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Cerebral Blood Flow Response Pattern during Balloon Test Occlusion of the Internal Carotid Artery

Jens-Peter Witt, Howard Yonas, and Charles Jungreis

PURPOSE: To evaluate the risk of temporary or permanent internal carotid artery occlusion.

METHODS: In 156 patients intraarterial balloon test occlusion in combination with a stable xenon-enhanced CT cerebral blood flow study was performed before radiologic or surgical treatment. All 156 patients passed the clinical balloon test occlusion and underwent a xenon study in combination with a second balloon test. Quantitative flow data were analyzed for absolute changes as well as changes in symmetry. **RESULTS:** Fourteen patients exhibited reduced flow values between 20 and 30 mL/100 g per minute, an absolute decrease in flow, and significant asymmetry in the middle cerebral artery territory during balloon test occlusion. These patients would be considered at high risk for cerebral infarction if internal carotid artery occlusion were to be performed. With one exception they belonged to a group (class I) of 61 patients who showed bilateral or ipsilateral flow decrease and significant asymmetry with lower flow on the side of occlusion. The other 95 patients, who showed a variety of cerebral blood flow response patterns including ipsilateral or bilateral flow increase, were at moderate (class II) or low (class III) stroke risk. In contrast to these findings, exclusively qualitative flow analysis failed to identify the patients at high risk: a threshold with an asymmetry index of 10% revealed only 16% specificity whereas an asymmetry index of 45% showed only 61% sensitivity for detection of low flow areas (<30 mL/100 g per minute).

CONCLUSION: For achieving a minimal hemodynamic related-stroke rate associated with permanent clinical internal carotid artery occlusion we suggest integration of a thorough analysis of quantitative cerebral blood flow data before and during balloon test occlusion.

Index terms: Arteries, carotid (internal); Catheters and catheterization, balloons; Interventional neuroradiology, provocative testing; Xenon

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Surgery for extensive skull-base tumors, unclippable intracavernous aneurysms, and arteriovenous fistulas often requires temporary and sometimes permanent occlusion of one of the internal carotid arteries (ICAs) (1-14). Because each ICA provides one-third of the brain's blood supply, acute occlusion must result in dramatic cerebral blood flow (CBF) redistribution if neuronal function is to be maintained. Many tests have been introduced to assess this capability (9, 15-24).

At our institution, stroke risk is assessed using temporary ICA balloon test occlusion (BTO) in patients who may require a permanent ICA occlusion (25-29). This test includes careful, continuous neurologic examination during a 15-minute BTO which, for those who clinically pass the first BTO, is followed by two xenon-enhanced computed tomographic (CT) CBF studies (30-32), one with the balloon deflated and the other during a second 5-minute BTO. The xenon CT CBF studies were performed to discriminate patients at increased hemodynamic risk for subsequent stroke if the ICA was therapeutically occluded.

Recent papers have proposed the use of qualitative CBF studies with technitium-99m-hexamethyl-propyleneamine oxime single-photon emission CT as an equally effective and technically simpler aid for reducing the associated risk of stroke after acute ICA occlusion (33-35). The authors used CBF symmetry analysis during BTO

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From Hannover University, Hannover, Germany (J.-P.W.), and the Departments of Neurological Surgery (H.Y.) and Radiology (H.Y., C.J.), University of Pittsburgh Medical Center.

Address reprint requests to Howard Yonas, MD, Department of Neurosurgery, Montefiore University Hospital, 3459 Fifth Ave, Pittsburgh, PA 15213.

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TABLE 1: Mean arterial blood pressure, end-tidal carbon dioxide, cerebral blood flow, and age in 156 BTO patients grouped into diagnostic subgroups

Diagnosis	Intracranial Tumor	Extracranial Tumor	ICA Aneurysm	All Patients
Patients	90	43	23	156
Age	43.8 ± 16.6	47.1 ± 16.1	50.4 ± 18.3	45.6 ± 16.9
MABP _(BL)	95.0 ± 14.2	97.9 ± 16.6	97.1 ± 19.1	96.1 ± 15.4
MABP _(BL/XE)	95.5 ± 14.7	97.0 ± 15.4	96.8 ± 15.9	96.1 ± 14.7
MABP _(BTO)	94.5 ± 15.7	97.3 ± 14.7	97.9 ± 15.2	95.8 ± 15.3
MABP _(BTO/XE)	96.2 ± 16.8	97.5 ± 13.4	97.5 ± 18.5	96.8 ± 15.8
pCO _{2(BL)}	41.7 ± 6.6	40.5 ± 7.0	39.8 ± 9.9	41.1 ± 6.9
pCO _{2(BL/XE)}	38.7 ± 6.1	38.7 ± 6.6	37.0 ± 8.6	38.1 ± 6.5
pCO _{2(BTO)}	40.4 ± 6.2	41.3 ± 6.2	39.7 ± 8.3	40.6 ± 6.4
pCO _{2(BTO/XE)}	38.1 ± 6.1	38.7 ± 6.6	35.5 ± 9.6	37.9 ± 6.7
CBF _{(BL)non}	48.5 ± 10.9	50.8 ± 10.9	46.1 ± 13.4	48.8 ± 11.3
CBF _{(BL)occ}	46.3 ± 10.4	49.3 ± 9.5	44.9 ± 14.1	46.9 ± 10.8
CBF _{(BTO)non}	48.6 ± 12.8	49.1 ± 10.7	47.9 ± 15.2	48.6 ± 12.6
CBF _{(BTO)occ}	48.6 ± 12.8	49.1 ± 10.7	47.9 ± 15.2	48.6 ± 12.6

