Predicting the Effect of Carotid Artery Occlusion During Carotid Endarterectomy

Comparing Transcranial Doppler Measurements and Cerebral Angiography

Dennis D. Doblar, PhD, MD; Nataliya V. Plyushcheva, PhD, MD; William Jordan, MD; Holt McDowell, MD

Background and Purpose—We correlated the mean transcranial Doppler blood flow velocity (FVm) during carotid endarterectomy with the functional collateral pathway(s) documented by angiography.

Methods—Three patient groups were established: group 1 was dependent on the anterior communicating artery, group 2 on the anterior communicating artery and ipsilateral posterior communicating artery, and group 3 on the ipsilateral posterior communicating artery. Continuous middle cerebral artery FVm and electroencephalographic monitoring were performed in 45 patients during carotid endarterectomy.

Results—Clamped FVm was lowest in group 3 at 17 ± 9 cm/s versus 36 ± 16 and 33 ± 11 cm/s for groups 1 and 2 (P < 0.01). FVm values in groups 1 and 2 were similar. There was significant cerebral arterial vasodilation in group 3 patients on the basis of a pulsatility index of 0.38 ± 0.15. The maximum FVm after clamp release was similar among the 3 groups. Normalized blood flow velocity 1 minute before release of the clamp was increased from the minimum flow velocity after clamping only in group 1 and 2 patients.

Conclusions—The ipsilateral posterior communicating artery is a minor collateral pathway during acute carotid occlusion that contributes little to the collateral flow if there is a functional anterior communicating artery. Collateral flow through the middle cerebral artery is not recruited during occlusion in group 3 patients. The reperfusion FVm transient is independent of the primary collateral pathway. Documentation of functional collateral pathways on the basis of Doppler or angiographic examination may be advantageous in future studies since it can provide the basis for comparison among studies. (Stroke. 1998;29:2038-2042.)

Key Words: carotid artery occlusion ■ carotid endarterectomy ■ collateral circulation ■ ultrasonography, Doppler, transcranial

The neurological deficits after temporary carotid artery occlusion and release during carotid endarterectomy (CEA) are the result of ischemia, emboli, combinations of both, or sustained hyperperfusion with or without superimposed embolic events in the postocclusion period. Monitoring the brain during surgical carotid occlusion to ensure adequate cerebral perfusion through collateral vessels is accomplished with the use of various combinations of electroencephalography (EEG), transcranial Doppler ultrasonography (TCD), near-infrared cerebral oximetry, somatosensory evoked potentials, and by communicating with the awake patient who receives local anesthesia and sedation.

The clinical tolerance of spontaneous, progressive carotid occlusion in stroke patients depends on the number of functional collateral pathways. The tolerance of acute carotid artery clamping or balloon occlusion depends on the functionality of the intracranial and extracranial cerebral collateral circulation and may be predicted with the Doppler carotid artery compression test. The finding of an impaired or exhausted response of cerebral blood flow to CO2 challenge is correlated with a higher incidence of ischemic stroke due to inadequate collateral circulation. The effect of contralateral stenosis or occlusion on the CO2 response is multifactorial. It is dependent on whether or not the patients were symptomatic, the type of stimulus used, and the specifics of the intracranial collateral circulation. In a study of stroke patients, contralateral stenosis of the internal carotid artery (ICA) did not correlate with CO2 reactivity or clinical outcomes, suggesting that intracranial collateral pathways in this group of patients play the more important role in...
compensation for reductions in arterial inflow. Muller and Schmrigk also concluded that vasomotor reactivity was not affected by the presence of contralateral ICA stenosis and that the results depended on the nature of the stimulus applied, either acetazolamide or Pco₂ increase through breath holding. In patients with ipsilateral ICA stenosis and contralateral ICA occlusion, however, vasomotor reactivity was low bilaterally, and in patients with reversed ophthalmic artery (OA) flow the vasomotor response was lower on the same sides than it was in patients with a normal direction of OA flow. Barzo et al reported normal or moderately reduced cerebrovascular reserve in half of their patients with unilateral or bilateral high-grade stenosis.

The functionality of the intracranial collateral circulation through the circle of Willis or extracranial collaterals may be assessed by cerebral angiography or by TCD examination. The carotid compression test, which mimics intraoperative carotid occlusion, is not practiced in some centers because of the risk of intra-arterial embolization to the brain. Since our patients were scheduled to undergo carotid cross-clamping as part of the surgical procedure, we did not perform the compression test. However, we did monitor Doppler blood flow velocity (FV) to judge the adequacy of the collateral circulation after the application of the carotid artery cross-clamp.

