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Effect of Carotid Endarterectomy on Primary Collateral Blood Flow in Patients With Severe Carotid Artery Lesions

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Background and Purpose—In patients with severe obstruction of the internal carotid artery (ICA), it is recognized that the preoperative failure to visualize collaterals of the circle of Willis increases the risk of hemispheric ischemia before, during, and after carotid endarterectomy (CEA). The purpose of the present study was to assess the effect of CEA on the anatomy and function of the circle of Willis.

Methods—Time-of-flight and phase-contrast MR angiography were used to study changes in vessel diameter and collateral flow of the circle of Willis in 48 patients with 70% to 99% ICA stenosis before and after CEA.

Results—In patients with unilateral ICA stenosis, all preoperative vessel diameters on both sides of the circle of Willis were larger than in control subjects. All demonstrated a significant diameter decrease to reach normal values after CEA. Furthermore, preoperative collateral flow patterns normalized after CEA ($P=0.03$). In patients with stenosis and contralateral ICA occlusion, CEA resulted in a significant increase in the prevalence of collateral flow via the anterior communicating artery (33% to 83%, $P<0.01$) and a significant increase in diameter of both A1 segments ($P<0.05$) in patients in whom collateral flow developed after CEA.

Conclusions—CEA reduces the caliber of compensatory collateral channels to normal levels by MR angiography measurements in the presence of severe unilateral stenosis; when the opposite side is occluded and the stenosis is removed ipsilaterally, a greater amount of compensatory collateral circulation can be measured on both the occluded side and the fully opened side. **(*Stroke*. 2003;34:1650-1654.)**

Key Words: carotid endarterectomy ■ cerebral ischemia ■ circle of Willis ■ collateral circulation

In patients with severe symptomatic stenosis of the internal carotid artery (ICA), carotid endarterectomy (CEA) reduces stroke risk by removal of the atheromatous plaque as a source of thromboembolism.[1–3] Moreover, improvement in cerebral perfusion and vascular reserve capacity after CEA may further decrease stroke risk by a better washout of cerebral embolisms from border-zone areas in which the collateral blood supply is minimal.[4–6]

In patients with severe ICA disease, the circle of Willis is the primary collateral structure to reroute flow from the contralateral side via the anterior communicating artery (ACoA) to the deprived hemisphere or to obtain blood flow from the posterior circulation via the posterior communicating artery (PCoA). The development of such detour routes depends on differences in arterial perfusion pressure and on the presence and size of the vessels involved.[7–10] Preoperatively, collateral flow is associated with preserved arterial perfusion pressure[7] and cerebral blood flow to the hemisphere distal to an ICA stenosis.[11,12] Perioperatively, patients with cross flow via the ACoA have a decreased incidence of ischemic electroencephalographic changes and a lower risk of stroke.[7,13,14] Postoperatively, Henderson et al showed, using data from the North American Symptomatic Carotid Endarterectomy Trial (NASCET), that patients with visualized collateral pathways on their preoperative angiogram had the lowest 2-year stroke risk among surgically treated patients.[14] However, in patients with unilateral ICA stenosis, the prevalence of collateral flow and the caliber of the collateral channels may diminish after CEA, and if so, these potential collaterals may become clinically significant only in the postoperative period when asymmetries between the flow in the 2 carotids are present, eg, when a restenosis occurs. In contrast, in patients with contralateral ICA occlusion, CEA may result in a higher prevalence of collateral flow via the anterior circulation and a reduction in long-term stroke risk.[15,16] Thus far, for both patient categories, little is known on how CEA affects the preoperative anatomy and function of the circle of Willis.

The purpose of the present study is to investigate changes in the primary collateral flow pattern and diameter of the individual vessel segments in the circle of Willis before and after CEA. To study the effect of severe ICA lesions on the

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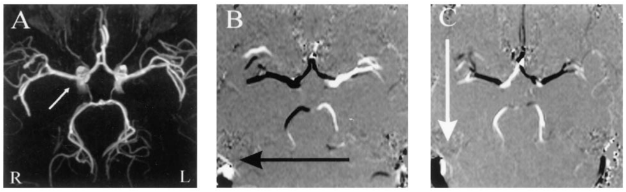

Figure 1. Example of MRA investigation in a patient with 75% stenosis of the right ICA. A, Maximum intensity projection of the circle of Willis as investigated with 3D TOF MRA (arrow indicates side of ICA stenosis). B and C, The 2D PC images phase encoded in the left-right (LR) and the anteroposterior (AP) direction, respectively. Middle, Blood flowing to the patient's right is black; blood flowing to the patient's left is white. Right, Blood flowing in the anterior direction is black; blood flowing in the posterior direction is white. These 2D PC images indicated collateral flow via the A1 segment toward the patient's right ICA, and no collateral flow was detected via the PCoA.

