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Stroke Risk after Abrupt Internal Carotid Artery Sacrifice: Accuracy of Preoperative Assessment with Balloon Test Occlusion and Stable Xenon–Enhanced CT

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PURPOSE: To evaluate stable xenon–enhanced CT cerebral blood flow with balloon test occlusion as a predictor of stroke risk in internal carotid artery sacrifice. **METHODS:** Abrupt internal carotid artery occlusion was performed by surgical or endovascular means below the origin of the ophthalmic artery in 31 normotensive patients who were assessed preoperatively by a 15-minute clinical balloon test occlusion followed by an internal carotid artery–occluded xenon CT cerebral blood flow study. **RESULTS:** One patient, who passed the clinical test occlusion but exhibited regions of cerebral blood flow less than 30 mL/100 g per minute on the occlusion xenon CT cerebral blood flow study went on to have a fatal stroke corresponding exactly to the region of reduced blood flow. Thirty patients passed both components of the preoperative stroke-risk assessment. Neuroimaging demonstrated possible flow-related infarctions, which subsequently developed in three patients. Two patients were asymptomatic, and one patient was left with a mild residual hemiparesis. **CONCLUSIONS:** Our protocol provided a statistically significant reduction in subsequent infarction rate and infarction-related death rate when compared with a control group of normotensive abrupt internal carotid artery occlusion patients who did not undergo any preoperative stroke-risk assessment (reported in the literature). The estimated false-negative rate for our preoperative assessment protocol ranged from 3.3% to 10% depending on the assessment of the cause of the three potentially flow-related infarctions. Although life-threatening major vascular territory infarctions have been avoided, our protocol is less sensitive to changes predicting smaller, often minimally symptomatic, vascular border zone infarctions and does not predict postoperative thromboembolic strokes.

Index terms: Arteries, carotid (internal); Cerebral blood flow; Brain, infarction; Xenon; Interventional neuroradiology, provocative testing

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Internal carotid artery (ICA) sacrifice remains a useful and sometimes necessary procedure for the treatment of certain aneurysms, carotid-cavernous fistulas, and cervical and skull-based neoplasms (1–17). Since the first attempts at therapeutic ICA sacrifice in the 1700s, surgeons have recognized that the major risks to their patients are subsequent cerebral infarction and infarction-related death (18). Over the years many tests have been developed to assess preoperatively the risk of infarction after permanent ICA sacrifice.

At our institution preoperative stroke risk is assessed with a 15-minute clinical balloon test occlusion of the cervical ICA followed by an ICA-occluded stable xenon–enhanced computed tomographic (CT) cerebral blood flow (CBF) study (19–21). Since 1982, we have performed these tests in more than 400 patients for various medical reasons. The purpose of this study is to report our incidence of infarction after abrupt ICA sacrifice below the origin of the ophthalmic artery in patients who had successfully completed our preoperative assessment, to discuss the relative

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strengths and weaknesses of our current protocol, and to contrast and compare the results achieved using our protocol with those achieved by others who either did not perform a preoperative stroke-risk assessment or who relied solely on a clinical temporary ICA occlusion test.

Materials and Methods

A retrospective review of records from our four medical center hospitals identified 45 patients who underwent abrupt therapeutic sacrifice of their ICAs between September 1982 and June 1991 (approximately 10 years). Fourteen patients were excluded from study for the following reasons: 7 patients underwent preocclusion assessment with a clinical balloon test occlusion but did not undergo a subsequent ICA-occluded xenon CT CBF study; 1 patient underwent only a preoperative 5-minute common carotid artery balloon test occlusion; 1 patient was preoperatively assessed only with a manual cross-compression angiogram; 1 patient had a very poor xenon CT CBF study because of motion, making that study uninterpretable for technical reasons; and 4 patients underwent abrupt occlusion of their ICAs above the origin of the ophthalmic artery (a scenario not tested by our stroke-risk assessment protocol). There were 3 infarctions (1 of which was fatal) in this group of 14 excluded patients. Thirty-one patients underwent both a 15-minute clinical balloon test occlusion and a technically adequate ICA-occluded xenon CT CBF study before abrupt sacrifice of their ICAs below the origin of the ophthalmic artery.

Patient Population

Mean patient age was 48 years (range, 18 to 77 years). There were 12 men and 19 women. The pathologic diagnoses of all 31 patients are presented in Table 1. All 31 patients underwent ICA-occluded stable xenon CT CBF studies, and 21 of these patients also had comparison studies performed with the balloon deflated. Twenty-nine ICA sacrifices were performed electively; 2 were performed in emergencies for epistaxis from postoperative petrous carotid pseudoaneurysms (Table 1). In both emergency cases blood pressure and hemoglobin levels were stabilized before ICA sacrifice. In 10 patients the ICA was either ligated or clipped surgically. In 21 patients the ICA was endovascularly occluded by detachable balloon. Seven of the 21 patients underwent preoperative endovascular ICA sacrifice before resection of a neoplasm, and in 5 of these 7, the ICA was also secondarily ligated or clipped at surgery.

TABLE 1: Pathologic diagnoses of 31 normotensive patients who underwent abrupt ICA sacrifice below the origin of the ophthalmic artery from 1982 through 1991

Vascular lesions (n = 14)
Cavernous-sinus aneurysm (6)
Unruptured supraclinoid aneurysm (4)
Carotid-cavernous fistula (2)
Postoperative petrous carotid pseudoaneurysm (2)[a]
Cavernous-sinus neoplasm (n = 9)
Meningioma (6)
Spindle cell carcinoma (1)
Adenoid cystic carcinoma (1)
Chordoma (1)
Cervical neoplasms (n = 7)
Squamous cell carcinoma (6)
Paraganglioma (1)
Temporal bone neoplasms (n = 1)
Osteogenic sarcoma (1)

[a] In both cases the ICA was immediately occluded endovascularly for epistaxis. In both cases the patient's blood pressure and hemoglobin levels were stabilized before ICA sacrifice.

Techniques

The details of the technique for performing the 15-minute clinical ICA balloon test occlusion and the subsequent ICA-occluded stable xenon CT CBF study have been published previously (19, 20). Intraoperative ICA ligation or clipping was performed at the discretion of the surgeon. Of the 10 surgically occluded cases, 5 were clipped or ligated just proximal to the ophthalmic artery, and 5 were ligated in the upper cervical region. In no case was a gradual occlusion technique (eg, tourniquet or gradual occlusion clamp) used. Details of the technique for performing endovascular detachable balloon ICA occlusion have been published previously (9). Of the 21 cases primarily occluded by detachable balloon, all were occluded at the level where the petrous segment of the ICA enters the cavernous sinus.

Xenon CT CBF Analysis

Each xenon CT CBF study yielded two levels of CBF maps in the axial plane. At each level, contiguous 2-cm-diameter regions of interest were placed over the cortical mantle as depicted in Figure 1. The number of regions of interest placed along the rim of each hemisphere varied slightly in each patient according to brain size and exact level chosen for the axial image. A quantitative value for the mean CBF within each region of interest was calculated according to previously published methods (22–24).