Note.—MABP indicates mean arterial blood pressure (mm Hg); pCO₂, end-tidal carbon dioxide partial pressure (mm Hg); baseline, balloon deflated; BL/XE, stable xenon CT CBF study during baseline; BTO/XE, stable xenon CT CBF study during BTO; non, nonoccluded side; and occ, occluded side.

and demonstrated evidence for the high sensitivity of this criterion in detecting patients at hemodynamic risk for permanent ICA occlusion. Concerns have been raised about the low specificity of this method (33, 36).

This study explores the range of CBF responses to clinical BTO. Unlike the qualitative character of most single-photon emission CT reports using hexamethyl-propyleneamine oxime or iodoamphetamine, stable xenon CT provides quantitative CBF measurements (37). With this method we are able to analyze not only changes in symmetry, but also absolute CBF alterations including a fall to below the normal CBF range (51 ± 10 mL/100 g per minute) (37) during BTO. We believe this provides a valuable predictor of a patient's possible cerebrovascular decompensation after permanent ICA occlusion.

Materials and Methods

Within the last 10 years more than 450 BTOs have been performed at our institution. More than 400 of these examinations were done in combination with xenon CT CBF measurements.

Patients

Of the 400 patients, 156 (89 female, 67 male) were randomly selected by alphabetical order. Only complete xenon CT CBF studies that included both occluded and nonoccluded measurements of high technical quality were included. Ninety patients presented with intracranial tumors (more than 80% meningioma), 43 patients showed extracranial tumors (more than 70% squamous cell carcinoma),

and 23 patients presented with ICA aneurysms (more than 65% cavernous sinus aneurysm).

The average age of these patients was 46 ± 17 years (range, 7 to 79). Mean arterial blood pressure and end-tidal carbon dioxide are recorded in Table 1. Measurements were acquired before, during, and after each xenon CT CBF study.

BTO Method

As described previously, a complete BTO examination consists of the following steps. After a baseline neurologic examination a four-vessel angiogram is performed, then a double-lumen catheter is introduced (Swan-Ganz, Edwards Laboratories, Annasco, Puerto Rico) into the femoral artery. The catheter is then advanced within the ICA to the level of the first or second cervical vertebral body. The patient is given 5000 to 7000 U of heparin intravenously during the procedure. While continuously measuring blood pressure in the distal ICA and intermittently measuring systemic blood pressure by an automatic cuff (Critikon Dynamap, Tampa, Fla), the intraarterial balloon is inflated until distal pressure falls and balloon deformation consistent with the vessel is observed. The patient undergoes a continuous neurologic examination for the initial 5 minutes and subsequently at 4- to 5-minute intervals. The balloon remains inflated over a 15-minute period but may be immediately deflated if the patient shows consistent neurologic alteration. If no neurologic alterations are observed during the BTO, the patient is transferred to the CT suite with the balloon deflated but still in place. Xenon CT CBF studies are performed both with the balloon deflated and during a second 5-minute period of balloon reinflation.

Xenon CT CBF Measurement

CBF studies were performed using the xenon CT CBF system including software and hardware adapted to the GE

9800 scanner (General Electric Medical Systems, Milwaukee, Wis). During the CBF studies the patients inhaled a gas mixture of 33% xenon/67% oxygen (Xe SCAN, Linde Medical Gases, Danbury, Conn). After two baseline scans the xenon enhancement was monitored with six scans during a 5-minute gas inhalation period (37). The radiodensity enhancement of brain tissue caused by the inhalation of stable xenon is used in a modified Kety equation (38) to calculate CBF.

Because each of our patients underwent both baseline (balloon deflated) and BTO (balloon inflated) studies, 312 xenon CT CBF studies were entered into the analysis. Each xenon CT CBF study included CBF calculations of two levels. Level 1 included the basal ganglia and paralleled the frontal skull base near the orbitomeatal line. Level 2 was a cut 2 to 3 cm above the first level. In this study we concentrated on level 1. By focusing on mixed cortical flow values CBF data were analyzed by placing 22 to 24 contiguous 2-cm regions of interest (each ≈ 314 pixels) within the cortical mantle (37) (Fig 1).

CBF Analysis

CBF was analyzed for both absolute and relative changes with BTO. To measure CBF corresponding to the three major vascular territories, the 2-cm regions of interest were grouped into three sets: anterior cerebral artery territory, middle cerebral artery territory (MCA), and posterior cerebral artery (Fig 1).

Absolute Xenon CT CBF Changes

BTO-induced CBF changes in each region of interest were calculated using the absolute differences between

identical regions of interest in the baseline xenon CT CBF study and the xenon CT CBF study during BTO. Values were calculated for each 2-cm region of interest and the major vascular territories (39, 40).