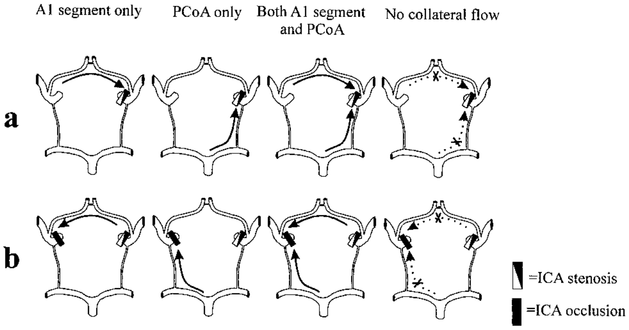

Figure 2. Four patterns of collateral flow via the circle of Willis defined as (a) flow toward the operated side, ICA stenosis, in patients with unilateral symptomatic carotid stenosis and (b) flow toward the nonoperated side, ICA occlusion, in patients with asymptomatic ICA stenosis and a contralateral symptomatic ICA occlusion.

contralateral side, these investigations were performed in a group of patients with unilateral symptomatic ICA stenosis only and in a group of patients with severe ICA stenosis with contralateral (symptomatic) ICA occlusion.

Methods

Subjects

Forty-eight patients (38 men, 10 women; mean±SD age, 64±9 years) with 70% to 99% stenosis of the ICA (on left side, n=26) were included in the study. Grading of ICA obstruction was performed with intra-arterial digital subtraction angiography according to NASCET criteria[17] (n=42) and/or duplex ultrasonography (n=6). All patients were selected by the Department of Vascular Surgery or Neurology as candidates for CEA. Of the 48 patients, 30 had severe (70% to 99% reduction in diameter) symptomatic ICA stenosis without significant ICA stenosis on the nonoperated side (median degree of stenosis on the contralateral side, 0%; first [Q1] to third quartile [Q3], 0% to 40%). These patients had transient monocular blindness (n=7), hemispheric transient ischemic attacks (n=14), or minor ischemic stroke (Rankin grade 3 or better)[18] (n=9). The remaining 18 patients underwent CEA of their asymptomatic 70% to 99% ICA stenosis because of a contralateral symptomatic ICA occlusion. Of these 18 patients, 3 had transient monocular blindness, 7 had hemispheric transient ischemic attacks, and 8 had minor ischemic stroke. Patients were investigated before CEA (median, 7 days; Q1 to Q3, 1 to 17 days) and after CEA (median, 4.5 months; Q1 to Q3, 112 to 167 days).

A control group was recruited from a population-based study[19] and consisted of 56 age-matched volunteers without vascular abnormalities in the cerebripetal arteries on MR angiography (MRA) (22 men, 34 women; mean±SD age, 66±3 years). We obtained informed consent from all patients and control subjects, and the hospital's commission on scientific research on human subjects approved the study protocol.

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 (2D PC) sagittal localizer survey through the circle of Willis, followed by a 3-dimensional time-of-flight (3D TOF) MRA sequence. The 3D TOF MRA scan (see Figure 1A) was made 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, 256×256; number of excitations, 2; slice overlap, 0.6 mm; number of slices, 50; and stack volume, 30 mm. With TOF MRA, a high signal is obtained in the arteries of the circle of Willis because the flowing blood is continuously refreshed. Diameter measurements of the A1 segments of the anterior cerebral arteries (ACAs), PCoA, and P1 segments of the posterior cerebral arteries were performed on the individual source slices of the 3D TOF MRA data set with a workstation (Easy Vision, Philips Medical Systems).[20] To determine the mean diameters for the control group, the left and right circle of Willis segments of the control subjects were averaged.