Eight vascular territories were defined as depicted in Figure 1. The middle cerebral artery distribution comprised the lateral regions of interest between the three anterior cerebral artery and posterior cerebral artery regions of interest. The anterior border zone territory consisted of the last anterior cerebral artery region of interest and the first middle cerebral artery region of interest; the posterior border zone consisted of the last middle cerebral artery region of interest and the first posterior cerebral artery region of interest. A mean CBF value for each of the eight vascular territories was calculated for each patient at each CBF study level by averaging the mean CBF values for each region of interest within each territory.

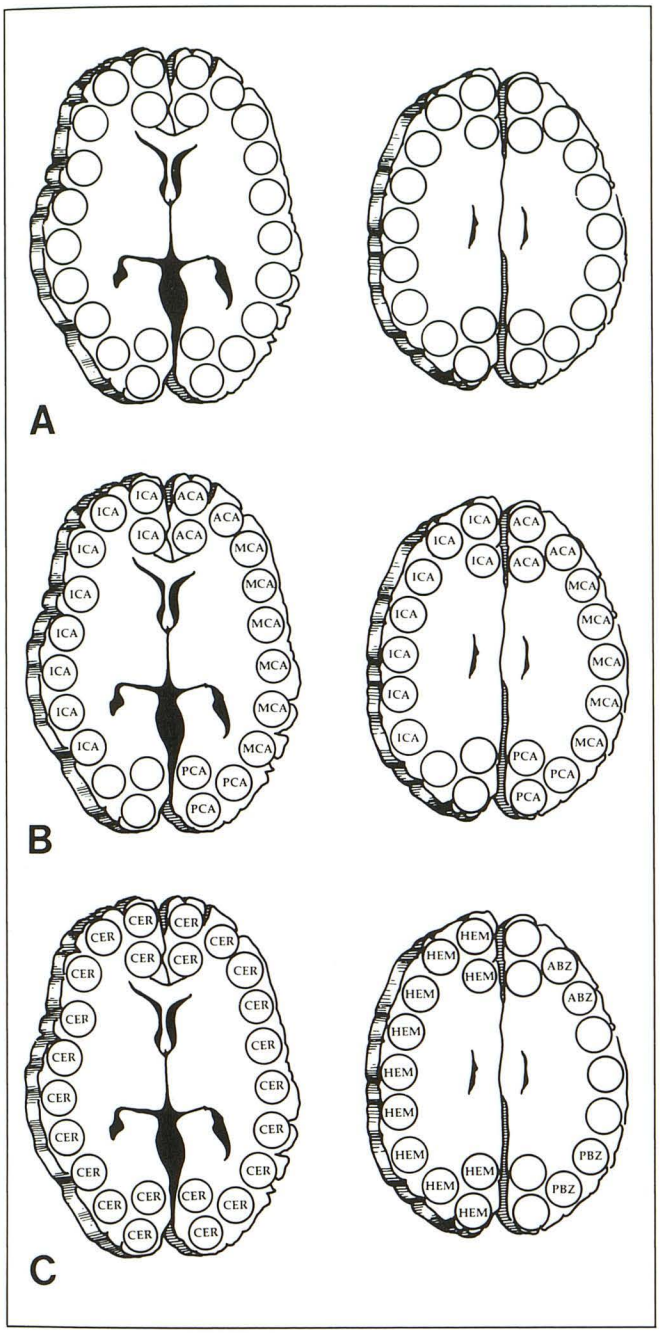


Fig. 1. Two axial levels were chosen for xenon CT CBF analysis. The first was centered at the level of the foramen of Monro and the second at the top of the ventricular system. At each level, contiguous regions of interest 2 cm in diameter were placed over the cortical mantle (*A*). Eight vascular territories were defined for each level as outlined in *B* and *C*. A mean CBF value for each of the eight vascular territories was calculated for each patient at each study level by averaging the mean CBF values for each region of interest within each defined vascular territory. *ACA* indicates anterior cerebral artery; *MCA*, middle cerebral artery; *ABZ*, anterior border zone; *PBZ*, posterior border zone; *HEM*, hemispheric territory; *CER*, cerebral territory; ICA, internal carotid artery; and PCA, posterior cerebral artery.

Criteria for Passing the ICA-Occluded Stable Xenon CT CBF Study

Our criteria for grouping patients is based on a minimum CBF value in any vascular territory (20). Normal CBF using the stable xenon CT CBF technique was 51 ± 10 mL/100 g per minute (mean ± SD) (25). From a statistical standpoint, 30 mL/100 g per minute was chosen as the cut-off for interpreting an abnormal CBF value because it was 2 SD from the mean. However, CBF at 30 mL/100 g per minute or less is not ominous if the lowest territorial flow value is not significantly different from the unoccluded CBF value in that same vascular territory. This is especially true in elderly persons who are known to have lower normal CBF (21, 25). Therefore, patients were deemed to have passed the stable xenon CT CBF study if their ICA-occluded CBF was more than 30 mL/100 g per minute in all vascular territories or if a region of CBF of 30 mL/100 g per minute or less was not significantly different from the value in the same vascular territory on the unoccluded CBF study (9, 14, 19, 26). All but 1 of the 31 patients met these criteria.

Follow-up and Definition of Study End Points

Neuroimaging follow-up was available for 25 of 31 (81%) of patients (mean, 1.3 years; range, 1 week to 5.4 years). Any patient who developed new neurologic symptoms after ICA sacrifice underwent neuroimaging with CT or MR. In addition, most asymptomatic patients underwent postoperative neuroimaging. Clinical follow-up was available for all 31 patients (mean, 1.5 years; range, 1 week to 5.4 years).

Any posttherapeutic infarction documented by neuroimaging, whether or not it was symptomatic, was considered a study end point. In contrast, a completely reversible neurologic deficit that did not result in an infarction on MR and/or CT was not considered an end point. Because the clinical balloon test occlusion and ICA-occluded stable xenon CT CBF study were designed only to predict infarction related to the loss of ipsilateral ICA blood flow, end points could be excluded only if there was direct positive evidence that the subsequent infarction was not flow-related. Direct positive evidence meant angiographic proof of a distal embolus or intraoperative recording of sacrifice of an end artery, either of which had to correspond to the vascular distribution of the resultant infarction. A strong clinical impression on the part of the surgeon or radiologist that the infarction was embolic in nature was not considered sufficient direct positive evidence. In the absence of direct positive evidence to the contrary, and to present the most conservative estimate of the false-negative rate for the stroke-risk assessment protocol, all other end points were considered flow-related infarctions.

Criteria for Inclusion in Control Groups

Two control groups were established based on extensive review of the English literature on therapeutic carotid artery sacrifice below the level of the origin of the ophthalmic

artery. Patients from previously published reports were eligible for inclusion into either group if the reports: 1) contained at least 15 evaluable patients (to reduce anecdotal bias); 2) adequately distinguished infarction-related deaths from other postoperative deaths; and 3) consisted of patients who underwent abrupt ICA occlusion without concomitant hypotension. Studies were specifically excluded if they failed to meet the above criteria, used partial or gradual ICA occlusion, or did not distinguish infarctions resulting from abrupt common carotid artery occlusion from those resulting from abrupt ICA occlusion and did not perform an internal analysis to demonstrate that the infarction rates from those two types of vessel sacrifice were equivalent.

