ELSEVIER

EVALUATION OF CEREBRAL BLOOD FLOW AND HEMODYNAMIC RESERVE IN SYMPTOMATIC MOYAMOYA DISEASE USING STABLE XENON-CT BLOOD FLOW

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Moyamoya disease is a vascular abnormality seen in children and adults characterized by progressive narrowing of the internal carotid, middle, anterior, and posterior cerebral arteries and the development of leptomeningeal and proximal internal carotid artery collaterals, which appear diaphanous on angiogram. Although adults tend to present with subarachnoid hemorrhage and children with ischemic events, the clinical sequelae in these two populations overlap. Expanding upon work done at this institution using stable xenon computer tomographic blood flow determinations with acetazolamide and carbon dioxide challenge to predict which population of patients with severe carotid disease and hemodynamic compromise would benefit from surgical intervention, we used similar rationale to determine which patients with moyamoya disease would likely benefit from revascularization. Data and outcome concerning four such patients make up the body of this report.

KEY WORDS
Moyamoya disease, Xenon cerebral blood flow, revascularization.

Idiopathic internal carotid artery (ICA) stenosis was originally described by Takeuchi in 1957 [61] and was eventually given the name moyamoya, the Japanese word for something hazy like a puff of smoke drifting in the air [54]. This vascular disease is characterized by primary narrowing of ICA and progressive stenosis of the middle, anterior, and in severe cases posterior cerebral arteries (MCA, ACA, PCA) [54]. As numerous collateral vessels develop from the more proximal ICA and the external carotid artery (ECA), the classic angiographic moyamoya appearance becomes apparent.

Symptoms of moyamoya disease relate directly to the abnormal vasculature. Children most commonly present with ischemic deficits, and adults develop intracranial hemorrhages; however, symptom crossover between the two age groups is common. The management of moyamoya disease has traditionally depended upon the angiographic appearance, the patient's age, and the presence of hypoperfused cerebral parenchyma. Hypoperfusion, per se, however, does not necessarily indicate the need for revascularization. Infarcted regions will, by definition, have reduced metabolic rates and concomitant low flows. On the other hand, areas that have normal requirements and inadequate blood supply and areas with marginal or normal baseline flows, which are compensating through maximally increased oxygen extraction and vasodilation would in our opinion benefit from a revascularization procedure. Available treatments include encephaloduroarteriosynangiosis (EDAS), extracranial-intracranial (EC-IC) bypass, encephalomyosynangiosis (EMG), placement of cranial burr holes over the affected region, encephaloomentalsynangiosis (EOS), encephalomyoarteriosynangiosis (EMAS), and the use of corticosteroids and calcium channel blockers. The technical aspects, indications, pitfalls, and results of each of these procedures have been discussed [1,5,9,10, 12,15,21,32,34–39,41,45,47,49,54,58,60,62].

Preoperative and postoperative patient evaluation includes neurologic examination, repeat angiography, computed tomography (CT), magnetic

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resonance imaging (MRI), single-photon emission-computed tomography (SPECT), proton emission tomography (PET), transcranial Doppler (TCD) and ^{133}xenon (Xe) or stable Xe inhalation blood flow measurement [4,11,19,24,25,42–44,59,63–67,69]. We used stable Xe-CT cerebral blood flow (CBF) along with acetazolamide (Diamox; Lederle) challenge or P_aCO_2 alteration to evaluate baseline and reserve CBF reserve in four moyamoya patients. Comparison of prechallenge and postchallenge CBF helped predict which patients would likely benefit from revascularization. We now report the decision process, procedure efficacy as demonstrated by postoperative blood flow studies, and patient follow-up.

Materials and Methods

CBF was measured in four patients (three adults, one child) with the clinical and angiographic diagnosis of moyamoya disease. The CBF protocol was identical to that used by Tarr et al [68], as originally described by Gur [18]. All four patients had baseline evaluations and two patients, who each had bilateral revascularization procedures, were also studied postoperatively. CBF was measured by means of the stable Xe-CT method [18]. All xenon-CT CBF measurements were performed on a GE 9800 CT scanner (General Electric Medical Systems, Milwaukee, WI) equipped with a CBF hardware and software package. CBF was measured at two different levels in each patient. Following the initial CBF study patients were subjected to a CO_2 alteration or administered intravenous acetazolamide (2 mg/kg). Repeat CBF studies were performed 20 minutes following drug administration.

CBF data for baseline and acetazolamide examinations at each level were analyzed using multiple, contiguous, region of interest circles (ROA) aligned along the outer cortical ribbon of both hemispheres. A diameter of 2.0 cm was chosen for the ROA circles to optimize inclusion of a mixture of gray and white matter.

On the basis of results from pre-Xe-CT and post-Xe-CT CBF studies with and without acetazolamide administration or CO_2 alteration one adult patient had bilateral STA-MCA bypasses and one pediatric patient had bilateral EDAS procedures. Two other patients with similar angiographic patterns did not have surgery.

