Collateral Ability of the Circle of Willis in Patients With Unilateral Internal Carotid Artery Occlusion

Border Zone Infarcts and Clinical Symptoms

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Background and Purpose—The circle of Willis is regarded as the major source of collateral flow in patients with severe carotid artery disease. The purpose of the present study was to assess whether the presence of border zone infarcts is related to the collateral ability of the circle of Willis in symptomatic (transient ischemic attack, minor stroke) and asymptomatic patients with unilateral occlusion of the internal carotid artery (ICA).

Methods—Fifty-one patients (35 symptomatic, 16 asymptomatic) and 53 control subjects were investigated. Patients had unilateral occlusion of the ICA and contralateral ICA stenosis between 0% and 69%. The directions of flow, on the side of the ICA occlusion, and the size of the component vessels in the circle of Willis were investigated with MR angiography.

Results—On average, 92% of the patients without border zone infarcts (n=26) had willisian collateral flow compared with 60% of patients with border zone infarcts (n=25; P<0.05). This increase in collateral flow was caused by the high prevalence of collateral flow via the posterior communicating artery in patients without border zone infarcts (50% versus 12%; P<0.05). No statistically significant relation was found between the pattern of collateral flow via the circle of Willis and the presence of clinical symptoms. Nevertheless, asymptomatic patients with ICA occlusion demonstrated an increased diameter of the anterior communicating artery (P<0.05).

Conclusions—In patients with unilateral ICA occlusion, the presence of collateral flow via the posterior communicating artery in the circle of Willis is associated with a low prevalence of border zone infarcts. Asymptomatic patients with an ICA occlusion do not have an increased collateral function of the circle of Willis. (Stroke. 2001;32:2768-2773.)

Key Words: carotid artery occlusion □ cerebral ischemia □ circle of Willis □ collateral circulation □ posterior communicating artery

Patients with occlusion of the internal carotid artery (ICA) have postocclusive diminished arterial pressure. In these patients collateral blood flow via the circle of Willis is important to keep the cerebral perfusion at a level sufficient to accommodate the metabolic demands.1,2 The anterior communicating artery (ACoA) and the ipsilateral posterior communicating artery (PCoA) are the collateral pathways via which the circle of Willis can redistribute blood flow to the deprived side of the brain. When collateral compensation mechanisms fail short, obstructive ICA lesions may result in a decreased cerebral perfusion pressure, which may lead to the presence of low-flow infarcts in border zone areas of the brain.3–7 Border zone areas are located in the most distal part of the perfusion territory of the main cerebral arteries or between the deep and superficial supply area of the middle cerebral artery (MCA). Recent studies have investigated the collateral potential of the circle of Willis.8–14 Although the role of the circle of Willis in protecting patients with carotid occlusive disease against ischemia is recognized, there is still much confusion about the importance of the individual pathways. A possible reason for these contradicting results is that in these studies only symptomatic patients with ICA stenosis or occlusion were included. No comparison with asymptomatic patients with ICA stenosis or occlusion or with control subjects was made.

It has been shown previously that patients with asymptomatic ICA occlusion have a more well-preserved hemodynamic status of the brain compared with symptomatic patients.15–18 The role of the circle of Willis in this respect is not fully understood. It has been suggested that collateral flow via the circle of Willis compensates for deprived perfusion in asymptomatic patients with ICA occlusion.18,19 However, at present, no study has directly compared symptomatic patients with asymptomatic patients with ICA occlusion.
In the present study the hemodynamic role of the circle of Willis in patients with unilateral ICA occlusion was studied by comparing the collateral ability of the circle of Willis between symptomatic and asymptomatic patients. In addition, we investigated whether differences in collateral flow pattern were present between patients with and without border zone infarcts.

Subjects and Methods

Subjects
Fifty-one patients with unilateral ICA occlusion and contralateral ICA stenosis between 0% and 69% were included. Symptomatic and asymptomatic patients were analyzed in combination and separately. Thirty-five patients with a symptomatic unilateral occlusion (28 men, 7 women; mean age, 58.6 years; range, 35.6 to 77.3 years) who presented with hemispheric transient ischemic attack (n=17) and minor stroke (n=18) were included in the study population. All patients were referred to the Department of Radiology by vascular surgeons or neurologists for diagnosis and grading of the ICA obstruction. All patients had transient or minor-disabling neurological deficits in the supply territory of an occluded ICA within 6 months before the MRI examination. Transient neurological deficits were defined as symptoms lasting <1 day. A minor-disabling deficit indicated symptoms lasting >1 day and that resulted in a mild or moderate invalidation (Rankin grade 3 or better). Grading of the ICA lesions was performed with intra-arterial digital subtraction angiography according to criteria of the North American Symptomatic Carotid Endarterectomy Trial (NASCET). The degree of the contralateral ICA stenosis was 19±21% (mean±SD). Sixteen patients with unilateral asymptomatic ICA occlusion were included (13 men, 3 women; mean age, 64.7 years; range, 46.8 to 78.0 years). The asymptomatic patients presented to the Department of Stroke and Neurology. The MR images were evaluated for the presence of ipsilateral border zone infarcts. None of the asymptomatic patients with ICA occlusion had any ischemic symptoms in the past. In this group the degree of the contralateral ICA stenosis was 17±18% (mean±SD).