The first control group consisted of patients from series in which abrupt ICA sacrifice was performed without any preoperative stroke-risk assessment (Table 2) (10, 11, 27–29). The second control group consisted of patients from series in which abrupt ICA sacrifice was performed after passing an up to 30-minute clinical temporary ICA occlusion test (Table 3) (1, 5, 6, 17, 18, 30–32). Patients who underwent external manual compression (Matas) tests were excluded because of the inability to assess the completeness of ICA occlusion. Adequacy of temporary occlusion required either direct intraoperative visualization for surgical clamping or fluoroscopic confirmation for balloon test occlusions. Occlusion tests lasting longer than 30 minutes were excluded. Series that used a clinical temporary ICA occlusion test coupled to any modality other than serial awake neurologic examinations were also excluded. For the purpose of this study, any hemispherically lateralizing neurologic deficit that lasted longer than 24 hours after ICA sacrifice in the historical report was counted as an instance of infarction.

Statistical Analysis

The mean CBF value of each of the 8 vascular distributions for each CBF axial level, and the average for both levels combined, were calculated for each patient from their ICA-occluded CBF study (31 patients) and their unoccluded CBF study (21 patients). These CBF values were used to calculate 7 derived variables (Table 4) for each vascular distribution at each CBF axial level and the average of both CBF levels for each patient.

The 7 derived variables from each patient who sustained a subsequent flow-related infarction were compared with the values for each patient without a defined end point using either an independent t test or a Mann-Whitney test, depending on violation or nonviolation of the statistical assumptions for data distribution necessary for each variable. The statistical test to be used was determined independently for each variable. Statistical computations were performed using Biomedical Data Program (University of California Press, Berkely, Calif, 1990). Statistical significance was set at a nondirectional α of less than .05. The rate of flow-related infarction and flow-related mortality for the 30 patients who passed the preoperative stroke-risk assessment protocol was compared with those rates for the two control groups of abrupt ICA sacrifice derived from the literature (Tables 2 and 3) using χ^2 analysis.

Results

Subsequent Infarctions

Follow-up neuroimaging showed subsequent infarctions in six patients. Two of these infarctions were excluded as study end points, one because of an angiographically confirmed posterior cerebral artery embolus and the other be-

TABLE 2: Infarction and mortality rates in previously published large series of unselected ICA sacrifice in normotensive patients

Author (Ref)	Number of Patients	Patient Diagnosis (%)	Number of Infarctions (%)	Onset of Neurologic Deficit	Number of Deaths from Infarction (%)
Schorstein (27)	49	Unruptured aneurysm (73) Ruptured aneurysm (27)	8 (17)	5 min 4 d	3 (6)
Olivecrona (28)	23	Unruptured aneurysm (48) Carotid cavernous fistula (26)	7 (30)	3.5 h 7 d	0[a]
Norlen (29)	17	Unruptured aneurysm (22) Ruptured aneurysm (78)	5 (29)	Unknown	0[a]
Moore and Baker (10)[b]	61[c]	Cervical neoplasms	17 (28)	Immediate–6 d	10 (16)
Moore, Karlan, and Siger (11)[b]	104[c]	Cervical neoplasms	28 (27)	Unknown	17 (16)
Total	254		65 (26)	Immediate–7 d	30 (12)

[a] There were no deaths from infarction in either of these two series, but in two patients in each series the ICA ligature was removed at the onset of their neurologic deficit. It is unknown whether they would have died if this had not been done.

[b] The same first author reported both series, but no patients overlapped: the first included patients from 1926 through 1953 and the second from 1954 through 1968.

[c] In both series the majority were ICA rather than common carotid artery sacrifices (75% and 80%, respectively). Internal analysis in both studies showed no difference in the stroke rates between the two types of sacrifice, but the instances of stroke and death were not subdivided by method of carotid sacrifice.

TABLE 3: Infarction and mortality rates in large series of normotensive patients who underwent a successful clinical temporary ICA occlusion test followed by abrupt ICA sacrifice

Author (ref)	Number of Patients	Patient Diagnosis	Method of Temporary ICA Occlusion	Number of Infarcts (%)	Onset of Neurologic Deficits	Number of Deaths from Infarction (%)
Voris (30)	39	Cerebral aneurysms[a] (83%), Carotid-cavernous fistula (8%), Miscellaneous (8%)	20–30 min intraoperative occlusion, local anesthesia	13 (33)[b]	Within 12 h	5 (13)[b]
Love and Dart (18)	15	Cerebral aneurysms[a]	20–30-min intraoperative occlusion, local anesthesia	6 (40)[c]	Unknown	2 (13)[c]
Landolt and Millikan (31)	16	Cerebral aneurysms[a]	15–30-min intraoperative occlusion, local anesthesia	3 (19)	hour/day	0
Fox et al (5)	57	Unruptured aneurysm (85%), ruptured aneurysm (15%)	15-min balloon test occlusion	3 (5)	5 h–2 wk	0
Weil et al (17)	21	Unruptured aneurysm	10-min balloon test occlusion	2 (10)	1–4 mo	0
Andrews, Valavanis, and Fisch (1)	24	Skull-based neoplasm	15-min balloon test occlusion	1 (4)	Unknown	0
Gonzalez and Moret (32)	22	Cervical carcinoma	30-min balloon test occlusion	2 (10)	24 h	0
Higashida et al (6)	68	Cavernous-sinus aneurysms	30-min balloon test occlusion	3 (4)[d]	48 h–6 wk	0
Total	262			33 (13)	hour–4 mo	7 (3)

[a] None of these three series reported the percentage of ruptured versus unruptured aneurysms.

[b] Four of these infarctions leading to death were confirmed to result from distal propagation of thrombus (two from site of ligation, two from the aneurysm origin).

[c] One of these infarctions leading to death was confirmed to result from distal propagation of thrombus.