We performed a comparison of the results of brain monitoring with the findings of cerebral angiography before surgery to seek a correlation between FV and the functional intracranial collateral pathways. Mean middle cerebral artery (MCA) flow velocity (FVm) was monitored before, during, and after surgical common carotid artery occlusion to determine the change in FVm with the stages of surgery. The percent change in FVm from baseline to occlusion level and the return to full flow after cross-clamp release were compared with the pathway of cerebral collateral circulation as determined by preoperative 4-vessel angiographic data.

### Subjects and Methods

Institutional Review Board approval and informed consent were obtained. Procedures followed were in accordance with institutional guidelines. Forty-five patients underwent routine 4-vessel cerebral angiography before CEA. The criteria of the North American Symptomatic Carotid Endarterectomy Trial were used for the determination of percent stenosis. On the basis of the angiography results, patients were divided into 3 groups. In group 1 patients the anterior communicating artery (ACoA) was the only collateral. In group 2 both the ACoA and the posterior communicating artery (PCoA) ipsilateral to the side of the surgery were functional. In group 3 the ipsilateral PCoA was the functional collateral vessel.

Seven patients underwent surgery awake, receiving local anesthesia and intravenous sedation with combinations of midazolam, fentanyl, and propofol with supplemental oxygen through nasal cannulas. Thirty-eight patients received general anesthesia with the use of thiopental 3 to 5 mg/kg or etomidate 0.3 to 0.5 mg/kg for induction of anesthesia. Intermittent boluses of low-dose fentanyl or sufentanil were used for analgesia to supplement inhalational anesthesia with oxygen/air/nitrous oxide and either isoflurane or desflurane. Muscle relaxation was achieved with either atracurium or vecuronium. Low-dose intravenous midazolam (20 to 50 μg/kg) was administered for amnesia. The patients’ tracheas were intubated, and end-tidal CO₂ was maintained in a narrow range throughout the study periods by adjustments in minute ventilation. Inspired and expired anesthetic agent concentrations were monitored on a breath-by-breath basis.

The attending anesthesiologists were not advised of the status of the intracranial collateral circulation on the basis of the angiography data. Standard anesthesia monitoring included (1) intra-arterial blood pressure through an indwelling 20-gauge radial artery catheter; (2) ECG; (3) end-tidal O₂, CO₂, N₂O, and inhalational anesthetic agent concentrations; and (4) oxyhemoglobin saturation monitored by means of a pulse oximeter placed on the patient’s finger. Study data recorded included TCD velocities, TCD spectra, continuous 10-channel raw EEG, arterial blood pressure, expired gas concentrations, and anesthetic agent concentration at key points during the surgery. A certified EEG technologist monitored the EEG during the operation. The EEG data were reviewed and interpreted by a neurologist not present in the operating room who was also unaware of the angiographic findings.

Before the induction of anesthesia, a Medasonics CDS or Medasonics Neurogard transcranial Doppler probe ( Nicolet, Inc) was secured with a commercial probe holder to the head over the temporal window to insonate the ipsilateral MCA. The timing and definition of each FVm measurement reported in Table 2 are shown in the table footnotes. FVm was calculated as FVm=diastolic FV + (systolic FV – diastolic FV)/3. The pulsatility index (PI) was calculated as PI= (systolic FV – diastolic FV)/FVm.

Baseline FVm data for each patient are the average of 3 to 5 steady state measurements either after induction of general anesthesia or after the performance of the regional and local nerve blocks. All data are presented as mean±SD. Data were analyzed for statistical significance with the Student’s t test and ANOVA for repeated measures. P<0.05 was considered significant.

### Results

Twenty patients were assigned to group 1, 15 to group 2, and 10 to group 3. Table 1 provides a summary of the angiographic and outcome data for all patients. In all group 3 patients, a nonfunctioning ACoA or anatomic hypoplasia or stenosis of the A1 segment of the anterior cerebral artery was found. Four patients were symptomatic in the preoperative period. In all groups, 5 patients experienced neurological events in the perioperative period, 1 of which was a stroke and 4 of which were transitory (Table 1).