Relative Xenon CT CBF Symmetry Changes in the MCA Territory

Degree of side-to-side asymmetry in the MCA territory was calculated by the following equation:

$$I_{\text{asym}} = \frac{(C_{\text{non}} - C_{\text{occl}})}{(C_{\text{avg}})} \times 100 = \frac{(C_{\text{non}} - C_{\text{occl}})}{\left[\frac{(C_{\text{non}} + C_{\text{occl}})}{2}\right]} \times 100,$$

where I_{asym} is index of side-to-side asymmetry in percent; C_{non} is xenon CT CBF value (mL/100 g per minute) on the nonoccluded side; C_{occl} is xenon CT CBF value (mL/100 g per minute) on the occluded side; and C_{avg} is xenon CT CBF value (mL/100 g per minute) averaged between ipsilateral and contralateral to BTO.

The index of side-to-side asymmetry (I_{asym}) is *positive* if xenon CT CBF values are lower on the side of occlusion and *negative* if xenon CT CBF values are lower on the contralateral side. Xenon CT CBF studies revealing I_{asym} values in the range of $\pm 10\%$ are regarded as having symmetrical CBF referring to a control group of age-matched healthy volunteers (37). Group differences were tested for significance using the nonparametric Wilcoxon-Mann-Whitney test.

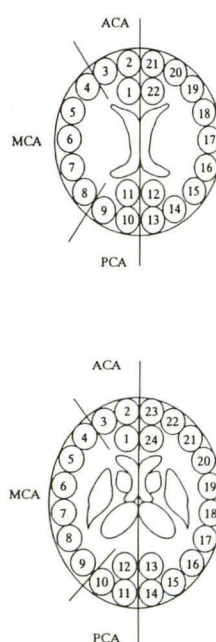
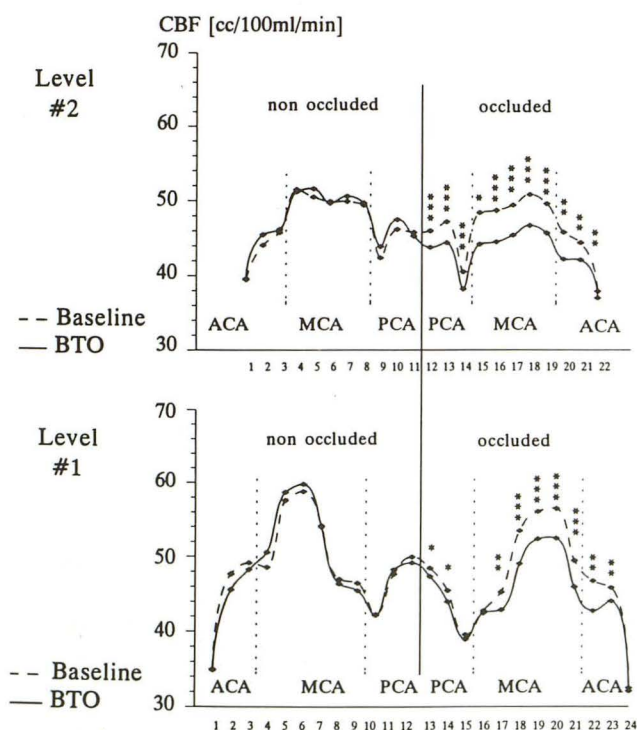


Fig. 1. Averaged CBF values ($n = 156$) (\diamond) in each 2-cm-circle region of interest on two levels during baseline and BTO study. Note significant CBF differences between baseline and BTO xenon CT CBF study (***, $P < .001$; **, $P < .01$; *, $P < .05$). ACA indicates anterior cerebral artery; PCA, posterior cerebral artery.

Classification

Quantitative and qualitative CBF responses to BTO were combined in an arbitrarily chosen classification. This classification was based on the clinical significance of the CBF responses to BTO and resulted in three main classes (I, II, and III, and certain subclasses). Class I included patients who showed both qualitative and quantitative signs of CBF compromise caused by BTO. Class II described patients who showed quantitative CBF compromise in combination with symmetrical CBF values or asymmetrical lower CBF on the contralateral side, and class III contained the rest of the patients who showed no clinically significant reduction of CBF during BTO. For the purpose of integrating the absolute (quantitative) and relative (qualitative) CBF changes, the CBF information was simplified in the following manner.

Absolute Xenon CT CBF Changes

The absolute change of CBF caused by BTO is categorized in increase (\uparrow) and decrease (\downarrow) on the side of occlusion and the contralateral side. The combination of side and change results in four different CBF response patterns: $\downarrow\downarrow$, $\uparrow\uparrow$, $\downarrow\uparrow$, $\uparrow\downarrow$ (occluded side/nonoccluded side).

Relative Xenon CT CBF Symmetry Changes in the MCA Territory

I_{asym} during the baseline xenon CT CBF study and BTO xenon CT CBF is described by two capital letters: the first for the baseline and the second for BTO: A indicates asymmetry of CBF with lower values on side of occlusion; B, balanced or symmetrical CBF; and C, contralateral lower values resulting in asymmetrical CBF. If CBF is asymmetric during both baseline and BTO and the lower value stays on the same side, that patient is labeled AA or CC. An indexed "1" indicates asymmetry increase caused by BTO, and an indexed "2" stands for decreased BTO asymmetry (A_1A , A_2A , C_1C , and C_2C). There are 11 possible types of CBF symmetry designations.