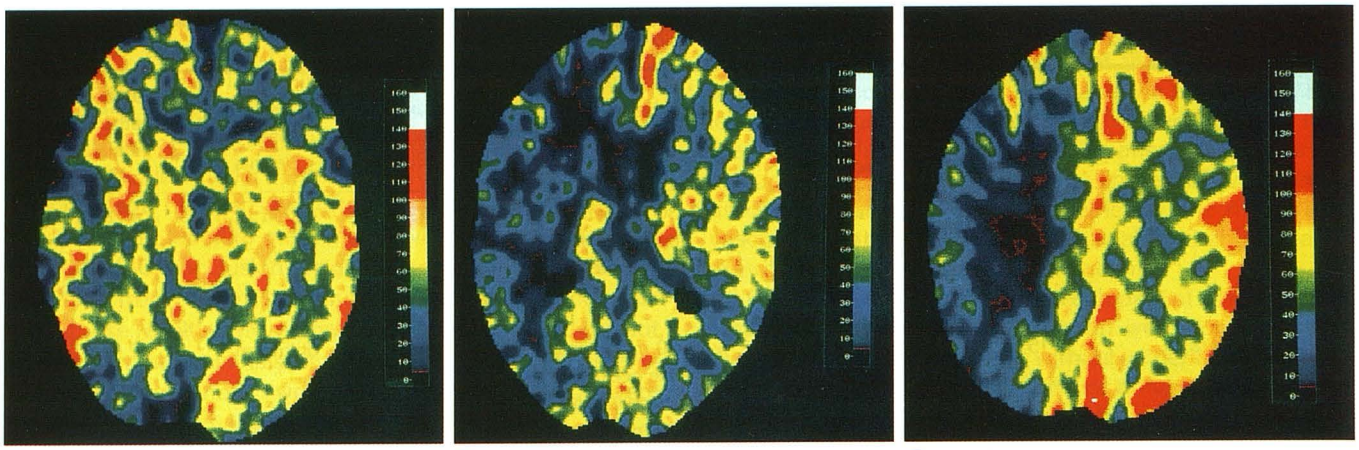
[d] One of these infarctions was confirmed to be a middle cerebral artery embolic stroke.

TABLE 4: Seven derived variables calculated for each vascular distribution at each CBF level and average of both levels for each patient

Variable[a]	Variable Derivation
1. Absolute CBF value =	ipsilateral occluded CBF value
2. Absolute change in CBF =	ipsilateral unoccluded CBF value − ipsilateral occluded CBF value
3. Relative change in CBF =	(ipsilateral unoccluded CBF value − ipsilateral occluded CBF value)/ipsilateral unoccluded CBF value
4. Absolute CBF asymmetry =	contralateral occluded CBF value − ipsilateral occluded CBF value
5. Relative CBF asymmetry =	(contralateral occluded CBF value − ipsilateral occluded CBF value)/contralateral occluded CBF value
6. Absolute change in CBF asymmetry =	(contralateral unoccluded CBF value − ipsilateral unoccluded CBF value) − (contralateral occluded CBF value − ipsilateral occluded CBF value)
7. Relative change in CBF asymmetry =	((contralateral unoccluded CBF value − ipsilateral unoccluded CBF value) − (contralateral occluded CBF value − ipsilateral occluded CBF value))/(contralateral unoccluded CBF value − ipsilateral unoccluded CBF value)

[a] Variables 1, 4, and 5 can be derived for all 31 patients, but variables 2, 3, 6, and 7 can be derived only for the 21 patients with both ICA-occluded and unoccluded CBF studies. Variables 1 through 3 are derived for all 8 vascular territories; variables 4 through 7 can be derived for all but the "cerebral" distribution (7 of 8 territories), because both sides are compared.

cause of known intraoperative sacrifice of the recurrent artery of Heubner. Four of these infarctions were considered potentially flow-related. One of the four flow-related infarctions (case 1) occurred in the one patient who passed the clinical balloon test occlusion but not the ICA-occluded stable xenon CT CBF study (Fig 2). This patient had had cervical squamous cell carcinoma, and his ICA had been ligated intraoperatively after laceration of that artery during tumor removal. A large, ultimately fatal, right hemispheric infarction developed in a region exactly corresponding to the region of reduced CBF on his ICA-occluded CBF study. Although he awoke



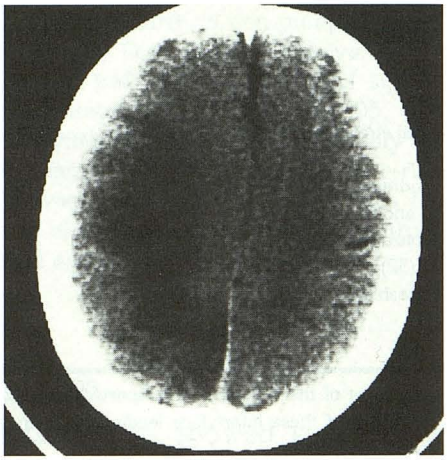


Fig. 2. Case 1. The unoccluded baseline xenon CT CBF study showed normal symmetric CBF (*A*). Although he tolerated the 15-minute clinical balloon test occlusion without any change in neurologic status, his right ICA-occluded xenon CT CBF study demonstrated a significant drop in blood flow in the right middle cerebral artery, right anterior border zone, and posterior right anterior cerebral artery territories (*B* and *C*).

D, CT without contrast 24 hours after carotid sacrifice demonstrated a major infarction (which was ultimately fatal) exactly corresponding to the region of CBF decrease observed in *B* and *C*.

from anesthesia without hemispheric deficits, a contralateral hemiplegia with hemihypesthesia developed 12 hours after ligation; the patient died of progressive brain swelling and herniation within 48 hours of ICA ligation. The three other flow-related infarctions were not fatal and occurred in patients who passed both components of their preoperative stroke-risk assessment.

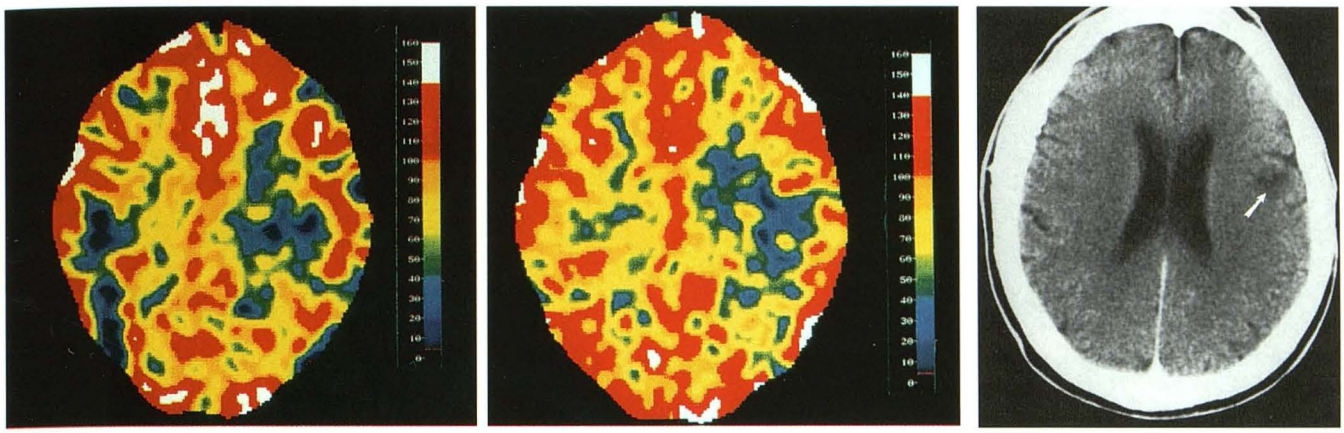
One of the patients (case 2) had a small left peripheral cortical infarction which occurred after detachable balloon occlusion of the left ICA for a bleeding petrous carotid pseudoaneurysm with a postoperative wound infection (Fig 3). A right pronator drift developed and resolved 48 hours after ICA occlusion. Despite the radiologist's strong clinical suspicion of distal embolization and a suggestive lesion size and location, the infarction was classified as flow-related because there was no proof of another cause.