### Table 1. Angiographic and Outcome Data

<table>
<thead>
<tr>
<th>Group</th>
<th>No. of Patients</th>
<th>Ipsilateral ICA Stenosis, %</th>
<th>Contralateral ICA Stenosis, %</th>
<th>Collateral Pathway</th>
<th>Neurological Deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>77±17 (35–96)</td>
<td>28±30* (0–80)</td>
<td>ACoA</td>
<td>2 (transient)</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>79±16 (35–99)</td>
<td>27±38* (0–80)</td>
<td>PCoA and ACoA</td>
<td>2 (transient)</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>78±18 (50–95)</td>
<td>71±38 (0–100)</td>
<td>PCoA</td>
<td>1 (stroke)</td>
</tr>
</tbody>
</table>

Functional collateral pathways were determined by cerebral angiography. PCoA indicates posterior communicating artery ipsilateral to the surgical site for endarterectomy. Four group 3 patients had contralateral ICA occlusion. Range of values is given in parentheses.

* Different from group 3 (P<0.01).
TABLE 2. Hemodynamic Data

<table>
<thead>
<tr>
<th>Group/Collateral Pathway</th>
<th>Minimum FVm During Occlusion, cm/s (% Baseline)</th>
<th>Average FVm During Occlusion, cm/s (% Baseline)</th>
<th>Prerelease FVm, cm/s (% Baseline)</th>
<th>Maximum FVm After Release, cm/s (% Baseline)</th>
<th>Average FVm 2 min After Release, cm/s (% Baseline)</th>
<th>PI During Occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/ACoA (n=20)</td>
<td>29±11* (53±15)</td>
<td>36±16* (65±16)</td>
<td>37±15* (70±36)§</td>
<td>68±25* (125±48)</td>
<td>51±19§ (93±22)</td>
<td>0.55±0.17</td>
</tr>
<tr>
<td>2/ACoA, PCoA (n=15)</td>
<td>30±10* (61±15)</td>
<td>33±11* (69±14)</td>
<td>35±10* (73±15)§</td>
<td>58±20 (110±38)</td>
<td>52±19 (98±32)</td>
<td>0.62±0.13</td>
</tr>
<tr>
<td>3/PCoA (n=10)</td>
<td>15±9* (24±3)</td>
<td>17±9* (27±5)</td>
<td>18±10* (31±11)</td>
<td>70±30 (138±86)</td>
<td>67±28 (125±70)</td>
<td>0.38±0.15</td>
</tr>
</tbody>
</table>

P (between groups)

<table>
<thead>
<tr>
<th></th>
<th>1–2 NS</th>
<th>1–3 &lt; 0.01</th>
<th>2–3 &lt; 0.01</th>
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<td>1–2 NS</td>
<td>1–3 &lt; 0.01</td>
<td>2–3 &lt; 0.01</td>
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<td>1–3</td>
<td>1–3 &lt; 0.01</td>
<td>1–3 NS</td>
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<td>2–3 &lt; 0.01</td>
<td>1–3 NS</td>
<td>2–3 NS</td>
</tr>
</tbody>
</table>

Data are mean±SD. Baseline value is average of FVm (3–5 measurements). Data in parentheses are as percentage of baseline value. FVm measurements were defined as follows: Minimum FVm during occlusion=single lowest value of FVm observed after carotid cross-clamping. Average FVm during occlusion=FVm, averaged during occlusion period. Prerelease FVm=single FVm value immediately before opening of carotid cross-clamp. Maximum FVm after release=single maximum FVm value observed after opening carotid cross-clamp. Average FVm 2 minutes after release=average of 3–5 FVm measurements beginning 2 minutes after opening carotid cross-clamp.

*Different from baseline within groups (P<0.01).
†Average FVm during occlusion (normalized to baseline) was greater than minimum FVm (normalized to baseline) (P<0.05).
‡Prerelease (normalized to baseline) was different from minimum FVm (normalized to baseline) (P<0.05).
§FVm 2 minutes after cross-clamp release was less than maximum FVm reached after cross-clamp release (P<0.01).

There was no difference in percentage of ipsilateral ICA stenosis, which averaged 77±17%, 79±16%, and 78±18%, respectively (mean±SD), for groups 1 through 3 (Table 1). Contralateral stenosis averaged 28±30%, 27±38%, and 71±38% in groups 1 through 3, respectively, with group 3 being higher than groups 1 and 2 (P<0.01). The degree of contralateral stenosis in group 3 patients ranged from 0% to 50% in 4 patients and 95% to 100% in 6 patients. For all 10 group 3 patients, there was poor correlation between percent contralateral stenosis and percent change in FVm (r=0.29). There was a decrease in FVm of 72±4% from baseline in the 4 group 3 patients with contralateral stenosis ≤50% and a decrease in FVm of 75±7% from baseline values in the 6 group 3 patients with contralateral stenosis ≥95%. The difference was not significant.