A 2D PC directional-flow MRA scan (see Figure 1B and 1C) was made with the following imaging parameters: repetition time/echo time: 16 ms/9.1 ms; flip angle, 7.5°; field of view, 250×250 mm; matrix size, 256×256; number of excitations, 8; slice thickness, 13 mm; single slice; and velocity sensitivity, 40 cm/s. Collateral flow patterns were analyzed according to the method of Schomer et al.[8] Figure 2 shows how the patterns of collateral flow via the circle of Willis were categorized. With 2D PC MRA, blood flowing in opposite directions causes opposite phase changes in the MR signal, which is the property used in the present study to detect reversed flow in the A1 segment and posterior-to-anterior flow via the PCoA (Figure 1B and 1C). Directional flow images were evaluated independently by 2 investigators (J.H. and J. vd G.) who were blinded to the status of the patient. Discrepancies between the 2 investigators were reevaluated in a consensus meeting.

Statistical Methods

In the patient groups, each side of the circle of Willis was designated the operated or nonoperated side. Differences in pattern of collateral flow via the circle of Willis before and after CEA were analyzed with Fisher's exact test or the χ^2 test with Yates' correction. Because the diameters of the circle of Willis components were not normally distributed, analysis of differences in vessel diameters between control subjects and patients was performed with the Mann-Whitney *U* and Wilcoxon rank-sum *W* test. Individual differences between vessel diameters before and after CEA were analyzed with the paired Wilcoxon test for 2 related samples. Vessel diameters were expressed as mean±SEM. A value of $P<0.05$ was considered statistically significant.

Results

In the total group of 48 patients, no stroke occurred in the postoperative period until the second MRI examination (4.5 months). Table 1 shows the diameter of the A1, PCoA, and P1 segment on the operated and nonoperated sides in patients with unilateral ICA stenosis. Before CEA, the PCoA and P1 segments on both sides demonstrated a significantly larger diameter compared with control subjects. Although both A1 segments of the ACA demonstrated a larger diameter compared with control subjects, this difference was not statistically significant. After CEA, the size of all vessel diameters

TABLE 1. Vessel Diameters in Patients With a Unilateral Symptomatic ICA Stenosis

Circle of Willis Segment	Before CEA, mm	After CEA, mm	Paired Difference (*P*)	Control Subjects, mm
A1, operated side	1.42±0.09	1.20±0.03	<0.05	1.28±0.05
A1, nonoperated side	1.39±0.08	1.16±0.04	<0.01	1.28±0.05
PCoA, operated side	0.91±0.10†	0.54±0.08	<0.001	0.57±0.06
PCoA, nonoperated side	0.90±0.09†	0.61±0.08	<0.001	0.57±0.06
P1, operated side	1.61±0.08*	1.26±0.05	<0.001	1.35±0.06
P1, nonoperated side	1.65±0.08*	1.27±0.05	<0.001	1.35±0.06

Vessel diameter (±SEM) of the A1, PCoA, and P1 segments on the operated side (CEA and symptomatic side) and nonoperated side in patients with a unilateral ICA stenosis before and after CEA (n=30) and in control subjects (n=56).

*$P<0.05$, †$P<0.01$, patients vs control subjects.

decreased significantly, falling into the range of the control subjects. Before CEA, 4 of 30 patients had collateral flow via the A1 segment on the operated side. After CEA, this normalized in all 4 patients (Fisher's exact test, $P=0.03$). Before CEA, the prevalence of collateral flow via the anterior circle of Willis in patients with unilateral ICA stenosis was significantly increased compared with control subjects (13% versus 0%; $P=0.015$). Before and after CEA, in 0 of the 30 patients, collateral flow via the PCoA toward the symptomatic ICA stenosis was found. In patients with unilateral ICA stenosis, no significant difference was found in the mean degree of ICA stenosis between patients with collateral flow (75%; 4 in 70% to 80% category) and patients without collateral flow (78%; 23 in 70% to 80% and 3 in 80% to 90% category) via the circle of Willis.

Table 2 shows the diameters of the A1, PCoA, and P1 segments on the operated side and nonoperated side (symptomatic and occluded side) in patients with ICA stenosis and contralateral ICA occlusion. Before and after CEA, all vessels demonstrated a larger diameter compared with control subjects, except for the A1 segment on the nonoperated side. The mean diameter of the A1 segment in control subjects was 1.28 mm (95% CI, 1.19 to 1.37) compared with 1.50 mm (95% CI, 1.30 to 1.70) in patients on the operated side and 1.23 mm (95% CI, 1.11 to 1.35) on the nonoperated side. The diameter of this A1 segment increased significantly ($P<0.05$) after CEA. Furthermore, CEA resulted in a significant overall increase in collateral flow in the circle of Willis (χ^2, $P=0.02$; Figure 3). More specifically, in patients who did not have collateral flow via the anterior circle of Willis before CEA, CEA resulted in a significant increase in collateral flow in the A1 segment on the nonoperated side (Fisher's exact test, $P=0.003$).

