The Value of Regional Cerebral Blood Flow Measurements Compared to Angiography in the Assessment of Obstructive Neck Vessel Disease

BY P. PROSENZ, M.D.,* W.-D. HEISS, M.D.,* H. TSCHABITSCHER, M.D.,† AND L. EHRMANN, M.D.*

Abstract:
The Value of Regional Cerebral Blood Flow Measurements Compared to Angiography in the Assessment of Obstructive Neck Vessel Disease

In 50 patients with internal carotid artery occlusion and 40 patients with internal carotid artery stenosis hemispheric and regional cerebral blood flow (rCBF) was measured by the \(^{133}\)Xenon clearance method. rCBF was evaluated according to the presence of ischemic or hyperemic foci and to the level of regional perfusion alteration. The degree of collateral circulation and diameter of stenosis were determined from the angiograms. The clinical symptoms were expressed in a score of motor deficiencies. In internal carotid artery occlusion no correlation of motor deficiency index with angiographically demonstrable collateral circulation was detectable, but there was good correlation with hemispheric CBF and an excellent correlation (P < 0.001) with the rCBF parameters. In internal carotid artery stenosis no correlation existed between motor deficiency and the degree of stenosis or hemispheric CBF, but good correlation was observed between motor deficiency and the rCBF parameters (P < 0.01).

According to these findings, angiographical demonstration of collateral circulation and of stenosis does not provide as accurate information on impending or already developed tissue infarction as does rCBF measurement. Presence of hyperemic foci and lack of ischemic foci were related to lesser motor disturbances. Borderlines of 30 ml/100 gm per minute for threatening tissue ischemia and of 25 ml/100 gm per minute for present tissue ischemia are established. Some points favor the thromboembolic theory of infarction in internal carotid artery stenosis.

Introduction

Neurologists as well as vascular surgeons and neurosurgeons have increasingly become aware of the importance of occlusive and stenotic processes of the neck vessels for transient and permanent cerebrovascular disturbances. However, some links of the pathogenetic chain which connects the vascular process situated in the neck to the functional and morphological damage of particular regions of the brain are still obscure, controversial or unknown.¹⁻⁷

Many authors have investigated the contribution of angiography to the elucidation of this pathogenetic chain.⁸ Evidence has been presented that the incidence of neurological disturbances as well as the danger of recurrences are higher in cases of stenosis or occlusion of the internal carotid artery than in an adequate control group.¹⁰

Results obtained from investigation on the significance of angiographically demonstrable collateral circulation⁶⁻⁻¹⁰ were not conclusive in all instances. This is due to several difficulties. In order to discuss collateral circulation in obstructive carotid processes, bilateral angiography, at least, must be performed; in order to fully survey all collateral channels, vertebral angiography and aortic arch opacification also are essential.¹⁰ These requirements are met only by a few investigators. In most instances homolateral angiography alone was performed, or no details are presented as to which criteria were used for the evaluation of the various collateral channels. Most authors did not separately evaluate occlusions and...
stenoses, intracranial and extracranial occlusions, and basal and leptomeningeal anastomosis. Thus, such questions as the significance of collateral circulation and the degree of a stenosis for brain perfusion are still open.

Until recently, only a few investigators have performed cerebral blood flow measurements in obstructive neck vessel disease. McHenry\textsuperscript{17} reported CBF measurements in two patients with internal carotid artery occlusion, Stewart\textsuperscript{18} commented on 12 stenotic and 10 occlusive carotid processes, and Herrschaft\textsuperscript{19} measured CBF in 60 patients with obstructive processes of the internal carotid artery. In previous reports we have presented rCBF measurements in seven patients\textsuperscript{20} and 45 patients.\textsuperscript{21} There is no information available which critically compares diagnostic and prognostic features of both angiography and CBF measurement in obstructive neck vessel disease.

This study is confined to the discussion of these problems on the basis of 90 patients, 50 of them with internal carotid artery occlusion and 40 with internal carotid artery stenosis. Occlusions and stenoses are dealt with separately because of the different angiographical problems in question.