Illustrative Cases and Results

Case #1

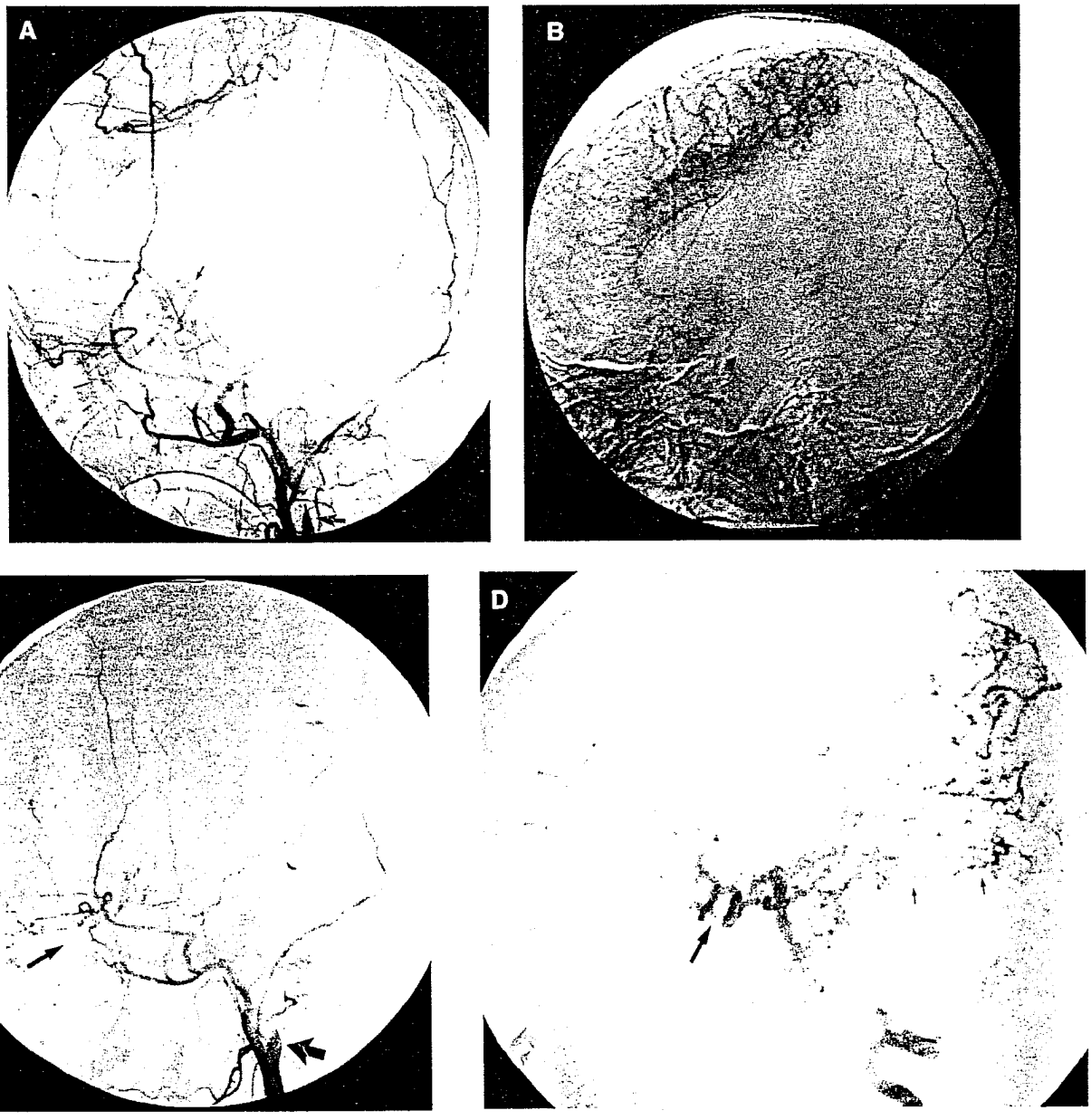
A 7-year-old boy presented with left hemiplegia and focal left hemispheric seizures. A CT scan confirmed the right hemispheric infarct. A right common carotid artery angiogram (CCA) (Figure 1 **A, B**) showed complete occlusion of the right ICA, just above the carotid bulb. The external carotid artery (ECA) via orbital collaterals reconstituted a short segment of the supraclinoid ICA. An enlarged middle meningeal artery (MMA) via meningeal collaterals along the falx cerebri reconstituted some of the distal anterior cerebral artery (ACA) territory. Left CCA and vertebral angiogram (Figure 1 **E, F**) showed the left ICA was occluded on this side also.

A Xe-CT CBF study was obtained at a P_aCO_2 of 51, 3 days after admission (Table 1). This study shows flows of 40–42 cc/100 g/minute in the left MCA distribution and 13–17 cc/100 g/minute in the right MCA distribution (Figure 1**C**). A repeat study at a P_1CO_2 of 30 showed flows of 27–31 cc/100 g/minute in the left MCA (27% decrease) and 21 cc/100 g/minute in the right MCA territory (55% increase). Similar increases in flow occurred in the right ACA territory (Figure 1 **D**) (Table 1).

