Correlation of Xenon-Enhanced Computed Tomography-Defined Cerebral Blood Flow Reactivity and Collateral Flow Patterns

Holly A. Smith, BS; Julie Thompson-Dobkin, DO; Howard Yonas, MD; Eric Flint, MD

**Background and Purpose** A chronic compromise of cerebral hemodynamics has been shown to identify a group of patients at an increased risk for stroke. Because autoregulation is implicated in a “steal phenomenon” induced by a vasodilatory challenge, it is assumed that these individuals would also have a severe compromise of primary collaterals and an increased dependence on leptomeningeal collaterals.

**Methods** Twenty-three patients with symptomatic cerebrovascular disease underwent angiography and xenon-enhanced computed tomographic cerebral blood flow studies before and after 1 g IV acetazolamide within 6 months of each other. Cerebral blood flow vasoreactivity was classified by whether cerebral blood flow increased (>5%) or was unchanged (±5%) (group 1) or fell by >5% (group 2) in any vascular territory. Angiographic collateralization was classified into four types: normal (type 1), willisian (type 2), ophthalmic (type 3), and leptomeningeal (type 4).

**Results** Twenty percent (2/10) of group 1 patients and 69% (9/13) of group 2 patients (P = .009) had leptomeningeal collaterals.

**Conclusions** A negative flow reactivity is significantly associated with a dependence on leptomeningeal collaterals and implies a state of maximal hemodynamic compromise. 

**Key Words** acetazolamide, cerebral blood flow, collateral circulation

Although symptomatic high-grade carotid stenosis is associated with an increased stroke rate, the primary cause is more often assumed to be an embolic and not a hemodynamic mechanism.1,2 The significance of a hemodynamic compromise of the cerebral circulation is far more difficult to assess.3 Even with detailed angiography it is difficult to predict if the remaining circulation will be able to adequately support metabolic needs, especially if a further compromise of perfusion pressure were to occur.3

The relation between cerebral circulation compromise and cerebral hemodynamics has been shown to be dependent on the extent of a potentially vast network of both the extracranial and intracranial collaterals.3-5 The presence of specific intracranial collateral patterns has been directly correlated with hemodynamic alterations defined by positron emission tomography (PET).3 A significant compromise of cerebral blood flow (CBF) is not commonly seen until the internal carotid artery is occluded and there is a lack of major collaterals in the circle of Willis. When the ophthalmic artery becomes the major source for hemispheric blood flow, a state of maximal vasodilatation is commonly found. When territorial flow becomes dependent primarily on leptomeningeal collaterals, not only is there evidence of maximal vasodilatation, but the oxygen extraction fraction (OEF) is increased.3 Blunting of the CBF response to vasodilatory challenge (compromised CBF reserves) has also been found in patients who have become dependent on ophthalmic collaterals4 and in patients found to have increased OEF.6,7

The identification of patients with compromised hemodynamics has become increasingly important with the recent evidence that these patients are at increased risk of subsequent stroke.8-11 Powers8 described a group of patients with an increased cerebral blood volume (CBV) and OEF who had a 28% (4/14) stroke rate at 2 years. Kleiser and Widder11 identified symptomatic patients with a blunted response to a transcranial Doppler vasodilatory challenge who had a 22% (8/37) 38-month stroke rate. Yonas et al10 reported a 36% 24-month stroke rate using stable xenon CBF studies accompanied by an acetazolamide challenge. In the latter study, identification of an increased stroke risk with decreased CBF to a vasodilatory challenge suggests that these patients may be highly dependent on leptomeningeal collaterals derived from adjacent vascular territories. This study seeks to confirm the assumption that patients with a steal response to vasodilatory challenge are dependent on leptomeningeal collaterals and have a maximal compromise of hemodynamic reserves.

**Subjects and Methods**

From a retrospective review of patients studied at the University of Pittsburgh Medical Center between 1984 and 1991, we identified 23 subjects who had undergone angiography, stable xenon-enhanced computed tomographic (Xe/CT) CBF studies with an acetazolamide challenge, and ocular pneumoplethysmography not more than 6 months apart. This
TABLE 1. Cerebral Blood Flow Reactivity and Collateral Flow Patterns In 23 Patients

<table>
<thead>
<tr>
<th>Pt No.</th>
<th>Xe/CT Cerebral VR Group</th>
<th>Angiographic Collaterals</th>
<th>Intracranial Disease</th>
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<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>...</td>
<td>WILL</td>
</tr>
<tr>
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<tr>
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</tr>
<tr>
<td>23</td>
<td>2</td>
<td>OA, LM</td>
<td>...</td>
</tr>
</tbody>
</table>

Pt indicates patient; Xe/CT, xenon-enhanced computed tomography; VR, vasoreactivity; WILL, willisian; LM, leptomeningeal; OA, ophthalmic artery; A1, A2, branches of anterior cerebral artery (ACA); and M1, M2, branches of middle cerebral artery (MCA). In cerebral VR group 1, cerebral blood flow increased (>5%) or was unchanged (±5%); in group 2, cerebral blood flow fell by >5%.

report examines the results of the comparative analysis of the CBF and angiographic data only.

