medical Sciences Section (Nederlandse organisatie voor Wetenschappelijk Onderzoek [NWO]) grant 920-02-090 (to Dr Hartkamp). Dr van der Grond is associated with The Netherlands Heart Foundation as a clinical investigator.

References

Circle of Willis Collateral Flow Investigated by Magnetic Resonance Angiography
Monique J. Hartkamp, Jeroen van der Grond, Kaspar J. van Everdingen, B. Hillen and Willem P. T. M. Mali

Stroke. 1999;30:2671-2678
doi: 10.1161/01.STR.30.12.2671
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1999 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

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/30/12/2671

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/