An external ventricular drain was placed on the fourth day of admission and the following day the blood flow study was repeated using two different arterial pCO_2 levels (24 mm Hg vs 39 mm Hg) (Table 1). In the normal cerebrovascular system, CBF should increase upon raising P_aCO_2 14 T. However, in this patient CBF paradoxically decreased 38%–50% in the right MCA territory, 0–1% in the left MCA territory, 36%–75% in the right ACA territory, and 32% in the left ACA territory (Figure 1 **G, H**).

Having made the angiographic diagnosis of bilateral moyamoya disease, documented marginal blood flow in the left and right hemispheres, and demonstrated absence of vasodilatory reserve, a revascularization procedure was considered indi-

1 (**A**) Right lateral CCA showing complete occlusion of the right ICA just above the carotid bulb (*large arrow*). Note orbital collateral reconstitution of the supraclinoid ICA (*small arrow*). (**B**) Reconstitution of the distal ACA territory by meningeal collaterals from an enlarged MMA. (**C**) Case 1—A Xe-CT blood flow at the level displayed on the adjacent axial CT image. Blood flow in cc/100gm/minute is related to the displayed colors. The color chart on the left side illustrates the blood flow valued assigned to each color. (**D**) Xe-CT blood flow post-Diamox. (**E**) Left lateral CCA showing left ICA occlusion (*large arrow*). Small orbital collaterals to the supraclinolid ICA are visible (*small arrow*).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Case Preoperative, Postoperative	Parameter	Vascular Territory	Right Level I cc/100g/minute	Right Level II	Left Level I	Left Level II
I	$PaCO_2$ (mm Hg) 51	ACA	11	16	17	19
		MCA	13	17	42	40
		PCA	70	58	75	40
	$PaCO_2$ (mm Hg) 30	ACA	17	20	14	15
		MCA	21	21	31	27
		PCA	34	31	37	21
	% Δ CBF ($PaCO_2$ 51–30)	ACA	44	23	−19	−23
		MCA	55	19	−27	−32
		PCA	−51	−46	−51	−48
	$PaCO_2$ 24	ACA	27	19	22	17
		MCA	39	33	37	29
		PCA	43	27	30	20
	$PaCO_2$ 38	ACA	6	12	15	20
		MCA	20	20	37	29
		PCA	48	47	34	25
	% Δ ($PaCO_2$ 24–38)	ACA	−75	−36	−32	18
		MCA	−50	−38	0	0
		PCA	10	72	15	25
Post Bilateral EDAS	Baseline	ACA	14	13	32	27
		MCA	38	35	46	42
		PCA	67	56	72	41
	Post-Diamox	ACA	13	8	32	35
		MCA	48	47	52	54
		PCA	89	80	88	53
	% Δ	ACA	−12	−40	0	31
		MCA	27	31	16	26
		PCA	31	42	21	28
II	Baseline	ACA	17	13	19	16
		MCA	27	17	24	28
		PCA	55	33	63	41
	Post-Diamox	ACA	19	14	21	27
		MCA	22	16	23	16
		PCA	64	34	71	31
	% Δ	ACA	14	10	8	70
		MCA	−19	−10	−4	−43
		PCA	17	4	13	−23
L MCA/STA	Baseline	ACA	43	21	35	40
		MCA	40	25	35	45
		PCA	43	55	43	59
R MCA/STA	Baseline	ACA	30	39	28	34
		MCA	40	51	39	35
		PCA	47	41	47	36
III	Baseline	ACA	33	40	33	38
		MCA	66	45	63	57
		PCA	57	38	53	35
	Post-Diamox	ACA	48	45	52	64
		MCA	72	64	75	69
		PCA	72	65	82	43
	% Δ	ACA	46	10	57	69
		MCA	9	42	19	21
		PCA	27	73	83	22
IV	Baseline	ACA	27	14	22	10
		MCA	26	19	18	12
		PCA	26	20	20	16
	Post-Diamox	ACA	36	35	27	24
		MCA	31	41	28	29
		PCA	36	31	32	27
	% Δ	ACA	33	144	22	130
		MCA	17	120	54	142
		PCA	37	53	32	68

cated. On postadmission days 11 and 22 the patient had left and right EDAS procedures, respectively. He had no postoperative complications.

After discharge, the child received 3 weeks of rehabilitation. His deficits at the completion of inpatient rehabilitation consisted of a moderate left hemisphere that affected the arm greater than leg and a left abducens palsy. He was able to walk short distances independently. His intellectual status appeared to be at the preinfarct level.