The combination of four absolute and 11 relative CBF response types theoretically results in 44 CBF response types. However, 10 types had to be excluded because they were physiologically not reasonable: $A_2A\downarrow\uparrow$, $AB\downarrow\uparrow$, $AC\downarrow\uparrow$, $BC\downarrow\uparrow$, $C_1C\downarrow\uparrow$, $A_1A\uparrow\downarrow$, $BA\uparrow\downarrow$, $CA\uparrow\downarrow$, $CB\uparrow\downarrow$, and $C_2C\uparrow\downarrow$.

Patients with bilateral CBF decrease resulting in asymmetry with lower CBF values on the side of occlusion (. . . $A\downarrow\downarrow$) were gathered in class I, subclass Ia. Patients with only ipsilateral CBF decrease who also showed CBF asymmetry during BTO (. . . $A\downarrow\uparrow$) were gathered in class I, subclass Ib.

Class II consists of patients in whom CBF decrease did not result in asymmetry with lower flow on the ipsilateral side. Subclass IIa consists of patients with bilateral CBF decrease; subclass IIb includes patients with ipsilateral decrease; and subclass IIc with contralateral decrease.

Class III includes patients with bilateral CBF increase (. . . $\uparrow\uparrow$), patients with diminishing asymmetry ($A_2A\uparrow\downarrow$, $C_2C\uparrow\downarrow$),

and patients in which ipsilateral CBF increase resulted in CBF symmetry.

We used the CBF threshold of 30 mL/100 g per minute as a validation test for this arbitrary classification because this value designates the break point at which CBF in the MCA region is significantly less than normal CBF in a group of healthy volunteers ($P < .05$) (37). We summed up the patients in each class who showed CBF less than 30 mL/100 g per minute only because of BTO and the patients who showed CBF values below this threshold during baseline and during BTO.

Results

Absolute Hemispherical Xenon CT CBF Changes

The overall mean xenon CT CBF changes in the two levels of both hemispheres were moderate (Fig 1), -6 mL/100 g per minute on the side of occlusion and $+2$ mL/100 g per minute on the contralateral side. Individual CBF response within a region of interest to BTO is, however, more unpredictable and of greater magnitude. Ninety-five percent of CBF responses ranged between -29 and $+21$ mL/100 g per minute. On the side of occlusion, CBF decrease caused by BTO on both levels was highly significant in all 2-cm regions of interest of the MCA-supplied area. However, on level 1 of the side of occlusion, changes in the regions of interest of the anterior and posterior cerebral arteries were not as marked as changes observed within regions of interest supplied by the MCA (Fig 1). The more dramatic effect of BTO on the MCA territory led us to concentrate on these regions of interest during the following analysis.

Sixty-one of 156 (39%) patients showed a CBF drop on both sides caused by BTO. In 34 patients the bihemispherical decrease resulted in asymmetrical xenon CT CBF during BTO with lower flow on occluded side. Of the remaining 27 patients, 20 were symmetric and 7 had lower CBF values on the contralateral side during BTO.

Thirty-seven of 156 (24%) patients demonstrated decreased xenon CT CBF values on the side of occlusion during BTO and increased flow on the contralateral side. In 27 of these patients lower ipsilateral CBF values were measured during BTO, and in 10 symmetric MCA CBF values were measured.

In 42 of 156 (27%) patients, we measured increased xenon CT CBF values in both hemispheres during BTO (Fig 2). In 18 patients, the bilateral increase resulted in asymmetrical CBF with less flow on the occluded side. In 20 patients, symmetric CBF was measured during BTO, and