The second nonfatal flow-related infarction (case 3) was a tiny new globus pallidus hypodensity in a patient with adenoid cystic carcinoma of the cavernous sinus and orbit (Fig 4). The patient remained clinically asymptomatic. This small infarction may have resulted from inadvertent intraoperative sacrifice of a small perforating artery or from hypertension (lacunar infarction); however, there was no proof of either, so it was included as a possible flow-related infarction.

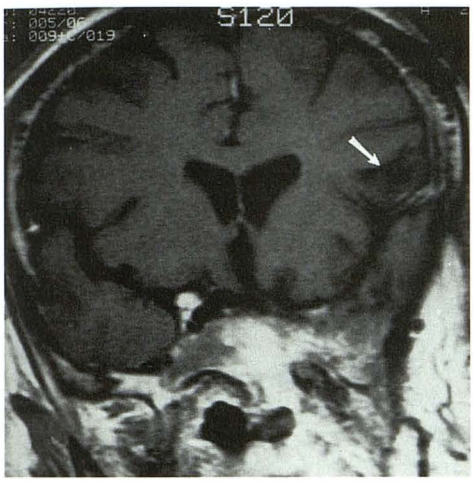
The third nonfatal flow-related infarction (case 4) was a moderate-size right parietal cortical border zone and deep white matter border zone infarction which occurred after surgical ICA ligation in a patient with a right cavernous sinus spindle cell carcinoma (Fig 5). Her postoperative dense left hemiparesis has since improved to a residual mild left hemiparesis with hyperreflexia, and she is independent in all activities of daily living.

False-Negative Rate

If the first two nonfatal infarctions (cases 2 and 3) were excluded as episodes of distal emboliza-



A B C



D

Fig. 3. Case 2. The unoccluded baseline xenon CT CBF study showed relatively normal symmetric CBF (*A*), which did not significantly change (except for possible flow augmentation in the right posterior parietal region) with temporary left ICA occlusion (*B*).

C, Noncontrast CT and *D*, T1-weighted (400/20/2 [repetition time/echo time/excitations]) noncontrast MR taken 48 hours after detachable balloon occlusion of his left ICA demonstrated a small peripheral cortical infarction (*arrow*). Distal embolization during the balloon procedure was suspected but could not be proved.

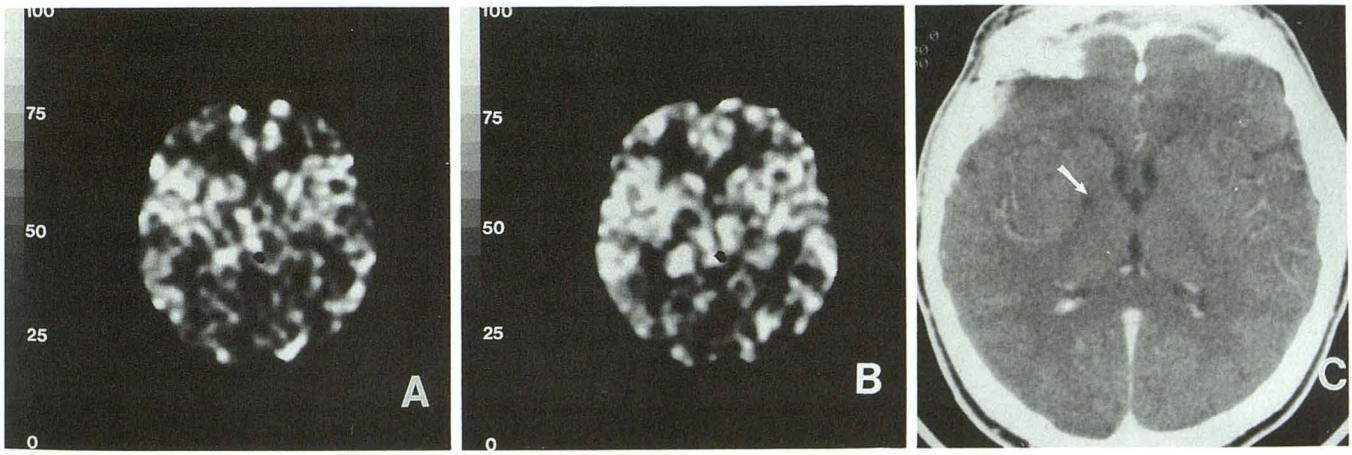


Fig. 4. Case 3. The unoccluded baseline xenon CT CBF study demonstrated normal symmetric CBF (*A*), which did not appreciably change with temporary right ICA occlusion (*B*).

C, Contrast-enhanced CT 48 hours after intraoperative sacrifice of the right ICA during resection of a right cavernous-sinus tumor revealed a tiny right globus pallidus hypodensity (*arrow*). Inadvertent intraoperative perforating artery occlusion or a lacunar infarction in this hypertensive patient were suspected but could not be proved.