Four months following EDAS revascularizations, the patient had a Xe-CT CBF study with and without intravenous acetazolamide administration. This study revealed the previously documented right frontal infarct and blood flows in the surrounding parenchyma in the mid-40s. Blood flow was augmented following Diamox administration in all areas except the infarcted region, indicating normal autoregulation and the presence of physiologic baseline vasodilatory reserve. There were no areas of vascular steal as seen in the preoperative P_aCO_2 altered studies (Table 1) (Figure 1 **I, J**). Follow-up magnetic resonance angiography (MRA) at 3 years demonstrated the bilateral EDAS with underlying vascular changes (Figure 1 **K**).

CASE #2

A 25-year-old woman was admitted to another hospital with paresthesias of the right arm and face, slurred speech, and a right hemiparesis. MRI showed a left frontal infarction and multiple periventricular white matter lesions. Angiography demonstrated left ICA, MCA, and ACA stenosis. She was treated for vasculitis with Cytoxan and Medrol. Despite this therapy, symptoms recurred. A brain biopsy revealed perivascular inflammation and necrosis. At age 26 she was admitted to our hospital with a right hemiplegia and expressive aphasia. Angiography showed bilateral severe intracranial ICA stenoses and prominent lenticulostriate vasculature indicative of moyamoya disease. A stable Xe-CT CBF study revealed abnormally low flows in the ACA and MCA territories bilaterally (Figure 2 **A**) (Table 1). A second CBF study, using acetazolamide challenge, demonstrated moderate flow augmentation in the ACA territories and a paradoxical 10%–19% and 4%–43% decrease in flow in the right and left MCA territories, respectively (Figure 2 **B**). Armed with the knowledge that this patient had only modest ability to vasodilate the ACA and PCA territories, and had steal from the MCA territories indicating maximum vasodilation and absent vasodilatory flow reserve, left and right STA-MCA bypasses were performed in two separate operations. Postoperative Xe-CT CBF study showed an increase in blood flow in the ACA and MCA territories bilaterally (Figure 2 **C**). She had continual improvement in her speech and her gait with no further ischemic episodes.

One year after surgery, the patient died from a subarachnoid hemorrhage.

CASE #3

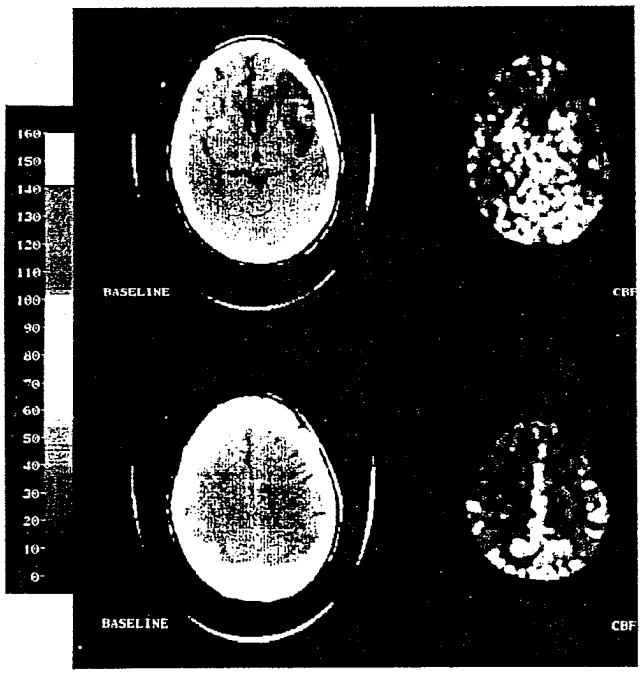
This 39-year-old woman presented with a left basal ganglia hemorrhage. Angiography showed right and left supraclinoid ICA stenosis, a left MCA that was reconstituted by fine pial vessels and flow through the left posterior communicating artery (Figure 9). A stable Xe-CT CBF study demonstrated normal flows through both hemispheres except in the hemorrhagic region (Figure 3 **A**). A stable Xe-CT CBF study following acetazolamide administration revealed diffuse-flow augmentation (Table 1) (Figure 3**B**). In the presence of adequate arterial dilatory reserve we thought that flow augmentation via a bypass procedure would provide no benefits. The patient has since been stable for 4 years.

CASE #4

This 56-year-old woman presented with a subarachnoid hemorrhage. Angiography showed right MCA and PCA occlusions with a collateral pattern suggestive of moyamoya disease. She was managed expectantly and followed. Nine months later she presented with weakness, expressive dysphasia, and incontinence. A CT scan revealed left frontal and temporal lobe atrophy. Xe-CT CBF studies with and without intravenous acetazolamide were performed (Table 1) (Figure 4 **A, B**). Due to the presence of blood flow augmentation following the acetazolamide administration, a revascularization procedure was not performed. She died the same month from subarachnoid hemorrhage. An autopsy was not performed.