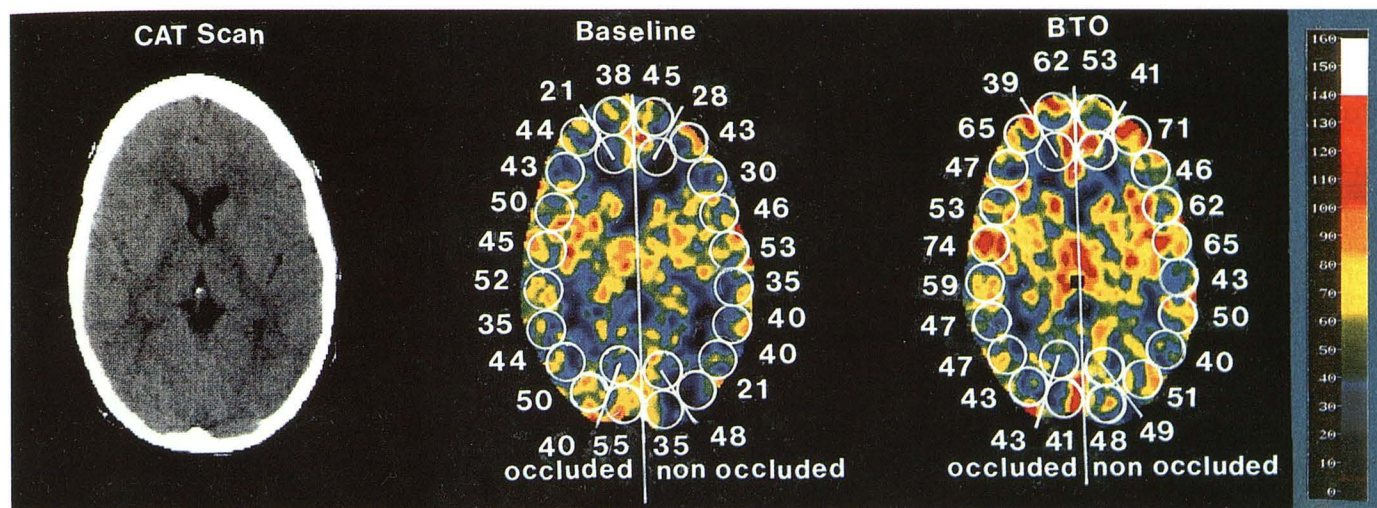


Fig. 2. Patient 122, 24-year-old woman, rhabdomyosarcoma right cavernous sinus. Xenon CT CBF study: baseline CT scan (left), CBF before (middle) and during BTO (right). CBF showed symmetrical values greater than 30 mL/100 g per minute for the vascular territories before BTO and showed symmetry during BTO, with CBF increased bilaterally in response to BTO. CBF response type is BB↑↑.

Xe/CT CBF in MCA territory

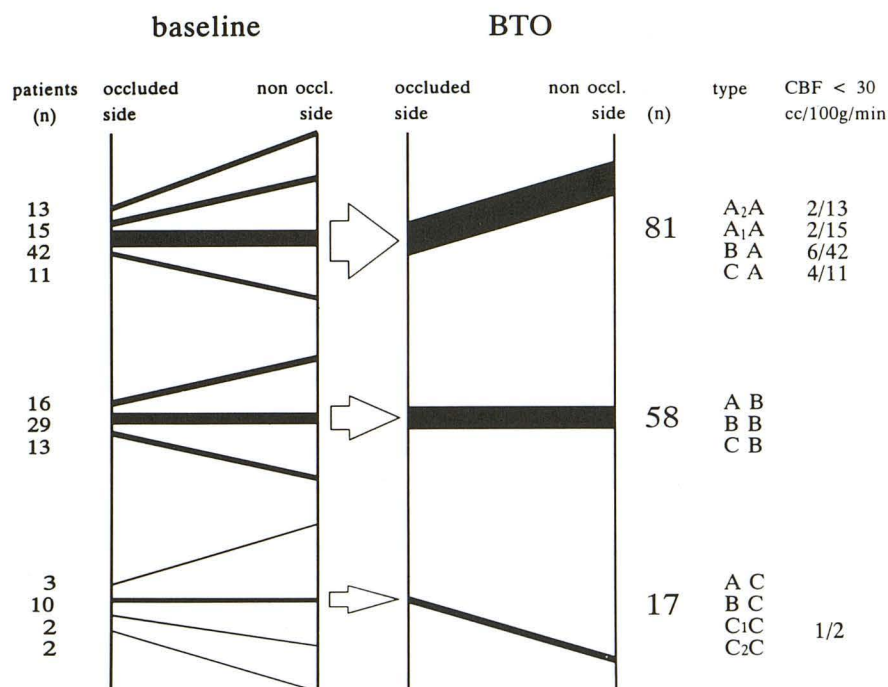


Fig. 3. CBF response pattern to BTO. Note number of CBF values less than 30 mL/100 g per minute associated especially with . . . A CBF response type. The width of line correlates with the number of patients. Response types are described in text.

in four patients lower CBF values were observed on the contralateral side.

In 16 of 156 (10%) patients, MCA CBF increased on the side of occlusion and decreased on the contralateral side because of BTO.

Relative Xenon CT CBF Symmetry Changes in the MCA Territory

Considering the entire group of patients ($n = 156$), there was a tight correlation ($r = .79$, $P <$

.001, $b = .8$) between observed BTO asymmetry values and recorded changes of asymmetry; this emphasizes that the asymmetry during BTO is caused not by preexisting CBF pattern but by the occlusion of the ICA.

A schematic summary of all types of relative CBF responses to BTO is provided in Figure 3. On the baseline xenon CT CBF study, 47 of 156 (30%) patients had asymmetric lower CBF on the side of test occlusion (A . . .), 81 of 156 (52%)

patients had symmetric CBF defined by limits of I_{asym} of $\pm 10\%$ (B . . .), and 28 of 156 (18%) patients had lower CBF on the contralateral side to occlusion (C . . .).

During BTO more than the half of all patients, 81 of 156 (52%), showed asymmetry with lower CBF on side of occlusion (. . . A), 58 of 156 (37%) patients revealed symmetric CBF (. . . B), and 17 of 156 (11%) patients presented with asymmetric CBF showing lower values on the contralateral side (. . . C). By combining the BTO results with those of the baseline study, we classified 11 different types of CBF response to BTO.