There were no significant differences in baseline FVm among groups 1, 2, and 3 (57±18, 49±17, and 62±37 cm/s, respectively). In comparisons of groups 1 and 3 and groups 2 and 3, the differences in minimum and average of FVm during occlusion were significant (P<0.001) (Table 2). In groups 1 and 2, the minimum FVm after clamping was different from the FVm immediately before clamp release when data normalized to baseline values were compared (P<0.05) (Table 2). The maximum differences in FVm after release of the carotid artery cross-clamp were not significant when groups 1 and 2, 1 and 3, and 2 and 3 were compared (Table 2). The PI during carotid occlusion differed between groups 1 and 3 (P<0.01) and groups 2 and 3 (P<0.001) but not between groups 1 and 2 (Table 2).

Within groups, FVm changes with the application and release of the carotid artery cross-clamp compared with baseline flows were significant (P<0.01) (Table 2). An intra-arterial shunt was used in 1 patient in group 1 who was awake and sedated for surgery. No patients in group 2 or 3 required the use of an intra-arterial shunt. Emboli were observed in the Doppler spectrum after the release of the external carotid artery (ECA) and the ICA in all 3 groups. No pattern of embolization was determined. In group 1, the maximum FVm reached after release of the cross-clamp (68±25 cm/s) was different from the average FVm during the first 2 minutes after release of the clamp (P<0.01) (Table 2). This difference was not observed in group 2 or 3 patients. The prerelease FVm normalized to baseline was greater than the minimum FVm reached after cross-clamping in groups 1 and 2 only.

The mean arterial blood pressure (MAP) and end-tidal PCO₂ data are summarized in Table 3. In groups 1 and 3, MAP was higher than baseline during occlusion. In group 3, MAP was higher than baseline after release of the cross-clamp (Table 3). There was no significant intragroup or intergroup differ-

TABLE 3. MAP and End-Tidal PCO₂

<table>
<thead>
<tr>
<th>Group</th>
<th>Collateral Pathway</th>
<th>MAP Baseline, mm Hg</th>
<th>MAP Occluded, mm Hg</th>
<th>MAP Release, mm Hg</th>
<th>CO₂ Baseline, mm Hg</th>
<th>CO₂ Occluded, mm Hg</th>
<th>CO₂ Release, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (n=20)</td>
<td>ACoA only</td>
<td>94±12</td>
<td>105±11*</td>
<td>97±14</td>
<td>33±3</td>
<td>33±2</td>
<td>33±2</td>
</tr>
<tr>
<td>2 (n=15)</td>
<td>ACoA and PCoA</td>
<td>97±16</td>
<td>99±10</td>
<td>94±10</td>
<td>33±2</td>
<td>33±2</td>
<td>33±2</td>
</tr>
<tr>
<td>3 (n=10)</td>
<td>PCoA only</td>
<td>93±13</td>
<td>111±11*</td>
<td>107±12*</td>
<td>33±4</td>
<td>33±3</td>
<td>33±3</td>
</tr>
</tbody>
</table>

P (between groups)

<table>
<thead>
<tr>
<th></th>
<th>1–2 NS</th>
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<td>2–3 &lt; 0.05</td>
<td>2–3 NS</td>
<td>2–3 NS</td>
</tr>
</tbody>
</table>

Data are mean±SD.

*Different from baseline (P<0.05).
ence in end-tidal PCO₂ for any period compared with baseline. End-tidal PCO₂ data are not included for awake patients.

Discussion

Patients with intracranial collateral blood flow through the ACoA, with or without a functional PCoA, have a smaller percent decrease in FVm during the period of carotid artery cross-clamping than patients dependent on the PCoA (Table 2). The presence of functioning ACoA and PCoA collateral pathways in the 15 patients of group 2 did not result in higher MCA FVm during carotid occlusion than in group 1 patients who lacked the PCoA. Patients with only PCoA collaterals experienced significantly greater decreases in FVm with cross-clamping than did those with ACoA collaterals (65±16% and 69±14% for groups 1 and 2 versus 27±5% of baseline for group 3). These data are consistent with previous findings that the collateral flow supplied by the posterior circulation alone was associated with a higher stroke rate than in patients with ACoA and PCoA collaterals.⁴,¹³ Our data also agree with the results reported for 175 CEA patients in whom clamping ischemia was seen with a FVm reduction to 21.8%¹⁴ and 15%¹⁵ of baseline.