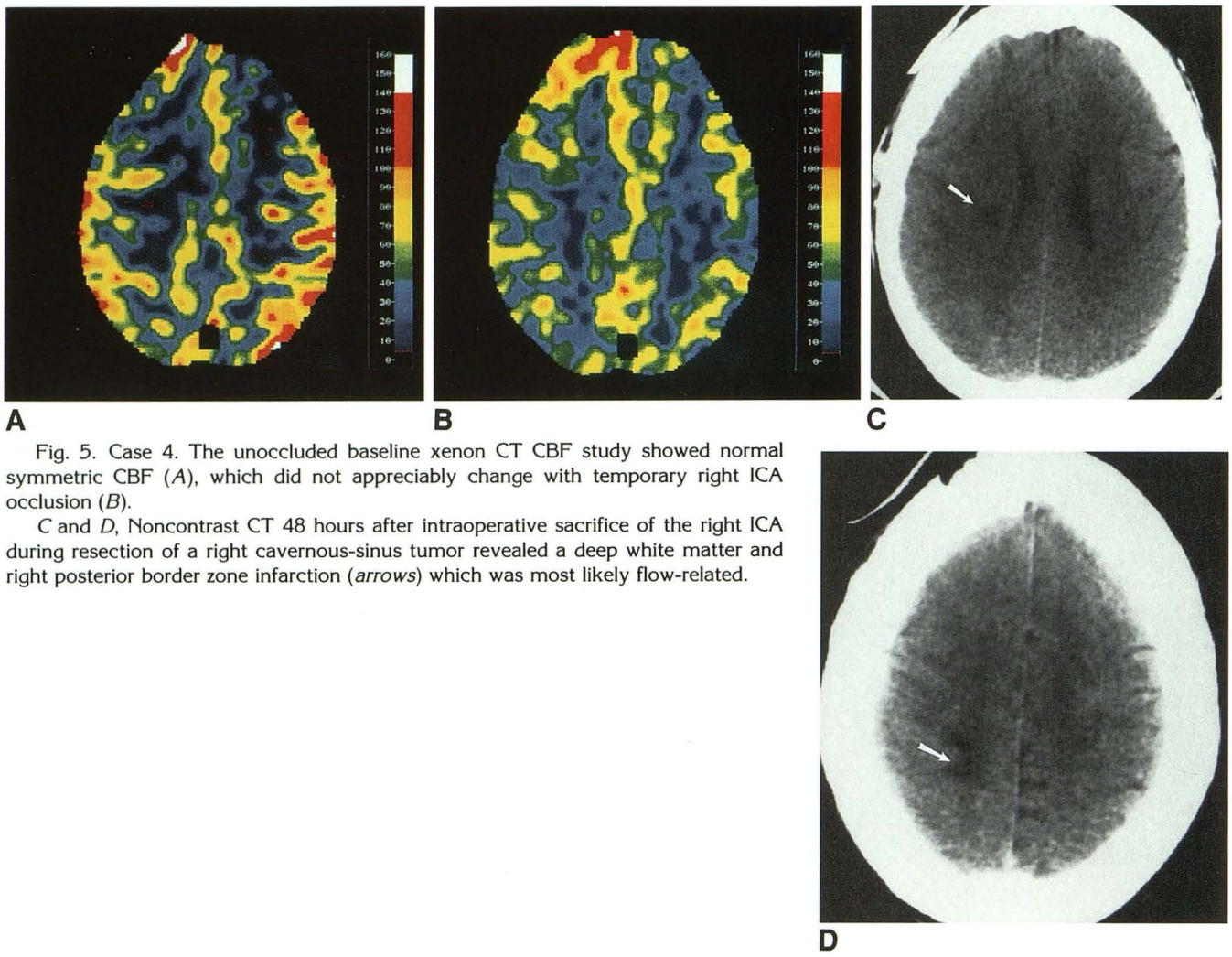


Fig. 5. Case 4. The unoccluded baseline xenon CT CBF study showed normal symmetric CBF (*A*), which did not appreciably change with temporary right ICA occlusion (*B*).

C and *D*, Noncontrast CT 48 hours after intraoperative sacrifice of the right ICA during resection of a right cavernous-sinus tumor revealed a deep white matter and right posterior border zone infarction (*arrows*) which was most likely flow-related.

tion and perforator occlusion, the false-negative rate for abrupt ICA occlusion below the ophthalmic artery was 3.3% (1 of 30). By attributing all 3 unpredicted infarctions to reduced CBF, despite the likelihood that some were not, we arrived at a conservative overall estimate of 10% (3 of 30) as the false-negative rate for the clinical balloon test occlusion with the ICA-occluded xenon CT CBF study.

There were no statistically significant differences between the 3 cases of unpredicted flow-related infarctions and the 27 cases without infarctions in any of the 7 derived variables at either CBF level, or both levels combined, for any of the 8 vascular territories studied.

Comparison with Previously Published Series

Table 3 presents the data from the previously published reports of large series of unselected normotensive patients who underwent abrupt ICA sacrifice (10, 11, 27–29). Unselected abrupt ICA sacrifice led to infarctions in 65 (26%) patients, of which 30 (46%) were fatal. Compared with this group, preoperative balloon test occlusion coupled with an ICA-occluded stable xenon CT CBF study led to a statistically significant reduction in postoperative infarction ($P < .05$) and infarction-related mortality ($P < .05$).

Table 4 presents the data from large series of normotensive patients who underwent abrupt ICA sacrifice after passing a clinical temporary ICA occlusion test but did not undergo any other means of assessing the adequacy of cerebrovascular reserve (1, 5, 6, 17, 18, 30–32). Abrupt ICA sacrifice led to infarctions in 33 (13%) patients, of which 7 (21%) were fatal. Isolated use of a clinical temporary ICA occlusion test also led to a statistically significant reduction in postoperative infarctions ($P < .05$) and infarction-related

mortality ($P < .05$) compared with the unselected ICA sacrifice. Addition of an ICA-occluded stable xenon CT CBF study to the preoperative evaluation led to a reduction in postoperative infarction and infarction-related mortality rates compared with sole reliance on a clinical temporary ICA occlusion test (13% versus 10%, and 3% versus 0%, respectively). However, this further reduction did not achieve statistical significance.

Discussion

Evolution of Preoperative ICA Occlusion Risk Assessment

One of the earliest attempts at preoperative risk assessment for subsequent ICA occlusion was the development of the external manual ICA compression test by Matas (33–35). Unfortunately this test has proved unreliable partly because of its inability to assure adequate ICA occlusion, to exclude common carotid artery or external carotid artery occlusion, and to eliminate confounding vasovagal responses (36). The next advance was to assure adequate ICA occlusion by performing the temporary ICA occlusion test intraoperatively, under direct vision using local anesthesia so that serial neurologic examinations could be performed (18, 30, 31). The clinical balloon test occlusion performed under local anesthesia is a variation on this theme, with the adequacy of occlusion assessed fluoroscopically (1, 2, 4–6, 17, 32). For situations in which it was not possible or desirable to keep the patient awake during risk assessment, electroencephalography (37–42) and compressed spectral array (43) and somatosensory-evoked-potential (39) monitoring provided sensitivity similar to that of serial neurologic examinations. Although confirmable temporary ICA occlusion did reduce the number of infarctions after abrupt ICA sacrifice, it did not completely eliminate them.

One approach for eliminating the small group of delayed postocclusion infarctions that remained was to ligate the ICA with ligatures or metallic bands that could be removed if problems later developed (28, 29, 34, 35). Another was to occlude the ICA partially then completely in a second stage if no ischemic symptoms developed (44–46). A third was to occlude the ICA gradually with a clamp that could be progressively closed over several days (47–48). Each of these strategies was tedious, labor-intensive, and often subjected the patient to more than one operation. Furthermore, each was applicable only to cervical ICA occlusion.

Under the assumption that many of the remaining delayed infarctions were caused by marginal postocclusion CBF, some tried to assess ICA-occluded CBF reserves preoperatively. The earliest of these tests was the assessment of collateral circulation by cross-compression angiography (49). Unfortunately, angiographic vessel opacification is a poor physiologic indicator of CBF, and it is not surprising that cross-compression angiography turned out to be a poorer method for assessing CBF reserves than subsequently developed techniques (50). Other popular tests included the measurement of intraoperative ICA-occluded stump pressure (38, 51, 52), angiographic catheter back pressure (53, 54), and retinal artery pressure (55, 56). Although more useful than cross-compression angiography, these techniques have subsequently been replaced by more accurate techniques (53, 57).

The most recent supplemental temporary ICA-occlusion techniques take direct intracranial measurements of parameters linked to CBF to measure CBF reserves. Examples of these techniques include transcranial Doppler (58, 59) dynamic CT scanning (60), xenon-133 CBF (3, 42, 49), single-photon emission CT (61–63), and stable xenon CT CBF (19–21).