Looking for the most common CBF response to BTO, we found 42 of 156 (27%) patients represented the "BA" group: no asymmetry during baseline xenon CT CBF study and CBF asymmetry during BTO with lower CBF values on the side of occlusion. Twenty-eight of 156 (18%) patients with asymmetrically lower CBF on the side of occlusion had asymmetrical CBF during baseline. Of these, 13 patients had a larger (A_2A) and 15 had a smaller (A_1A) degree of asymmetry.

Twenty-nine of 156 (19%) patients showed no asymmetry at all, either during baseline or during BTO, and were classified as type BB. Ten of 156 (6%) patients who revealed baseline CBF symmetry, group BC, showed contralateral lower CBF values during BTO.

Twenty-eight of 156 (18%) patients started with significantly lower flow on the contralateral side to the later occlusion (CA, CB, and $C_{1,2}C$), and only 4 of 28 continued to show asymmetry on the contralateral side during BTO ($C_{1,2}C$). CBF in most of these patients (24 of 28) became balanced (13 of 28, CB), or the side with lower flow values switched to the occluded side (11 of 28: CA).

Sixteen of 156 (10%) patients who started with significantly lower CBF values on the side to be occluded during the baseline xenon CT CBF study presented with symmetric CBF during BTO (AB).

Finally, in 3 of 156 (2%) patients, we found a switched asymmetry from lower CBF on the side of occlusion during baseline to contralateral lower CBF during BTO (AC).

Classification

See Table 2 for final classification. Assessing the clinical significance of this arbitrary classification by enumerating the occurrence of CBF less than 30 mL/100 g per minute, 13 patients were found in class I (Fig 4). Ten of these patients

TABLE 2: Clinical classification in response to BTO

Class	Type	Patients	CBF < 30, BTO	CBF < 30, BL and BTO
Ia	$A_1A \downarrow \downarrow$	34	6 (18%)	2 (6%)
	$A_2A \downarrow \downarrow$			
	$BA \downarrow \downarrow$			
	$CA \downarrow \downarrow$			
Ib	$A_1A \downarrow \uparrow$	27	4 (15%)	1 (4%)
	$BA \downarrow \uparrow$			
	$CA \downarrow \uparrow$			
	$AB \downarrow \downarrow$			
IIa	$BB \downarrow \downarrow$	27	1 (4%)	
	$CB \downarrow \downarrow$			
	$AC \downarrow \downarrow$			
	$BC \downarrow \downarrow$			
IIb	$C_1C \downarrow \downarrow$	10		
	$C_2C \downarrow \downarrow$			
	$BB \downarrow \uparrow$			
	$CB \downarrow \uparrow$			
IIc	$AC \downarrow \downarrow$	6		
	$BC \downarrow \downarrow$			
	$C_1C \downarrow \downarrow$			
	$all \uparrow \uparrow$			
III	$A_2A \uparrow \downarrow$	52		1 (2%) ^a
	$AB \uparrow \downarrow$			
	$BB \uparrow \downarrow$			
	$C_2C \uparrow \downarrow$			

Note.—BL indicates baseline; A, CBF lower on occluded side; B, symmetrical CBF; C, CBF lower on contralateral side; 1, asymmetry increased because of BTO; 2, asymmetry decreased because of BTO; and $\downarrow \uparrow$, absolute CBF change (eg, decrease occluded side/increase nonoccluded side).

^a This patient tolerated BTO despite low flow resulting from subarachnoid hemorrhage.

showed CBF less than 30 mL/100 g per minute only during BTO, the other 3 patients showed CBF less than 30 mL/100 g per minute during baseline and during BTO.

In class IIa only one patient presented with CBF less than 30 mL/100 g per minute during BTO on the side contralateral to occlusion.

Class III as well, only had one patient, who had recovered from a severe subarachnoid hemorrhage after aneurysm rupture, with flow values less than 30 mL/100 g per minute before and during BTO. Despite these low CBF values this patient tolerated the BTO procedure without any clinical signs of additional neurologic deterioration. BTO revealed a slight CBF increase during BTO, and the preexisting asymmetry on the side of occlusion was reduced ($A_2A \uparrow \uparrow$). Three additional patients showed CBF less than 30 mL/100 g per minute on the contralateral side exclusively before BTO.

Considering the level of the asymmetry index I_{asym} , of 81 patients who showed significant ($>10\%$) asymmetry with lower CBF on the side

of occlusion, 14 (17%) patients showed CBF less than 30 mL/100 g per minute. We found that in all patients (8 of 8) in whom more than 45% CBF asymmetry with lower flow on the side of occlusion developed, CBF became less than 30 mL/100 g per minute in the MCA territory (Fig 5).