DISCUSSION

Moyamoya disease is a slowly progressive unilateral or bilateral occlusive arterial condition that preferentially affects the distal ICA and the proximal MCA and ACA. The age distribution appears to be bimodal with peaks occurring in the first and fourth decades [54]. Children typically present with cerebral ischemia attributable to insufficient blood supply through existing collateral pathways. Symptoms include paresis or plegia, involuntary movement disorders, sensory disturbances, dysphasia, visual disturbances, headache, altered consciousness, seizures, apraxia, and altered cognitive abilities [33,54]. Seventy-seven percent of untreated children followed for at least 2 years



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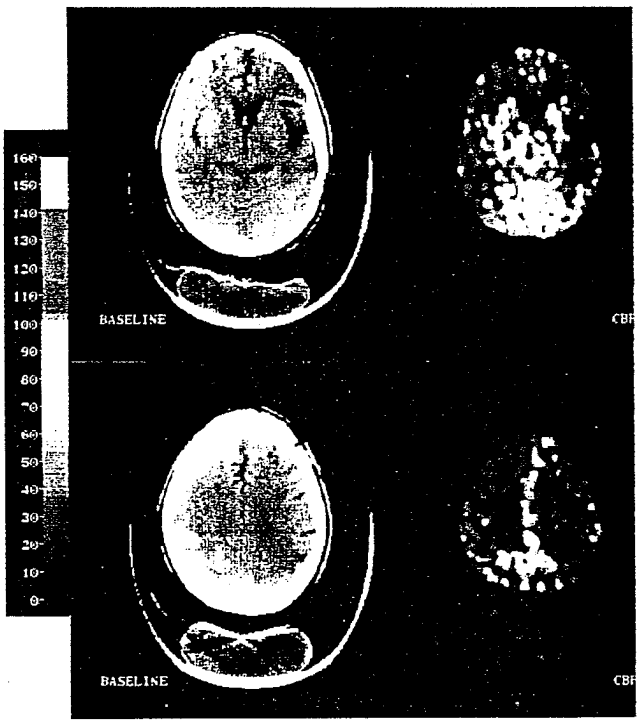

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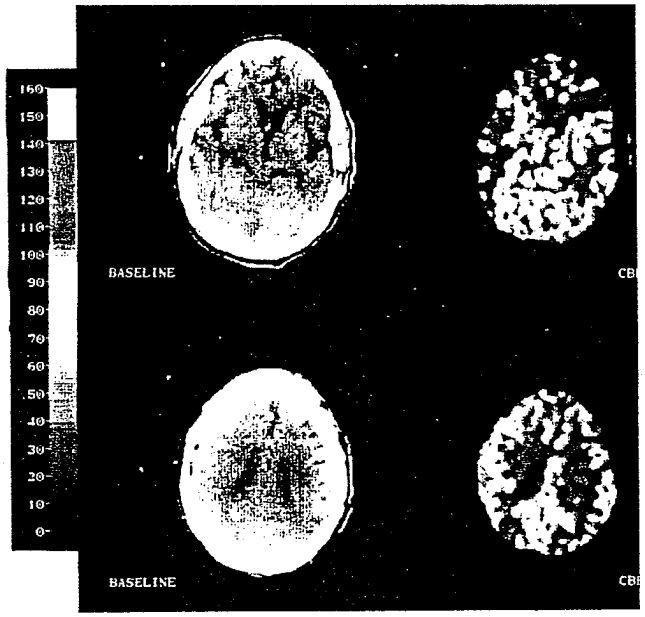