Of the 23 patients, 13 were men and 10 were women, aged 38 to 88 years (mean, 65 years). Thirteen patients presented with stroke, 9 with transient ischemic attacks, and 1 for evaluation of bilateral carotid disease. Angiography identified 13 with bilateral carotid disease, 6 with unilateral disease, 2 with intracranial stenosis, and 2 with combined intracranial/extracranial disease. In all but 2 of the patients, the symptoms correlated with the side of greatest vascular narrowing.

Stable Xe/CT CBF Methodology

CBF was measured by means of the stable Xe/CT CBF technique described by Gur et al.,12-13 Within 5 minutes after a baseline CBF study, the patient received 1 g of acetazolamide by rapid intravenous infusion; approximately 20 minutes later, a repeat CBF measurement was made. The patient maintained the same position in the scanner for the duration of the two studies. CBF measurements were taken on two levels. Level 1 was at the basal ganglia, a level that provided bilateral mixed cortical CBF measurements of the anterior, middle, and posterior cerebral artery distributions. Level 2 was approximately 20 mm higher at the level of the centrum semiovale. This level also provided bilateral measurements of the anterior, middle, and posterior cerebral artery distributions. Contiguous 2-cm-diameter circular regions of interest (ROIs) were placed around the cortical mantel on each of the two CBF images. Individual ROIs encompassed approximately 314 voxels, each measuring 1x1x10 mm.1 CBF values for each vascular territory were computed by averaging the three to six ROIs within each territory on each level before and after acetazolamide administration. The change in CBF after the administration of acetazolamide was computed for each of the 12 vascular territories per study. Territories with >50% infarction defined by CT were excluded from analysis. Patients were classified into groups based on least change in CBF after acetazolamide in a single vascular territory. CBF group 1 included those with CBF increase of >5% or no change (±5%) in the territory of least reactivity. Statistical analysis revealed no difference between the group of patients with >5% and the group with ±5% least reactivity, and therefore the two were combined to form one group. CBF group 2 included those with CBF decrease >5% in any single territory (Table 1).

Cerebral Angiography

All 23 patients had two- to four-vessel, biplanar cerebral angiography. Eight patients underwent selective two-vessel angiography of the carotid circulation, and 15 had three- or four-vessel angiography inclusive of at least one vertebral artery injection. These studies were reviewed independently by a neuroradiologist (E.F.) and neurologist (J.T.-D.) who had no knowledge of the Xe/CT CBF studies. Angiograms were...
vasodilatation, has also been shown to correlate with
the observation of this study that patients who have
prior observations. Thus, a steal response to vasodila-
tory capacity, which implies a state of maximal
hemodynamics should have direct impact on clinical
management. An immediate therapeutic implication in
the group of patients identified with such a disorder
should be to maintain a normal or even elevated blood
pressure. In the subgroup of patients with recurrent
ischemic events within the hemodynamically threat-
ened region despite maximal medical therapy, extra-
cranial and intracranial surgical options that have the
potential to increase CBF should be considered. Fu-
ture studies will have to explore whether additional
treatments, either medical or surgical, will prove to be
of benefit for these patients.

The ability of the Xe/CT CBF technique to identify
patients at increased risk is encouraging because this is
a potentially widely available, noninvasive, and cost-
effective technology. Through its sensitivity to a de-
crease of CBF, the stable Xe/CT CBF technique has
allowed us to gain physiological insight into the relation
of CBV and OEF without the use of PET. 679 Through its
ability to identify anatomy with a flow analysis is
important for identification of areas of low flow due to
atrophy as distinguished from those due to compro-
mised supply. It is hoped that with the greater availability
of the Xe/CT CBF technique or other similarly capable
technology, patients with severe hemodynamic
compromise due to severe occlusive vascular disease will
be increasingly recognized, allowing earlier prophylactic
intervention and therapy that is guided by more patient-
specific information.

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effect of hemodynamically significant carotid artery disease on the
1987;106:27-35.
occlusion resting and hypercapnic flow related to collateral pat-

### Table 2. Type of Collateralization by Cerebral Vasoreactivity Grade

<table>
<thead>
<tr>
<th>Cerebral VR group</th>
<th>1 (Carotid)</th>
<th>2 (Willisian)</th>
<th>3 (Ophthalmic)</th>
<th>4 (Leptomeningeal)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
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<td>2</td>
<td>2</td>
<td>9*</td>
<td>13</td>
</tr>
</tbody>
</table>

VR indicates vasoreactivity. In cerebral VR group 1, cerebral blood flow increased (>5%) or was unchanged (±5%); in group 2, cerebral blood flow fell by >5%.

*P < .0009.
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