Discussion

Unilateral ICA occlusion has an abrupt and profound impact on the entire cerebral circula-

tion. The distal ICA pressure commonly falls from approximately 100 mm Hg to about 60 mm Hg with proximal vessel occlusion (29). Cerebral perfusion pressure in one territory may drop even more precipitously if collaterals are not able to replace the supply of blood lost with ICA occlusion. Causes for CBF alteration are most likely found in preexisting extracranial occlusive vascular disease (41, 42), inherent morphologic insufficiencies of the circle of Willis (43, 44), alter-

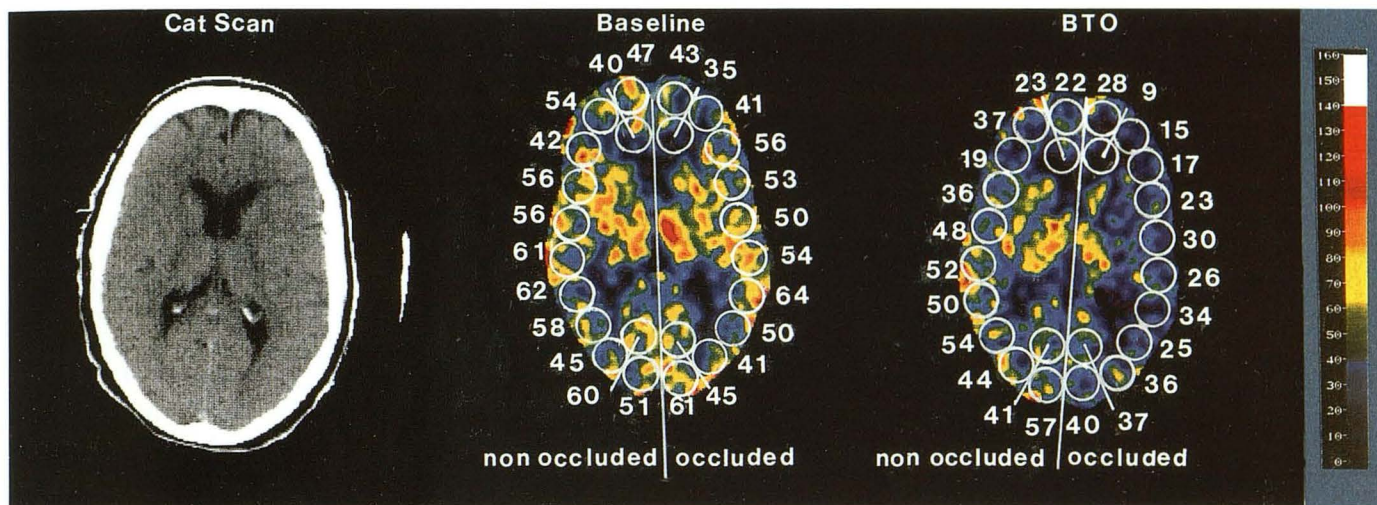


Fig. 4. Patient 107, 61-year-old man, left maxilla squamous cell tumor with intracranial extension. Xenon CT CBF study: baseline CT scan (left), CBF before (middle) and during BTO (right). This patient showed symmetrical CBF greater than 30 mL/100 g per minute before BTO and dropped CBF on both sides resulting in asymmetry with flow values less than 30 mL/100 g per minute on the side of occlusion during BTO. CBF response type is BA↓.

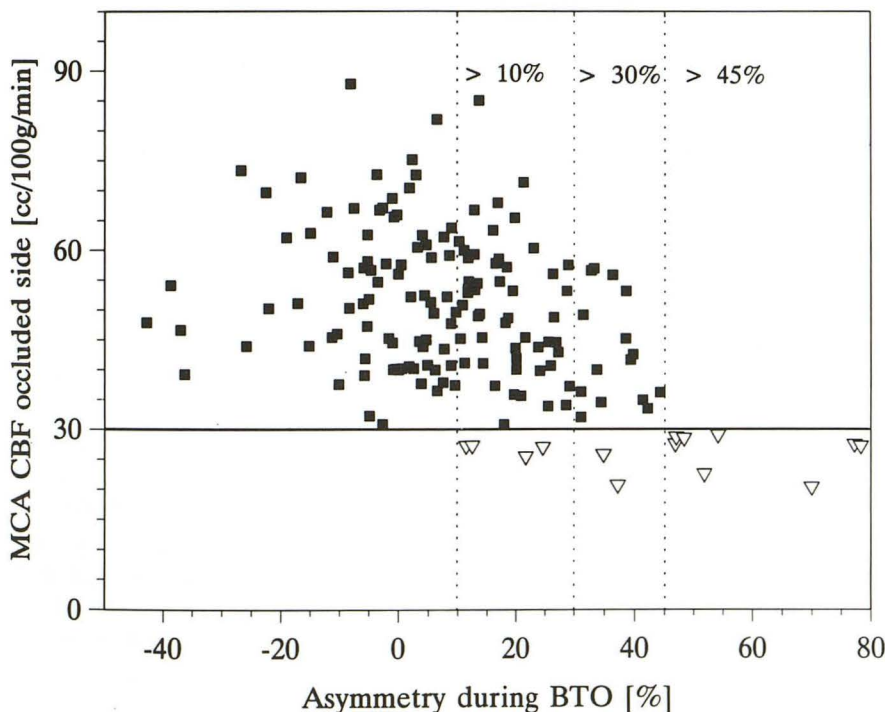


Fig. 5. Interhemispherical asymmetry and MCA CBF on the occluded side during BTO. Note high sensitivity but low specificity when asymmetry threshold is 10%.

ation of the autonomic vascular innervation partly induced by ICA manipulation (45–48), or compromised vasodilatory capacity most likely related to small vessel disease (42, 49). In addition, large and small vessel narrowing induced by vasospasm caused by ruptured aneurysms (50), local brain edema, and mass effect caused by intracranial tumors may also result in flow alteration.