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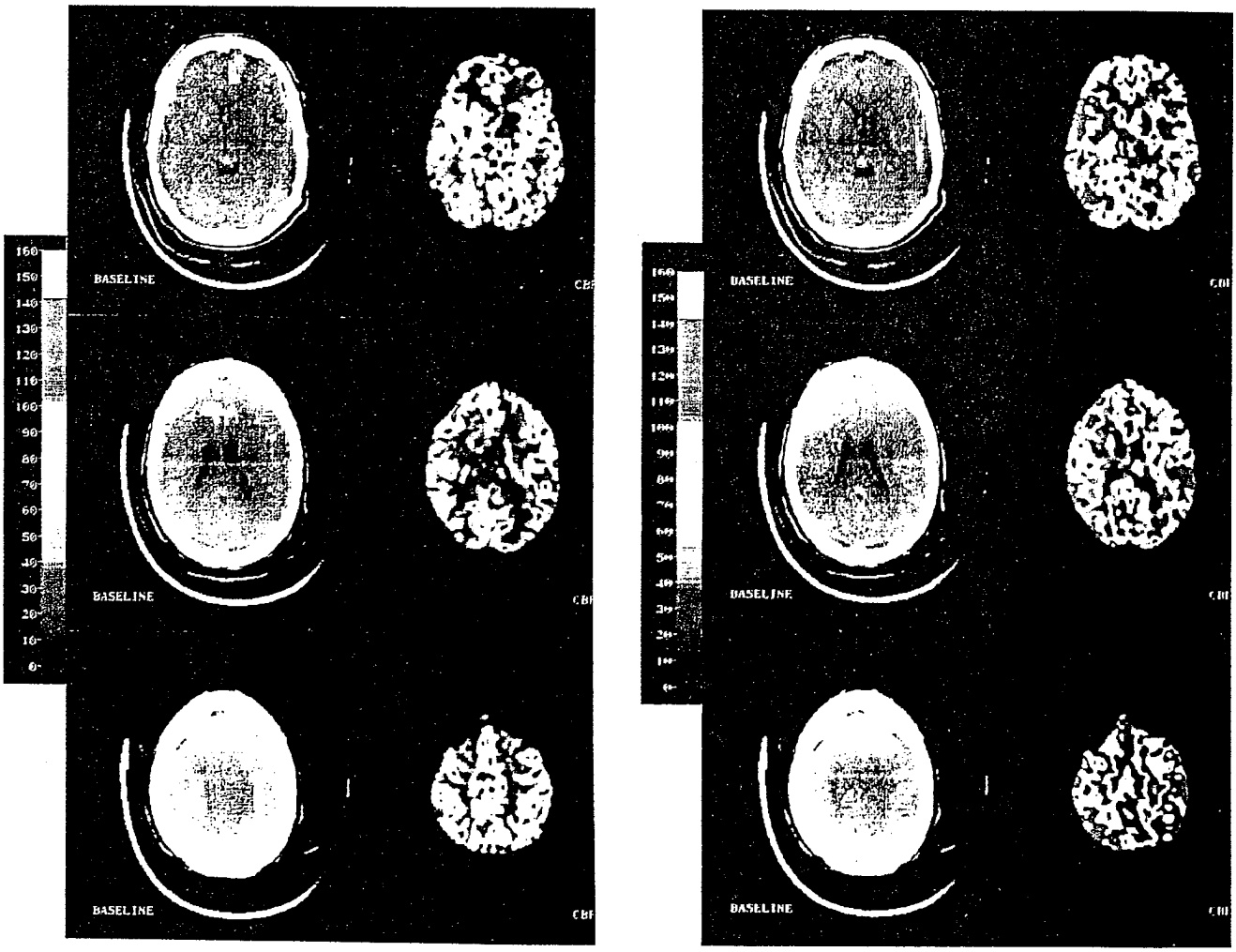
2 (**A**) Case 2. Baseline Xe-CT blood flow. (**B**) Case 2. Xe-CT blood flow post-Diamox. (**C**) Case 2. Postbypass Xe-CT blood flow.

can be expected to die or develop a severe neurologic deficit [45]. While adults can present with any of the previously listed symptoms, they most commonly succumb to an intracranial hemorrhage [33,54].

EVALUATION

The primary angiographic finding in moyamoya disease is gradual stenosis of the supraclinoid portion of one or both internal carotid arteries with extension of this stenosis to the circle of Willis and the middle, anterior and, eventually, posterior cerebral arteries [32]. Sources of collateral blood supply subsequently develop. These collaterals can be divided into four groups. Group 1 consists of branches from the supraclinoid carotid, ACA and PCA. Group 2 includes collaterals originating from the ophthalmic artery and cavernous sinus arteries. Group 3 consists of ECA branches and group 4 involves PCA leptomeningeal vessels [51].



A B

3 (A) Case 3—Baseline Xe-CT blood flow. (B) Case 3—Xe-CT blood flow post-Diamox.

The classic moyamoya vessels are those that supply the basal ganglia and thalamus [47]. These vessels initially arise from the ICA; however, with progressive stenosis of this vessel the PCA and ECA provide additional vascular collaterals. Eventually the PCA and infraclinoid carotid stenose, moyamoya vessels disappear, and the only visible bypasses are near the cranial vault in leptomeningeal vessels [32]. With the development of leptomeningeal transdural anastomoses (natural EC-IC bypasses), patients may enter a phase characterized by clinical stability or even improvement [32].

Findings on CT include low-density zones scattered in a honeycomb fashion, a dilated ventricle secondary to ischemia and volume loss, enlarged subarachnoid spaces, and poor visualization of the A1 and M1 vessel segments after contrast administration. Some enhanced CT scans even demonstrate the moyamoya vessels along the base of the brain [32].

MRI permits visualization of occluded and stenotic vessels while at the same time demonstrating collaterals an characteristic signs of infarct and hemorrhage [4,11,56]. In its ability to define vessel status and visualize collaterals, MRI is superior to CT, and represents an excellent modality for screening and follow-up of patients with moyamoya disease [19]. As MRA improves it may obviate the need for conventional angiography.

