Collateral Cerebral Vascular Resistance in Patients with Significant Carotid Stenosis

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SUMMARY This study tests the hypothesis that asymptomatic patients with hemodynamically significant internal carotid artery stenosis have a lower ipsilateral collateral cerebral vascular resistance and hence greater blood flow than their symptomatic cohorts. We measured internal carotid artery blood flow and cerebral perfusion pressures intraoperatively prior to and after carotid endarterectomy in 35 symptomatic and 10 asymptomatic patients with hemodynamically significant internal carotid artery stenosis. When the stenosis produced 30% or greater reduction in blood flow the calculated nondimensional normalized ratio of collateral cerebral vascular resistance to ipsilateral hemisphere cerebral vascular resistance was 1.15 ± 0.83 (mean ± SD) for the 10 asymptomatic patients and 2.98 ± 1.89 for the 35 symptomatic patients (p = 0.0044). For the subgroup of 22 patients with 50% or greater reduction in internal carotid artery blood flow the resistance ratios were 0.782 ± 0.541 for the 5 asymptomatic patients and 3.21 ± 2.26 for the 17 symptomatic patients (p = 0.029). These results suggest that asymptomatic patients with hemodynamically significant internal carotid artery stenoses have a lower collateral cerebral vascular resistance than their symptomatic cohorts. The low collateral resistance may provide an adequate collateral cerebral blood flow to prevent ischemia and symptoms.

MOST TRANSIENT ISCHEMIC ATTACKS and strokes attributed to carotid artery atherosclerotic disease are thought to be due to emboli. However, “high grade” or “hemodynamically significant” internal carotid artery stenosis producing low cerebral blood flow can cause cerebral ischemia and symptoms. Acute or progressive occlusion of an internal carotid artery will produce cerebral infarction in 25 to 35% of patients.1-3 The reason that most patients do not have a cerebral infarction when an internal carotid artery is permanently occluded is unclear, but it is generally assumed that the collateral cerebral blood flow is adequate to maintain cell viability and function. This hypothesis is tested by calculating collateral cerebral vascular resistance in patients who have hemodynamically significant internal carotid artery stenosis to see if the asymptomatic patients have a lower collateral vascular resistance than their symptomatic cohorts.

Methods

Cerebral vascular pressure and flow measurements were made in 45 patients with high grade internal carotid artery stenosis undergoing carotid endarterectomy. All patients had preoperative selective biplane carotid anterograms with extracranial and intracranial views. No patient had angiographic evidence of significant contralateral extracranial carotid artery stenosis or significant intracranial disease. Twenty-nine patients had a preoperative recent transient ischemic attack or mild stroke, six had nonlateralizing transient symptoms and ten were asymptomatic. The asymptomatic patients were operated upon because of the presence of high grade stenosis and planned cardiac or abdominal vascular surgical procedures. After exposure of the common, internal and external carotid arteries at the time of surgery, electromagnetic blood measurements (Statham Model SP2204 electrical zero) were made on the common and internal carotid arteries. Jugular venous pressure at the base of the brain was measured by a retrograde #8 or #5 French catheter in the internal jugular vein. Carotid back pressure and systemic mean arterial pressure were measured. At the completion of carotid endarterectomy and re-establishment of blood flow, electromagnetic flow measurements were repeated. All patients in this study had a pre endarterectomy to post endarterectomy internal carotid artery blood flow ratio of less than 0.70. That is, all patients in this study had at least a 30% reduction in cerebral blood flow due to internal carotid artery stenosis. Percent diameter stenosis measured from arteriograms was greater than 60% in all patients and averaged 87%. All operations were done with general anesthesia, 31 with halothane, nitrous oxide and oxygen and the remainder with balanced anesthesia. Normocarbia or slight hypocarbia was maintained with arterial pCO2 values between 32 and 38 mm Hg. Arterial oxygen saturation was greater than 95% in all patients.

Collateral cerebral vascular resistance was calculated as follows using a fluid mechanics model.4 Since mean pressure gradient equals vascular resistance times blood flow, ipsilateral hemisphere cerebral blood flow during carotid clamping is equal to the difference between mean systemic arterial pressure and carotid back pressure divided by the collateral vascular resistance. Similarly, ipsilateral hemisphere blood flow also equals the mean carotid back pressure minus cerebral venous pressure divided by the cerebral hemisphere vascular resistance. If Pc is the mean systemic arterial pressure, Pp is the mean carotid back pressure, Pp is the mean cerebral venous pressure, Rc is the cerebral vascular resistance, and Rh is the cerebral hemisphere vascular resistance, the two relationships for hemisphere collateral cerebral blood flow, Q, are:

\[ Q = \frac{(P_c - P_p)R_h}{(P_p - P_v)R_h} = \frac{(P_c - P_p)}{(P_p - P_v)} \]

Rearranging terms algebraically, we have \( R_h/R_c = (P_c - P_p)/(P_p - P_v) \). Or, the ratio of the collateral cerebral vascular resistance to...
cerebral hemisphere resistance is equal to the difference between mean systemic arterial and carotid back pressure divided by the cerebral perfusion pressure, \((P_c - P_v)\). The measured values of mean arterial pressure \((P_a)\), carotid back pressure \((P_b)\), and jugular venous pressure \((P_j)\), allow the nondimensional normalized ratio of collateral vascular resistance to cerebral hemisphere resistance, \(R_c/R_h\), to be calculated for each patient.