Etiology of Postocclusion Infarction

Development of a contralateral neurologic deficit immediately after ICA occlusions is usually caused by inadequate CBF in an eloquent area of the ipsilateral hemisphere. In our series of more than 400 balloon test occlusions we found that this occurred in 5% to 10% of patients tested (9, 14, 19). Both our group and others have shown that this type of deficit occurred within 10 minutes (usually within 3 minutes) of complete carotid occlusion and rapidly and completely reversed on balloon deflation (5, 32). Coupling the clinical occlusion test to a stable xenon CT CBF study was an attempt to detect patients with marginal CBF reserves who are able to tolerate temporary ICA occlusion but who are at increased risk for developing a flow-related infarction with prolonged occlusion, especially if periods of hypotension, anemia, hypoxemia, or hypoglycemia occur during the postoperative period (4, 14, 19, 20). That patients in group B are at greater risk for stroke than patients in group A was evident in a series of ICA vein-graft reconstructions re-

quiring 1.5 to 2.5 hours of temporary ICA occlusion, published by Sen and Sekhar (26). Despite moderate hypothermia (32°C) and barbiturate-induced coma during temporary occlusion, 5 of 9 (56%) group B patients awoke with hemispheric neurologic deficits compared with 1 of 14 (7%) group A patients. In our series of balloon test occlusions, 10% to 15% of patients fell into this moderate-risk category.

Not all delayed infarctions after abrupt ICA occlusion are flow-related. In 1868, LeFort was the first to propose that delayed infarction after ICA sacrifice might occur from distal propagation of thrombus from the point of ICA ligation up into the circle of Willis (64). Several necropsy reports have confirmed that this sequence of events occasionally occurred, with thrombus beginning either at the point of ICA ligation or from another source such as an aneurysm lumen (18, 30, 64–66). Another possible mechanism of infarction is distal embolization from a blind ICA stump.

Anecdotal necropsy evidence (65) led Dandy to make the influential and dogmatic statement that immediate infarctions (up to 12 hours) were attributable to inadequate circulation, late ones (after 12 hours) to thrombosis and/or embolization (44). Since that time adequate evidence has accumulated to suggest that thromboembolism actually accounted for only a subset of delayed infarctions after ICA occlusion. The majority of autopsies after infarction-related deaths from ICA sacrifice did not show ICA or major distal branch thromboembolism (28). In addition, surgical reexploration after the development of a neurologic deficit often failed to identify intraluminal thrombosis, and release of the occlusive ligature often led to good distal pulsations with improvement of the neurologic deficit (18, 28, 31, 35, 45).

Thresholds of Ischemia

Normal adult cortical CBF is 50 to 55 mL/100 g per minute (21, 24, 25). The CBF threshold at which reversible clinical symptoms first begin to appear in awake humans has not been determined. However, in awake nonhuman primates the CBF threshold for reversible clinical neurologic symptoms was 21 to 23 mL/100 g per minute; the threshold for infarction with permanent flow reduction was 17 to 18 mL/100 g per minute (67). Clinical studies in normothermic and normocapnic anesthetized humans and in anesthetized nonhuman primates demonstrated that the CBF threshold for neurophysiologic changes (eg, electroencephalography, somatosensory evoked potentials, or central conduction time) was 15 to 22 mL/100 g per minute (37, 42, 68–73). Thus, clinical temporary ICA occlusion tests were likely to identify a similar (but not identical) group of patients as neurophysiologic ICA occlusion tests. The reversibility of these ischemic changes was related to both the degree of CBF reduction and the duration of the reduction. Even severe reductions in CBF could be tolerated for very short periods, but permanent CBF drops below 15 to 18 mL/100 g per minute tended to lead uniformly to infarction (67, 74).

Studies of extracellular potassium clearance in nonhuman primates after cortical stimulation demonstrated an abnormally elevated clearance half-time when CBF was between 20 to 40 mL/100 g per minute (75). Thus, measurable ionic disturbances were present at CBFs above the threshold for clinical and neurophysiologic changes. With CBF reduction to 8 to 11 mL/100 g per minute massive spontaneous rises in extracellular potassium occurred; CBF reduction to 5 to 6 mL/100 g per minute led to failure in membrane ionic homeostasis (71, 72, 76).

Control Subjects

Because of our own strong beliefs in the validity of our preoperative risk-assessment techniques, we could not proceed with abrupt ICA sacrifice for patients who failed the clinical balloon test occlusion or for those who demonstrated major drops in CBF by ICA-occluded stable xenon CT CBF study. As a result, we had to rely on literature-based control groups for comparison. Obviously, historical literature-based controls have major drawbacks, including the nonuniformity of treatment techniques, the evolution of basic supportive medical care, and the improvement in medical diagnosis and complication management over time.

Although we eliminated series with cases of concomitant hypotension from hemorrhage as the major confounding variable leading to stroke after ICA sacrifice (10, 12, 77), other weaker confounding factors such as ruptured cerebral aneurysms and distal arteriovenous malformations were not excluded. Subarachnoid hemorrhage could lead to an overestimation of the postocclusion infarction rate because of ischemic contributions by vasospasm; including arteriovenous malformations could lead to overestimation

of the postocclusion infarction rate because of preferential shunting of collateral blood supply through the fistula rather than to the surrounding normal brain.

Another confounding variable in the literature-derived control group was the site of ICA occlusion and the possibility of distal thromboembolism. Most of the surgical ligation series involved cervical ICA ligations, which resulted in a long column of stagnant blood in the ICA from the ligature to the entrance of the next major collateral (usually the ophthalmic artery). Several cases of proved thromboembolus (18, 30) could not be excluded from the control groups because all patients in the group did not undergo angiography or necropsy to confirm the mechanism of infarction. The infarction rates in the control groups must therefore be viewed as comprising both thromboembolic and flow-related infarctions, and therefore slightly overestimating the flow-related infarction rates in these groups.

On the other hand, modern neuroimaging was not available before 1976. As a result, earlier studies included only patients with clinically symptomatic neurologic deficits. There was no way to identify small, clinically silent infarctions. This factor could lead to an underestimation of infarction rates after ICA sacrifice in the literature-derived control groups compared with our series in which neuroimaging-detected infarction was the defined end point. In addition, our series included surgical intracranial ICA occlusions along with cervical ICA occlusions. Regional pressure from brain retraction is a known contributor to underlying parenchymal ischemia (78–82), and this confounding factor could lead to an overestimation of the infarction rate resulting purely from loss of ICA blood flow in our study group.

Infarctions after False-Negative ICA-Occluded Stable Xenon CT CBF Studies

Cases 2 and 3 (Figs 3 and 4) seem to have infarctions atypical in size and location for flow-related infarctions. They were included as end points in this study for the sake of maintaining a rigorously conservative analysis. Case 4 (Fig 5) almost certainly had a flow-related infarction. The infarction involved deep white matter and posterior cortical border zone regions between the middle cerebral artery and posterior cerebral artery distributions. The main middle cerebral artery and posterior cerebral artery parenchymal territories were spared.