Various methods have been used to evaluate CBF in patients with moyamoya disease. These include SPECT, PET, TCD, ^{133}Xe inhalation, and stable Xe enhanced CT [23–25,28,40,42–44,50,57–59,63–67,69,

72]. The theory behind the safety and reliability of stable Xe-enhanced CT has been shown by a number of investigators and topic review have been published [2,7,16,26,29,31,52,53,71,73,74]. We favor the use of stable Xe-enhanced CT CBF at our institution because of the method's ability to topographically record low-flow values and anatomically represent flow data with a high degree of resolution. In addition, the ease with which tests can be rapidly repeated at the same sitting permits the physician to perform a variety of "challenge" studies to test cerebrovascular reserve and autoregulation. Finally, stable Xe-enhanced CT scanning is safe. For those patients who do not tolerate the stable Xe-CT or who are too unstable to be transported to the CT scanner, ^{133}Xe CBF (with and without acetazolamide or CO_2 challenge) can be performed.

The validity and accuracy of stable Xe CBF has been challenged by some on the basis of Xe-induced flow activation. Using transcranial Doppler, Giller, et al [14] demonstrated a rise in MCA velocities 2 minutes after the initiation of Xe inhalation and raised a question concerning the effects of such velocity changes on the rate constant (k) in the Kety-Schmidt equation. If the rate constant is sufficiently altered by the increasing velocity, they reasoned that the calculated blood flow values as obtained through the Kety-Schmidt equation will fail to represent the patient's true physiologic blood flow value when not under the effects of Xe activation. While such concerns are valid, they fortunately fail to be significant [2,16,71]. The rate constant (k) is calculated using the first postinhalation scans that are obtained within 2 minutes of inhalation and, thus, not influenced by Xe-induced flow activation. The partition coefficient (λ), which is the other important variable used to calculate flow, is dependent only upon tissue characteristics and, therefore, not affected by flow activation. Good and Gur [16], Witt et al [71], and Lindstrom [2] studied the effects of flow activation and calculated blood flow. These investigators found no significant changes in the derived flow values for white and gray matter. We therefore feel Xe CBF provides an accurate, reproducible means by which to assess CBF.

While a single Xe-CT CBF study provides the physician with CBF values, it does not yield information concerning CO_2 reactivity and vasodilatory reserve. This information can be obtained by elevating the P_aCO_2 or administering the carbonic anhydrase inhibitor acetazolamide [26,70]. This medication is known to induce vasodilation and increase CBF although the exact mechanism by which this occurs is currently unknown [6,8,17,20,55]. We have favored the use of acetazolamide in the evaluation of patients with questionably compromised vasodilatory reserves because of the ease of administration, rapidity of vasodilation in the normal individual, and safety [48,55,68]. However, in intubated patients we have found it equally as effective to test the reactivity and vasodilatory reserve by elevating P_aCO_2 concentrations through alteration of ventilator settings.

Four basic regional CBF responses have been documented when patients with hemodynamic abnormalities secondary to occlusive cerebrovascular disease are given acetazolamide and administered a repeat stable Xe-CT CBF study. Type 1 demonstrates normal baseline CBF of at least 35 mL/100 g/minute and a normal postacetazolamide CBF augmentation of at least 10%. Type 2 has a normal baseline CBF and less than normal postacetazolamide augmentation. Type 3 has a low baseline CBF and 10% flow variation after Diamox. Type 3a would have a regional flow reduction of >10% postacetazolamide. Type 4 has a low preacetazolamide CBF with normal postacetazolamide augmentation [48,68]. These various schema illustrate five different states of physiologic CBF reserve. Type 1 represents a normal individual. Type 2 represents an individual who has cerebrovascular disease and in his resting state requires arteriolar vasodilation to provide baseline CBF. The patient with type 3 response has a below-normal baseline CBF, either due to diminished delivery or decreased metabolic needs. While this patient may have the ability to augment flow, he does so suboptimally. Type 3a steals from the maximally dilated region to the acetazolamide-induced dilated area. [47,70]. A type 4 response represents a patient with below-normal baseline CBF secondary to decreased metabolism, yet the ability to adequately augment flow should the need arise.

In case 1, the paradoxical increase in blood flow within the right MCA and ACA territories at the lower P_aCO_2 indicated that these regions were probably already maximally dilated with minimal or no vascular dilatory reserve. When other regions were induced to constrict by reducing P_aCO_2, the right MCA and ACA territories simply acted as sinks for blood from the surrounding regions (reverse seal phenomenon). When P_aCO_2 was elevated in this patient from 24 to 38 mm Hg, the MCA and ACA territories bilaterally experienced a decrease in CBF instead of an expected 43% increase. The explanation for such paradoxical results lies in the fact that, with P_aCO_2 induced vasodilation in the normal parenchyma, a steal phenomenon developed with

blood entering the new, low-resistance regions. This pattern indicates that the region with reduced flows has exhausted its physiologic reserve and is at risk for significant ischemia, if baseline blood flow through existing collaterals is reduced or if regional demand is increased.