The presence of 1 or more major collateral pathways supplying the ipsilateral hemisphere was positively associated with better outcome in 61 patients experiencing unilateral stroke.¹ Although retrograde blood flow through the ipsilateral OA was a significant collateral pathway in some of their patients, we did not measure FVm in the OA because the ECA was clamped. It has also been shown that patients without collateral capacity through the ACoA had the lowest stump pressure and were at increased risk for perioperative stroke.¹⁶ Similarly, the presence of a functional PCoA did not influence stump pressure during the period of carotid occlusion.¹⁶

The presence of the PCoA did not improve blood flow during carotid artery occlusion in group 2 compared with group 1. The collateral pathway common to both groups was the ACoA. During the period of carotid occlusion, the averaged, normalized FVm in group 1 was higher than the minimum FVm in group 1 (Table 2). Similarly, the normalized FVm prerelease in groups 1 and 2 was greater than the minimum, normalized FVm (Table 2), providing evidence of progressive recruitment of collaterals during the occlusion period.

Although we and others¹⁴,¹⁵ present data to the contrary, it has been suggested that the “safe limit” for a reduction of Doppler FVm in the MCA is 30% to 40% of the baseline value.²,¹⁷ This threshold is higher than those based on cerebral blood flow/TCD comparisons.¹⁶,¹⁸ It is possible that their patients who were intolerant of carotid occlusion lacked a functional ACoA and that pooling data from patients with PCoA as a primary collateral with those dependent on the ACoA resulted in a higher overall FVm threshold for shunting. Strict application of this lower limit of FVm would have resulted in the insertion of intra-arterial shunts in 9 patients of group 3. However, it should be noted that they found higher FVm after release in shunted patients, and shunts were used in 23 of 45 of their patients.²⁰ Two minutes after cross-clamp release, the average FVm was not different from the maximum FVm after release in groups 2 and 3 (Table 2).

The source of collateral circulation, ACoA, PCoA, or both, appears to have little effect on the transient response to reperfusion during CEA. We, like Naylor et al,²⁰ found no association between the degree of ipsilateral or contralateral stenosis, type of anesthesia, or occurrence of emboli on the magnitude of the transient hyperemia. We observed no sustained hyperemia in this group of patients that would place them at risk for stroke.²¹–²³ There was, however, evidence of near-maximal dilation during the cross-clamp period, as evidenced by the PI of 0.38±0.15 in group 3 patients.

The degree of hyperemia after cross-clamp release was similar among the groups. Careful blood pressure control after cross-clamp release may minimize passive hyperemia in patients with impaired cerebral pressure autoregulation,²⁴ such as those who lack a functional ACoA.¹³ The response to clamp release involves all collateral pathways such as the leptomeningeal arteries.¹²,¹⁸,²⁶

It is unlikely that differences in MAP influenced our results since there were no differences during baseline in groups 1 to 3 or during occlusion in groups 1 and 2, and MAP was highest in group 3 during occlusion where FVm was lowest (Tables 2 and 3). If pressure autoregulation had been impaired during carotid
artery cross-clamping, the effect of higher MAP would have minimized the differences between groups 1 and 2 compared with group 3. Similarly, there were no significant differences in arterial Pco2 that could explain any significant aspect of the observations in this study (Table 3). Five patients experienced neurological deficit in the immediate postoperative period; 4 were transient and 1 was permanent. In groups 1 and 2 the deficits were likely embolic in origin since FVm was ≧65% of baseline.

In conclusion, the posterior collateral circulation does not enhance FVm during carotid occlusion in patients with functional ACoA, nor does the PCoA contribute significantly to the maintenance of the adequate FVm in the MCA in patients with bilateral occlusion during cross-clamp. Other pathways that do not involve the circle of Willis, such as the lenticulostriate vessels and retrograde flow through the OA,27 may play a role in this population of patients who experience a slow, progressive occlusion of the ICAs before surgery. The ipsilateral ECA/OA collaterals, however, are not functional during common carotid cross-clamping, as in the present study. Recruitment of collateral flow through the MCA does not occur in patients dependent on the ipsilateral PCoA but does occur in patients with a functional ACoA. If MAP is well controlled during reperfusion, the transient hyperemia is independent of the collateral pathway.

Multimodality monitoring of patients undergoing CEA awake with sedation may enhance our understanding of the role of the collateral circulation and the ability of patients to tolerate relative ischemia during carotid occlusion. It would appear that the use of absolute thresholds for the use of intra-arterial shunts requires further investigation and consideration of the nature of the collateral circulation.

Acknowledgments
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References
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