The control group consisted of 53 volunteers (20 men, 33 women) aged 60 to 70 years, with a mean age of 65.7 years. This group was recruited from a population-based study as described previously. In all control subjects morphological scans of the circle of Willis were performed, whereas in 36 of the control subjects directional flow measurements of the circle of Willis were available. Informed consent was received from all subjects, and approval was received from the hospital’s commission on scientific research on human subjects.

MR Angiography
MR angiography (MRA) of the circle of Willis was performed on a 1.5-T system (Philips Gyroscan NT, Philips Medical Systems). The MRA protocol consisted of a 2-dimensional phase contrast sagittal localizer survey through the circle of Willis, followed by a 3-dimensional time-of-flight (TOF) MRA sequence with the following imaging parameters: repetition time/echo time (TR/TE), 30 ms/6.9 ms; flip angle, 20°; field of view, 100×100 mm; matrix size, 256×256; 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. Diameter measurements were performed on the individual (transverse) source slices of the 3-dimensional TOF MRA data set with the use of a workstation (Easy Vision, Philips Medical Systems). The diameters of the component vessels in the circle of Willis were measured in all patients and control subjects: ACoA, A1 segment of the anterior cerebral arteries (ACA), and PCoA. The direction of blood flow in the A1 segment of the ACA and in the PCoA was measured with two 2-dimensional phase contrast sequences, of which one was phase encoded in the anterior-posterior direction and another in the left-right direction. The imaging parameters of the 2-dimensional phase contrast directional flow acquisition were as follows: TR/TE, 169.1 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, 40 cm/s. Two primary collateral pathways were analyzed: retrograde flow (toward the ICA) in the proximal segment of the anterior cerebral artery on the occluded (and symptomatic) side and posterior to anterior (retrograde) flow in the ipsilateral PCoA. In each patient the pattern of collateral flow via the circle of Willis was categorized as collateral flow (1) via the A1 segment only, (2) via the PCoA only, (3) via both the A1 segment and the PCoA, or (4) no collateral flow via either the A1 segment or the PCoA (Figure 1).

Cerebral Infarct Locations
Dual-echo T2-weighted spin-echo sequences were acquired to determine the presence of cerebral infarcts. Imaging parameters were as follows: TR/TE1/TE2, 2462/24/120 ms; 220×220-mm field of view; matrix size, 256×256; slice thickness, 6.0 mm; interslice gap, 0.6 mm; number of slices, 19; number of excitations, 2; and slice orientation, transverse angulated to the orbitomeatal line. Both the proton density–weighted images (first echo images) as well as the T2-weighted images (second echo images) were used to determine the location of infarction.

Each side of every circle was designated symptomatic or asymptomatic, corresponding to the side causing clinical symptoms. In all patients the symptomatic side corresponded with the side having the most severe ICA lesion. The MR images were evaluated for the presence of ipsilateral border zone territory and territorial infarcts by 2 senior neuroradiologists blinded to the angiographic results. In the study we focused especially on the presence of border zone infarcts. The following 3 types of border zone infarcts were considered: (1) between the superficial territory of the MCA and the ACA; (2) between the superficial territory of the MCA and posterior cerebral artery; and (3) between the superficial and the deep territory of the MCA. Mixed infarcts containing both border zone and territorial areas were included in the number of border zone infarcts.

Statistical Analysis
Differences between patients with unilateral ICA occlusion and control subjects in vessel diameter were analyzed with ANOVA. The same test was used for the diameter comparison of patients with versus without border zone infarcts and symptomatic versus asymptomatic patients.
tomatic patients. To demonstrate the interaction between flow pattern and diameter we used the $t$ test for independent samples. The $x^2$ test was used to compare the direction of flow in the A1 segment and the PCoA between control subjects and patients with a unilateral ICA occlusion, patients with versus without border zone infarcts, and symptomatic versus asymptomatic patients. The Bonferroni procedure (flow direction) and the Scheffe post hoc test (diameter) were used to correct for repeated measures. Vessel diameters were expressed as mean±2 SEM. $P<0.05$ was considered statistically significant.