### Results

The table gives the means and standard deviations of the ratio of collateral to cerebral hemisphere vascular resistance for the three groups of patients. Patients with vertebral-basilar or nonlateralizing symptoms have similar collateral to hemisphere resistance ratios as those patients with symptoms of mild stroke and lateralizing transient ischemic attack. By contrast, the asymptomatic patients have statistically significantly lower resistance ratios. When patients with a 50% or more reduction in pre endarterectomy internal carotid artery blood flow are considered, the difference in resistance ratios between the asymptomatic and symptomatic subsets are even greater. We also calculated the ratio of collateral vascular resistance to cerebral hemisphere resistance in 13 symptomatic patients with non hemodynamically significant stenosis (pre to post endarterectomy blood flow ratio greater than 0.70). The mean resistance ratio for this group was 2.13 with a standard deviation of 1.81, not statistically different from the symptomatic hemodynamically significant patients by analysis of variance.

### Discussion

These data support the hypothesis that asymptomatic patients with hemodynamically significant internal carotid artery stenoses have lower collateral cerebral vascular resistance than do their symptomatic cohorts. Since most symptomatic patients may be symptomatic from emboli, not low blood flow, the wide distribution of resistance ratios found (table) in the symptomatic group is expected. Perhaps the patients with symptoms due to low blood flow are the subset with high resistance ratios. Whatever the reasons, there are enough symptomatic patients who have high resistance ratios to cause this group to have statistically significantly higher resistance ratios than the asymptomatic group.

Unfortunately, both angiography\(^5\) and oculoplethysmography\(^7,8\) are poor predictors of the adequacy of collateral circulation. If resistance ratio measurements could be obtained noninvasively or by catheter technique, then one could identify patients at risk for stroke should their carotid stenosis progress to impede flow. Examination of the equation for the collateral to cerebral hemisphere vascular resistance ratio, \((P_c - P_v)/(P_c - P_a)\), indicates that a low value of the resistance ratio is associated with a high carotid back or stump pressure, \(P_c\), and conversely. Others have suggested that high back pressures are associated with safe permanent occlusion of the common or internal carotid artery,\(^9\) and our results support this concept.

There are advantages of using the resistance ratio described herein. First, it normalizes, or removes, a number of variables that affect cerebral vascular resistance, namely the effect of \(pCO_2\), anesthesia and other pharmacal agents on both the collateral and cerebral hemisphere blood vessels, as well as the effect of blood viscosity and temperature on vascular resistance. Thus, the normalized nondimensional resistance ratio used herein allows comparison of values between patients.

The effect of autoregulation on these measurements should be examined. When there is high grade carotid stenosis it is safe to assume that the effective cerebral perfusion pressure above the circle of Willis will be reduced, triggering the normal autoregulatory adjustment which is reflex reduction in cerebral vascular resistance. This may change the ratio of collateral to hemisphere resistance. In this study we measured cerebral pressure\(^6\) when the ipsilateral common and external carotid arteries are clamped, which probably produces an autoregulatory response. While we do not know if maximal vasodilatation of the collateral and hemisphere vessels occurred in any patients, the stimulus was similar for all patients, that is, carotid clamping. It would be interesting to know the regional ipsilateral cerebral blood flow during carotid clamping in these patients as they might confirm our tentative conclusions regarding the symptomatic patients having higher collateral vascular resistance than the asymptomatic patients. Similarly, it would be of interest to know the specific source of collateral flow, namely flow from the epicerebral anastomoses of the posterior and anterior cerebral arteries and flow via the anterior circle of Willis and ipsilateral middle cerebral artery. However, our method of estimating the collateral vascular resistance from fluid mechanics and pressure measurements does not permit a breakdown of the total collateral resistance into its component parallel components. Clearly, the most important value is the total collateral resistance.
In order to interpret the data to mean that the collateral vascular resistance is lower in asymptomatic patients than in symptomatic patients one must assume that the hemisphere vascular resistance, which is the denominator of the resistance ratio, is similar between these two groups of patients. There is no data available to support the hypothesis that asymptomatic patients have higher nor that symptomatic patients have lower cerebral hemisphere vascular resistance than normal, and in the patients studied herein there was no angiographic evidence of significant intracranial stenosis or occlusion. Thus, any difference found in the resistance ratio between the two groups is most likely due to collateral resistance. Because it is rare to have an indication for carotid endarterectomy in asymptomatic patients with non hemodynamically significant internal carotid artery stenosis, we do not have any patients in this subgroup.

It has been shown that cerebral blood flows below 30 ml/min/100 gm (40% reduction in flow) for extended time periods may lead to cerebral ischemia, and that cerebral flow below 18 ml/min/100 gm (65% reduction in flow) is always associated with ischemia. Since total cerebral flow is internal carotid flow plus collateral flow, when internal carotid stenosis is significant enough to reduce flow by 40% or more then the collateral circulation must make up the difference. If the collateral resistance is high then collateral flow may not be adequate to maintain adequate blood flow and ischemia may result. The low resistance ratio in our asymptomatic patients with hemodynamically significant internal carotid stenosis suggests that they may be asymptomatic because they have adequate collateral flow to prevent ischemia.

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References

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