Although in patients with contralateral occlusion an overall significant increase in diameter of the A1 segment on the nonoperated side (symptomatic and occluded side) was observed, the largest diameter increase was found in patients who developed collateral flow via the anterior circulation after CEA (Figure 4). In these patients, a significant diameter increase was found on the operated side also. In patients who already had collateral flow before CEA or did not develop collateral flow in the anterior circulation after CEA, no significant diameter changes were observed.

Discussion

The most important findings of this study are 2-fold. First, in patients with unilateral ICA stenosis, the preoperative vessel diameters in the circle of Willis on the operated and nonoperated sides are increased compared with control subjects and return to control values after CEA. In this patient group, CEA resulted in a normalization of the collateral flow in the circle of Willis. Second, in patients with ICA stenosis and contralateral ICA occlusion, all vessels except the A1 segment on the nonoperated side showed a significantly increased vessel

TABLE 2. Vessel Diameters in Patients With Asymptomatic ICA Stenosis and Contralateral Symptomatic ICA Occlusion (mm)

Circle of Willis Segment	Before CEA, mm	After CEA, mm	Paired Difference (*P*)	Control Subjects, mm
A1, operated side	1.50±0.10*	1.64±0.10†	NS	1.28±0.05
A1, nonoperated side	1.23±0.06	1.48±0.06	<0.05	1.28±0.05
PCoA, operated side	0.95±0.09*	1.09±0.14*	NS	0.57±0.06
PCoA, nonoperated side	1.02±0.09*	1.11±0.09*	NS	0.57±0.06
P1, operated side	1.65±0.06†	1.66±0.08*	NS	1.35±0.06
P1, nonoperated side	1.63±0.06†	1.64±0.07*	NS	1.35±0.06

Vessel diameter (±SEM) of the A1, PCoA, and P1 segments on the operated side (and asymptomatic side) and nonoperated side (occluded and symptomatic side) in patients (n=18) with ICA stenosis and a contralateral ICA occlusion and in control subjects (n=56).

*$P<0.05$, †$P<0.01$, patients vs control subjects.

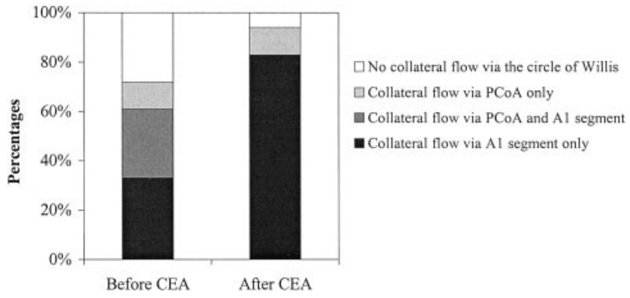

Figure 3. Preoperative (left) and postoperative (right) pattern of collateral flow via the circle of Willis in patients with ICA stenosis and a contralateral symptomatic ICA occlusion (n=18). Postoperatively, the prevalence of collateral flow via the anterior circle of Willis toward the nonoperated side (occluded and symptomatic side) was significantly increased ($P<0.01$).

diameter that did not change after CEA. However, CEA resulted in a significant increase in the prevalence of collateral flow via the ACoA and a significant increase in diameter of both A1 segments in the subgroup of patients in whom collateral flow was visualized after CEA.

The present study shows that in patients with unilateral ICA stenosis only, CEA resulted in a normalization of both the anatomy and collateral function of the circle of Willis. Previously, an association was found between the presence of collateral flow via the circle of Willis before CEA and long-term outcome after CEA.[14] Consequently, one would expect that preoperative differences in collateral ability of the circle of Willis remain present after CEA. However, we hypothesize on the basis of the presented data that in the postoperative situation, after removal of the flow obstruction, the unneeded collateral flow may disappear with no change in the underlying presence of the potential collaterals, which may become of clinical significance when asymmetries between the flow in the 2 carotids become present, eg, when a restenosis occurs. Still, the presence of preoperative collateral flow may influence stroke risk indirectly because the presence of collateral flow is associated with a more favorable