**Results**

First we compared patients with unilateral ICA occlusion with control subjects. Figure 2 shows the 4 patterns of collateral flow in 51 patients with ICA occlusion and 36 control subjects. Collateral (retrograde) flow in the PCoA segment was found in 31% of the patients (11% PCoA only, 20% PCoA plus A1 segment) and in 10% of the control subjects (10% PCoA only; $P<0.05$). Collateral flow in the A1 segment was found in 65% of the patients (45% A1 segment only, 20% PCoA plus A1 segment), whereas in none of the control subjects was retrograde flow in any of the A1 segments found ($P<0.001$). Patients with ICA occlusion demonstrated increased vessel diameters of the PCoA and ACoA compared with control subjects (Figure 3). For the A1 segment, no difference in diameter was found between patients and control subjects.

In Figure 4, the diameter of the PCoA is shown as a function of the 4 patterns of collateral flow in the circle of Willis. The PCoA vessel diameter in patients with collateral flow via the PCoA (PCoA only or PCoA plus A1 segment) was significantly increased ($1.70±0.23$ mm) compared with patients without collateral flow via the PCoA ($1.31±0.14$ mm; $P<0.01$). No differences in the ipsilateral and contralateral A1 and ACoA vessel diameters were found in the comparison of patients with or without collateral flow via the A1 segment.

Of the 51 patients with ICA occlusion, 25 patients had border zone infarcts and 26 patients had no border zone infarcts (7 with territory infarcts and 19 with no infarct visible on MRI). Figure 5 shows the comparison of collateral flow patterns via the circle of Willis between patients with and without border zone infarcts. In patients with border zone infarcts, collateral flow in the PCoA segment was found in 12% (12% collateral flow via the PCoA only). In patients without border zone infarcts, this percentage was significantly increased to 50% (23% PCoA only, 27% PCoA plus A1 segment; $P<0.01$). The prevalences of collateral flow via the A1 segment (A1 segment only or A1 segment plus PCoA) were in the same range for patients with and without border zone infarcts (60% and 69%, respectively). Figure 6 shows the corresponding vessel diameters of the PCoA, A1 segment, and ACoA. In patients without border zone infarcts on MRI, we found a corresponding increase in PCoA diameter ($1.59±0.20$ mm) compared with patients with border zone infarcts ($1.31±0.16$ mm; $P<0.05$). No differences in vessel diameters were observed for the A1 segment and the ACoA.

When we compared symptomatic and asymptomatic patients with unilateral ICA occlusion, no significant differences were found in the collateral flow pattern in the circle of Willis. The prevalences of collateral flow via the A1 segment only, PCoA plus A1 segment, PCoA segment only, and no collateral flow were 56%, 13%, 18%, and 13% for asymptomatic patients and 43%, 20%, 11%, and 26% for symptomatic patients, respectively. However, in asymptomatic patients
we found a significant increase of the ACoA diameter (1.51 ± 0.17 mm) compared with symptomatic patients (1.13 ± 0.09 mm; \(P < 0.05\)) (Figure 7). When we compared asymptomatic and symptomatic patients with border zone infarcts only, we found that the difference in ACoA diameter increased (1.83 ± 0.24 and 1.16 ± 0.11 mm, respectively; \(P < 0.01\)), whereas no difference was found in the collateral flow pattern.

**Discussion**

The most important findings of this study are 3-fold. First, in patients with ICA occlusion, the presence of collateral flow via the PCoA is associated with a lower prevalence of border zone infarctions. Second, asymptomatic patients with ICA occlusion do not have more well-developed collaterals in the circle of Willis than symptomatic patients. Third, for the PCoA there was a strong association between the presence of collateral flow and PCoA vessel diameter, whereas no such relation in the anterior part of the circle of Willis (ACoA and A1 segments) was found.