A series of mechanisms function to prevent ischemic brain tissue damage. First, in a phase of hemodynamic compensation (positron emission tomography stage 1) (51), CBF is maintained by decreasing the peripheral cerebrovascular resistance. This slows down the mean transit time and increases cerebral blood volume (51–53). Second, if the vasodilative capacity has been exceeded (ie, cerebrovascular resistance has reached its lowest value) and cerebral blood volume expansion has peaked, CBF will drop passively with a further fall in cerebral perfusion pressure as oxygen extraction fraction increases (54–56). This is referred to as positron emission tomography stage 2 (51). With an oxygen extraction fraction of approximately 60% and a minimal cerebrovascular resistance (55), any further drop in cerebral perfusion pressure, CBF, or cerebral blood volume will cause the cerebral metabolic rate of oxygen to decrease, resulting in neurologic deficits and subsequently in neuronal damage (57). In the past decades, reliable CBF thresholds have been established. At CBF values less than 18 to 23 mL/100 g per minute neuronal function gradually decreases (41, 58–60) and neurologic deficits occur. CBF values less than 8 to 15 mL/100 g per minute in mixed gray and white matter are tolerated for a very short period before irreversible infarction occurs (15, 50, 61–63). Our results are consistent with these earlier clinical and experimental studies, because no patient who passed the clinical examination during BTO without developing neurologic deficit had CBF values in the MCA territory less than 20 mL/100 g per minute.

In our studies we are most concerned about 15 of our 156 (10%) patients who passed the neurologic examination during BTO but showed xenon CT CBF values between 20 and 30 mL/100 g per minute. CBF values less than 30 mL/100 g per minute are not only more than 2 SD below the mean CBF shown in normal studies (37), but they also describe the maximal deterioration of CBF possible without neurologic deficits. These individuals have, therefore, entered a state of hemodynamic decompensation consistent with

positron emission tomography stage 2 (51). In this state cerebral perfusion pressure is insufficient, cerebral vascular resistance is minimized, and cerebral blood volume maximized, CBF drops, and an increasing oxygen extraction fraction is the only protection to prevent ischemic damage. These criteria should identify a group in whom cerebral perfusion depends on blood pressure. Such patients should benefit from bypass surgery and intraoperative brain protection, including pharmacologic and hypothermic procedures (12, 28) if temporary or permanent ICA occlusion should become necessary.

However, in cases in which CBF is below the threshold of 30 mL/100 g per minute before BTO and does not change with it, ICA occlusion without extracranial/intracranial bypass, in our eyes, should be tolerable. In these patients cerebrovascular vasodilative reserve capacity was maintained, although the absolute CBF level was reduced presumably as a result of decreased metabolic demand. Guided by this concept and clinical appearance, one elderly patient who suffered subarachnoid hemorrhage and had CBF less than 30 mL/100 g per minute before and during BTO (class III), underwent ICA sacrifice without subsequently developing cerebral ischemia.

Recent studies (33–35) concentrating on the assessment of qualitative CBF changes during BTO have recommended CBF asymmetry evaluation as a measure for stroke risk after permanent ICA occlusion. Because CBF in healthy control subjects is symmetrically distributed between both hemispheres in a range of $\pm 10\%$ variation, larger deviations with BTO are believed to indicate CBF maldistribution between both hemispheres (64–68). The shortcomings of solely qualitative CBF evaluation are the increased number of false-positive and false-negative decisions regarding the inability to proceed directly to ICA occlusion. It would be oversensitive to consider all patients who showed significant asymmetrical CBF during BTO as being at an elevated stroke risk after ICA occlusion, because it withholds from 81 (52%) patients the option of a relatively safe direct ICA sacrifice, whereas only 14 patients in this group had CBF less than 30 mL/100 g per minute. Raising the asymmetry threshold increases the specificity as the sensitivity decreases. Above 45% asymmetry, we found that all patients ($n = 8$) had CBF values less than 30 mL/100 g per minute. However, this method failed to identify 6 patients with CBF less than 30 mL/100 g per minute but less asymmetry. Com-

binning a baseline CBF study with the BTO CBF study and considering only qualitative CBF changes as predictive for CBF compromise after straight ICA sacrifice, 53 (34%) of our patients would have been identified to be at high risk. In this group, however, CBF in only 10 patients fell below 30 mL/100 g per minute.

Our current protocol, which divides patients into high-, moderate-, and low-risk groups, combines neurologic assessment during BTO with identification of new regions with absolute low CBF values (<30 mL/100 g per minute) (28). In applying these criteria in the surgical decision-making process, the rate of flow-related strokes that cause persistent neurologic deficits after permanent ICA occlusion dropped to 3% (1 of 30).

Conclusion

An exclusively qualitative assessment of CBF either during BTO alone or before and during BTO has not enough efficacy to guide individual case management properly. We are convinced that a quantitative CBF study before and during BTO followed by a detailed analysis of absolute CBF changes and symmetry changes identifies the different types of CBF response, and determines patients' location within their specific CBF-cerebral perfusion pressure autoregulation curves.

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