Positron emission tomography (PET) determination of CBF, regional cerebral blood volume (rCBV; an indirect measure of vascular dilation), cerebral metabolic rate of oxygen ($CMRO_2$), and regional oxygen extraction fraction (rOEF) have provided additional means by which to assess the adequacy of regional cerebral blood supply in the face of vascular occlusive disease [2,3,13,29,46]. In acute stroke, PET has demonstrated that a drop in rCBF relative to $CMRO_2$ leads to a compensatory increase in rOEF and CBV (misery perfusion) so that a steady state can be maintained in terms of energy needs and supply [2,13]. Gibbs et al found that mean CBV was significantly higher in cases of bilateral occlusion [13]. In patients with an occluded ICA the ipsilateral ratio of CBF/CBV, therefore, was considered an important indicator of an area's hemodynamic reserve with a low ratio indicative of an exhausted or nearly exhausted cerebral circulatory reserve [22]. This relationship became especially apparent when it was realized that a low CBF/CBV correlated with elevated rOEF [2].

Herold et al subsequently subjected patients to both PET and ^{133}Xe CBF studies and compared the results from ^{133}Xe blood flow scanning with CO_2 challenge to those of PET with CBF/CBV and rOEF determinations. These investigators found that a decreased capacity to vasodilate in response to inhaled CO_2 correlated with a decrease in CBF/CBV [22]. A significant correlation was obtained between CO_2 reactivity and CBF/CBV ratio [22]. They also demonstrated an association between reduced CO_2 reactivity and a rise of rOEF [22]. In view of the similar effects on intracranial vessels of CO_2 elevation and acetazolamide, it is fair to assume, as Herold did, that similar correlations exist between acetazolamide-induced Xe-CT CBF changes and PET-calculated CBF/CBV and rOEF observations.

Other investigators have shown that patients demonstrating patterns of reduced flow, steal, and poor flow augmentation overwhelmingly suffered with the most severe carotid occlusive disease [13]. Baron revealed the reversibility of such findings by documenting normalization of CBF and rOEF, following EC-IC bypass in a patient with bilateral carotid disease and preoperative PET studies showing severe reduction in CBF and abnormal elevation in rOEF.

In addition, studies that evaluate vasodilatory reserve have shown a capacity to predict stroke. Kleisser and Widder studied 85 patients with ICA occlusions using Diamox challenge. They documented a 0% incidence of stroke in patients with normal CO_2 reactivity and a 22% incidence of ipsilateral stroke in patients with diminished or absent cerebrovascular reserve [27]. A study utilizing Xe-CT CBF and diamox challenge by Yonas et al [75] showed a 12.6 times greater chance of stroke in individuals with atherosclerotic carotid disease, who had a low initial CBF, reduced vascular reserves, and a steal response.

Conclusion

Although our data concerning the management of moyamoya is limited to observations in four patients, we feel it is reasonable to evaluate this disease as we evaluate other occlusive vascular disorders. By extrapolating from the results of studies by ourselves and others, it is safe to conclude that the presence or lack thereof of vasodilatory and CBF reserve as documented by xenon-CBF challenge studies will help surgeons identify patients who are hemodynamically unstable and who are most likely to benefit from revascularization procedures.

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COMMENTARY

This paper reviews and discusses the surgical indications of moyamoya disease from the viewpoint of cerebral blood flow. It is educational, although these cases are not like the typical moyamoya disease we see in Japan. I completely agree with the idea discussed in this manuscript; it is important to know the hemodynamics of the brain with moyamoya disease. Surgical intervention will provide benefits to a hemisphere with decreased hemodynamic reserve. Reverse steal phenomenon after administration of acetazolamide and CO_2 challenge is important to consider when one examines a patient with this disease.

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This is an interesting paper on the diagnosis and management of hemodynamically compromised patients, although it deals with moyamoya disease.

First of all, I want to make clear the definition of moyamoya disease. It is a disease with a stenotic lesion of the terminal portion of the bilateral carotid arteries and the development of angiographical moyamoya vessels. A unilateral lesion is called an *atypical* moyamoya disease, not moyamoya disease.

The authors say that the mechanism of Diamox is unclear, and CO_2 inhalation and Diamox may have a similar action for dilating the cerebral vessels. But it is thought that CO_2, which is produced in the brain tissue metabolically, is blocked to be changed with H_2O by this Diamox into HCO_2 plus H+, and this blocked CO_2 itself dilates the cerebral vessels. This means Diamox does not show its vasodilating action where the tissue is already infarcted and does not produce CO_2 anymore. In this regard, it is clearly different from inhalated CO_2.

As the authors describe, we are of the opinion that SPECT or stable Xe-CT examining both rCBF and rCBV or rCBF with and without Diamox loading will help us detect hemodynamically compromised patients and select the candidates for revascularization procedures, or evaluate its effects postoperatively.

For reference, we have data [1] that there is a significant correlation between the value of preoperative rCBV measured by SPECT, and the bypass flow which was measured intraoperatively by a magnetic flow meter. The more the preoperative rCBV increased—that is, more vasodilation—the more the bypass flow was. This indicates that the more the rCBV of an occlusive CVD patient increases, the more a revascularization procedure such as EC-IC bypass may be necessary. Of course, to get a definite conclusion on this issue, more data accumulation is needed.

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