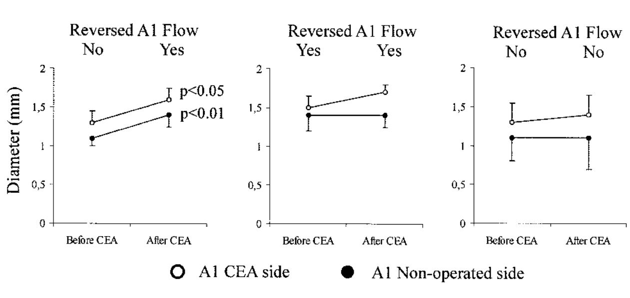

Figure 4. Vessel diameters (mean±SEM) of the A1 segments of the ACA before and after CEA on the operated side (○) and nonoperated side (occluded and symptomatic side) (●) in patients with ICA stenosis and a contralateral symptomatic ICA occlusion according to the collateral flow patterns in the anterior circle of Willis. Left, Patients who developed collateral flow to the symptomatic side via the anterior circle of Willis after CEA (n=7). Middle, Patients who did have collateral flow to the symptomatic side via the anterior circle of Willis before and after CEA (n=8). Right, Patients who did not have collateral flow to the symptomatic side via the anterior circle of Willis before and after CEA (n=3). Probability values represent the paired difference of mean vessel diameters before versus after CEA.

cardiovascular risk profile with a lower prevalence of hypertension and a lower prevalence of intracranial stenosis.[14,21]

Compared with patients with unilateral ICA stenosis, patients with severe ICA stenosis and a contralateral ICA occlusion are especially at risk for an ischemic event.[22] In these patients, the purpose of CEA is to reduce the risk of thromboembolism and to improve the hemodynamic status on the side of the occluded ICA. Several studies have shown the beneficial effect of CEA for patients with a contralateral ICA occlusion.[22,23] However, it is important to mention that a randomized trial of CEA in patients with contralateral symptomatic ICA occlusion has never been conducted. Furthermore, some reports found a relatively high perioperative stroke risk associated with CEA compared with the expected natural outcome when an asymptomatic ICA stenosis is operated on with ICA occlusion on the contralateral side.[22] Postoperatively, the long-term outcome in patients with contralateral ICA occlusion will depend largely on the presence of collateral flow via the circle of Willis with the lowest stroke risk in patients with adequate collateral flow toward the hemisphere distal to the ICA occlusion.[24]

In patients with ICA stenosis and contralateral ICA occlusion, the present study shows an increase in collateral flow via the anterior circle of Willis and a decreased prevalence of collateral flow via the posterior circle of Willis after CEA compared with the preoperative status. This shift in collateral flow pattern after CEA suggests that the degree of stenosis and the presence of cross flow via the primary collateral pathways are closely related, as suggested previously by Powers.[25] In the present study, the higher postoperative prevalence of collateral flow via the ACoA and the lower prevalence of collateral flow via the PCoA may be caused by a increase in blood pressure on the operated side. For the postoperative situation with an occlusion on the nonoperated side, several model-based studies already predicted that the ACoA is the preferred collateral pathway when the circle of Willis is intact.[10,26]

In general, MRA is regarded as a reliable technique to evaluate both the anatomy and function (flow direction) of the circle of Willis and high correlations have been found between non–contrast-enhanced MRA and angiography or transcranial Doppler ultrasonography measurements.[27,28] Patrux et al[27] showed that with techniques similar to those used in our study, the sensitivity of 2D PC MRA to detect collateral flow via the anterior circle of Willis was 89% with conventional angiography as the gold standard.[27] However, when blood flow is relatively low, collateral flow may be missed. Moreover, when blood flow is low, MRA diameter measurements may slightly underestimate the actual value because of the very slow flow near the vessel wall. Recently, several transcranial Doppler ultrasonography studies examined the collateral flow via the circle of Willis in patients in whom either a balloon test occlusion or permanent ICA occlusion was performed for the treatment of giant aneurysms of the carotid artery. These studies showed that the collateral function of the circle of Willis can predict the tolerance of ICA occlusion.[29,30]

In conclusion, in patients with unilateral ICA stenosis, the anatomic features and collateral flow patterns of the circle of

Willis normalized after CEA. It may be presumed that these potential collaterals again become clinically significant when asymmetries between the flow in the 2 carotids become present, eg, when a restenosis occurs. On the other hand, in patients with contralateral occlusion, CEA resulted in an increased prevalence of collateral flow and a subsequent increase in collateral vessel diameter.

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