The potential of the circle of Willis to provide alternative flow routes in case of diminished arterial flow to the brain has been known since Sir Thomas Willis first described the collateral function of the arterial anastomoses in 1664.24 Still, the importance of the individual pathways in the circle itself is not clear. Several studies have suggested that the presence of border zone infarcts may identify patients with poor hemodynamic status of the brain.25,26 Our study shows that in patients with a unilateral ICA occlusion, the presence of collateral flow via the PCoA in the circle of Willis is associated with a low prevalence of border zone infarcts, indicating that the presence of retrograde PCoA flow may protect against low-flow infarctions. Our results agree with previous studies that suggested a protective effect of the collateral flow via the PCoA14 or showed that a small (<1 mm in diameter) or absent ipsilateral PCoA is correlated with the presence of low-flow infarctions in patients with ICA occlusions.12

Additionally, the present study indicates that an increase in PCoA diameter is strongly associated with the presence of collateral flow in the PCoA. Therefore, retrograde collateral flow via the PCoA and the PCoA diameter cannot be considered independent parameters of hemodynamic compensation in patients with unilateral ICA occlusion. This correlation can be caused by 2 phenomena: (1) better visualization of the PCoA on MRA caused by an increased sensitivity of MRA in case of higher (retrograde) PCoA flow or (2) a real anatomic increase in PCoA diameter. The potential of the circle of Willis collaterals to increase in size may be a mechanism of the collateral arteries to adapt to hemodynamic changes.11,27–29 On the other hand, a well-known problem of MRA is that visualization of cerebral arteries is dependent on the flow through the arteries. When blood flow is relatively low, its visibility on a TOF MRA decreases, and diameter measurements may underestimate the actual value because of very slow flow near the vessel wall. In addition, a small underestimation in the prevalence of collateral flow in small circle of Willis components may be
expected. Indeed, Patrunx et al. showed that with techniques similar to those used in our study, the sensitivity of MRA to detect PCoA collateral flow was 81.3%, with conventional angiography used as gold standard. The corresponding prevalence of retrograde PCoA flow in this study (54 subjects) was 15% (16/108) for angiography and 12% (13/108) for MRA.30 The prevalence of 10% retrograde flow via the PCoA found in our control population is in agreement with these results. From a hemodynamic point of view, MRA imaging of collateral flow has advantages over conventional angiography. Very low (retrograde) flow in the PCoA is not expected to contribute substantially to cerebral perfusion and has limited value in protecting against low-flow infarcts. These insignificant collateral vessels are invisible on the MRA directional flow images but are detected with conventional angiography. Although we do not have any proof, it is likely that when collateral flow is visible on MRA, it contributes significantly in maintaining the regional cerebral blood flow. In general, for morphological as well as hemodynamic (flow direction) measurements in the circle of Willis, MRA is regarded as a valuable technique.31–33 In addition to the MRA method described, transcranial Doppler ultrasonography can be used for the assessment of intracranial hemodynamics in patients with carotid artery disease.34,35 Studies that compare transcranial Doppler ultrasonography with MRA show a high correlation in the prevalence of collateral flow via the PCoA and/or ACoA.36 However, an advantage of transcranial Doppler is that it can also visualize collateral flow via the ophthalmolic artery, which is hardly possible with MRA.

In asymptomatic patients we found an increased ACoA vessel diameter compared with symptomatic patients as well as with control subjects. Previous studies have suggested that the ACoA is a more important collateral pathway than collateral flow via the PCoA to maintain normal cerebral hemodynamics.13,37,38 Computerized flow prediction models indicated that the ACoA is the major conduit of collateral blood supply, whereas the PCoA is presumed to be more important as source of collateral flow in patients with a small ACoA.39–41 Compared with control subjects, we found a significantly increased prevalence (65%) of collateral flow via the A1 segment, which is in accord with the prevalences described in the literature that varied between 46% and 80%.13,32,42 However, although we found an increased diameter of the ACoA in asymptomatic patients, it is remarkable that in asymptomatic patients the same prevalence of collateral flow in the anterior part of the circle of Willis is found compared with symptomatic patients. In contrast to the predictions of mathematical models, no association was found between the ACoA diameter and the presence of collateral flow. Furthermore, between patients with and without border zone infarcts, no significant difference in vessel diameter or in the prevalence of retrograde flow in the A1 segment was found. These results are in agreement with a previous study in which no difference in collateral flow patterns was found between patients with asymptomatic ICA occlusion and those with mild or moderate stroke.19 Probably collateral flow via the anterior part of the circle of Willis alone is not enough to compensate for the deprived cerebral perfusion in patients with unilateral ICA occlusion, and additional flow via other collateral pathways is needed.

In conclusion, in patients with unilateral ICA occlusion, the presence of collateral flow via the PCoA in the circle of Willis is associated with a low prevalence of border zone infarcts. Between symptomatic and asymptomatic patients, either with or without border zone infarcts, no difference in collateral flow patterns was present, whereas an (unexplained) increase in anterior communicating artery diameter was found in asymptomatic patients.

References

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