Careful examination of Figure 1, which demonstrates our method of placement of regions of interest for CBF analysis, revealed a possible explanation. All regions of interest were placed to measure regions of mixed cortical flows (average of both gray and white matter). No regions of interest were placed to assess deep white matter CBF. In addition, the small size of the cortical posterior border zone region meant that it was sampled by at most two regions of interest. The CBF value in these two regions of interest may not have been accurate if their areas also overlapped some of the non–border zone middle cerebral artery or posterior cerebral artery vascular territories. It would appear that the major limitation of the ICA-occluded xenon CT CBF study was insensitivity to reduction in deep white matter and small cortical vascular border-zone regions, which reflected our selection of only cortical mantle regions for sampling.

Although the ICA-occluded stable xenon CT CBF study did not completely eliminate flow-related infarctions after abrupt ICA sacrifice, it certainly changed their character. In the literature-derived control group of abrupt ICA sacrifice in unselected patients (Table 3), 46% of subsequent infarctions were fatal; in the control group preoperatively assessed solely with a clinical temporary ICA occlusion test (Table 4), 21% of subsequent infarctions were fatal. These higher infarction-related death rates most likely resulted from infarction of major vascular territories with resulting cerebral swelling, increased intracranial pressure, and, finally, death. We saw no major vascular territory infarctions. Most vascular border zone infarctions are not fatal and result in much less residual morbidity than major vascular territory infarctions. One of our patients was asymptomatic from her infarction throughout her course (case 3); one became asymptomatic within 48 hours (case 2); and the third was left with a mild residual hemiparesis but was independent in all activities of daily living (case 4).

Stable Xenon CT CBF versus Other Methods of Assessing ICA-Occluded CBF Reserve

Stable xenon CT CBF noninvasively provides relatively high-resolution, accurate, quantitative local CBF information coupled with CT anatomy (21). The quantitative flow information derived by xenon CT correlates well with a variety of cerebral blood flow techniques (25, 82–91). A xenon CT study is repeatable at 20-minute inter-

vals, allowing for direct comparison of ICA-occluded and unoccluded CBF values. Stable xenon, at a concentration of 33%, is clinically safe. The most common effects of inhalation are a mild alteration in sensorium that occasionally induces patient motion, but this can be minimized by careful positioning, prestudy education, and patient reassurance during the study (21). Spontaneous respiratory depression longer than 10 seconds occurred in only 3.6% of patients (92). The balloon test occlusion has been associated with a 3.7% risk of any complication (including asymptomatic intimal dissections) and a 1.7% risk of neurologic deficit persisting beyond the testing period (93).

The major drawbacks of this preoperative risk-assessment protocol are the need to transport the patient from the angiography suite to the CT scanner with the balloon catheter in place (balloon deflated), the limited availability of stable xenon CT CBF technology, and the prolonged image reconstruction time once the data are acquired. Pending improvements in software speed, quality, and CT compatibility should soon eliminate the latter two drawbacks.

ICA-occluded regional xenon-133 CBF studies also provide accurate, quantitative CBF data which can be obtained in the angiography suite. Unfortunately, this test is slightly more invasive and does not provide the cortical or intraparenchymal CBF spatial resolution of tomographic methods. ICA-occluded transcranial Doppler studies provide rapid, noninvasive, accurate quantitative information about blood velocity and direction which are related to collateral CBF and can be performed in the angiography suite. Doppler studies are limited by: 1) inability to provide a direct measure of CBF; 2) dependence on technicians for reproducible, accurate studies; 3) of an acoustic window in up to 15% of patients; and 4) flow values only from major vascular trunks, which give little information about more distal or even border-zone CBF.

ICA-occluded technitium-99m-hexamethylpropyleneamine oxime single-photon emission CT studies provide fair tomographic spatial resolution of CBF (61–63). They are simple to perform, and the tomographic portion can even be performed several hours after the clinical balloon test occlusion. As generally applied, they are able to provide only relative CBF values and thus rely solely on the development of CBF asymmetry (61–63). Almost all significant reductions in CBF with ICA occlusion that we have studied with stable xenon CT CBF techniques have been associated with asymmetric drops in CBF. As a result, single-photon emission CT is very sensitive in identifying these patients. Unfortunately, without the benefit of accurate quantitative CBF values, ICA-occluded single-photon emission CT may be too sensitive (94). Some patients had baseline asymmetries before ICA occlusion that did not significantly change with occlusion. Moreover, asymmetry in some cases was caused by paradoxical CBF increases in one territory without surrounding decreases, minor asymmetric reductions of CBF, and minor reductions of CBF in some areas associated with asymmetric CBF increases in others. None of these situations would place a patient in the moderate stroke-risk group according to our criteria. Without the specificity afforded by accurate CBF quantitation, ICA-occluded single-photon emission CT might erroneously exclude some patients from potentially beneficial therapy.

Current Criteria

We currently divide our adult patients into 3 groups based on the results of their preoperative risk assessment. The 5% to 10% of patients who fail the clinical balloon test occlusion fall into group A. They probably experience drops in CBF to levels less than 21 to 23 mL/100 g per minute and are at high risk for infarction with even temporary ICA occlusion. The 10% to 15% of patients who pass the clinical balloon test occlusion but have CBF values less than 30 mL/100 g per minute fall into group B. These patients do not have normal ICA-occluded CBF from a statistical standpoint (greater than 2 SD from mean) and most likely represent a group with marginal CBF reserves who compensate tenuously for the ICA-occluded state. We believe that, although they may tolerate short periods of temporary ICA occlusion, they are at moderate risk for infarction with permanent ICA sacrifice. Those 80% of patients in group C who have ICA-occluded CBF values greater than 30 mL/100 g per minute are at low risk for flow-related infarction. These basic guidelines must be adapted on a case-by-case basis for patients at the extremes of age and for those with chronically accommodated areas of low baseline CBF. An area of CBF less than 30 mL/100 g per minute on the ICA-occluded study may not necessarily be abnormal in the occasional case in which the CBF in that same region is also low on the baseline unoccluded CBF study.

Internal analysis of the present study suggests that an asymptomatic region of CBF up to 30 mL/100 g per minute may not increase stroke risk if this value represents a CBF drop of less than 30% from the baseline CBF value in that region.

Using a preoperative clinical balloon test occlusion coupled with a stable xenon CT CBF study will significantly reduce but will not eliminate post-ICA-occlusion infarctions. Recognizing that two of the post-ICA-occlusion infarctions in our series may have been attributable to thromboembolic events or perforating artery occlusion, the data suggest that the false-negative rate for flow-related infarction falls between 3.3% and 10%. Analysis of the remaining infarction suggests that the stable xenon CT CBF studies, which examine only cortical blood flow, are incompletely sensitive to vascular border zone regions in the deep white matter and/or cerebral cortex. Adjusting our CBF sampling technique to pay more attention to deep white matter blood flow may eliminate this area of insensitivity in the future. Fortunately, infarctions in these regions are not usually fatal and carry far less morbidity than the major vascular territory strokes seen after ICA sacrifice when appropriate preocclusion techniques are not used.

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Please see the Commentary by Eskridge on page 845 in this issue.