**Occlusion of the Internal Carotid Artery**

This study consisted of 50 patients admitted to the Neurological University Hospital and to the Neurological Hospital of the City of Vienna Rosenhflgel (Austria) during the years 1968 to 1972. The patients were admitted either in the acute stage or days to weeks after the stroke for the purpose of establishing an accurate diagnosis and for the consideration of surgical treatment.

The ages ranged from 16 to 81 years, with a mean age of 57; 15 patients were females and 35 were males. All 50 patients suffered from occlusive processes of the neck vessels. Thirty-one patients had an occlusion of only one internal carotid artery, while other neck vessels were patent. A total of 19 patients showed an occlusion of both internal carotid arteries (three patients), or, in addition to the occlusion of one internal carotid artery, a stenosis of the other internal carotid artery (ten patients), or an occlusion of the homolateral external carotid artery (three patients), or occlusion or stenosis of the subclavian or vertebral arteries (three patients). The latter figure perhaps is not accurate, because vertebral or aortic arch angiography was not performed in all patients.

In 45 patients the case history, clinical and laboratory findings, and lack of signs of an "inflammatory" vascular disease pointed to general atherosclerosis as being etiologically responsible for the vascular process. In five patients other causes were obvious: physical exhaustion in one patient (\#16a), electrical accident in one patient (\#26a), and severe head trauma in one patient (\#47a). In two cases (\#58a and \#70a) clipping of the siphon because of intracranial arteriovenous malformations had been performed 15 and 25 years, respectively, before the sudden worsening of the symptoms causing hospitalization.

All patients underwent routine examinations (ECG, x-rays, complete medical examination, blood-glucose tolerance tests, blood lipids, EEG, orbital ophthalmoscopy, peripheral ophthalmoscopy) and routine treatment (cardiac therapy, normalization of glucose, blood gases, electrolytes, and fluid balance, osmolarly active agents [e.g., dextran 40, human albumin], dehydrating agents [e.g., furosemide], and physiotherapy).

**CLINICAL EVALUATION**

In order to minimize inherent errors and uncertainties due to subjective judgment of hardly quantifiable symptoms, evaluation was confined to motor deficiencies\textsuperscript{22, 23} and a simple rough score was used: 0 = no motor deficiencies, 1 = motor function disturbed but still useful, and 2 = not useful, plegic.

This score was applied to the cranial nerves (central facial paresis, etc.), the upper extremities, and the lower extremities. The sum of these scores established the clinical deficiency index (Id) with a maximum of 6 in a hemiplegic patient (0 = seven patients, 1 = two patients, 2 = seven patients, 3 = nine patients, 4 = seven patients, 5 = eight patients, 6 = 12 patients. Totally, measured 52 hemispheres in 50 patients).

**ANGIOGRAPHICAL EVALUATION**

A bilateral percutaneous serial carotid angiography was performed in all patients several hours up to 14 days after the onset of the stroke, the time interval being evenly distributed over that period with no preponderance of a certain time interval. Local anesthesia was used, and 8 to 10 ml of Urografin\textsuperscript{8} was injected manually. In ten patients a percutaneous vertebral angiogram also was obtained, and in 15 patients with signs of multilocular occlusive processes the neck vessels were additionally visualized by aortic arch angiography using the Seldinger technique.

In evaluating the angiographical picture the following items were examined:

1. **Localization and extension of the occlusion:** It was determined whether it was an occlusion of the internal carotid artery only, or of the common carotid artery, and whether the siphon was patent, which was not the case in eight patients.

2. **Condition of the other neck vessels:** It was determined whether there were additional stenotic or occlusive processes demonstrable, involving the other carotid, vertebral or subclavian arteries.

3. **Degree and pattern of collateral circulation:** It was determined whether there was a homolateral collateral flow via the ophthalmic artery, resulting in a filling of the middle and/or anterior cerebral arteries, or a collateral flow via the anterior communicating artery with filling of the anterior or middle cerebral artery and, in case vertebral angiography was performed, whether the anterior and/or middle cerebral arteries were filled via the posterior communicating artery.

A score was used to express semiqualitatively the degree of the angiographically demonstrable collateral circulation: 0 = no filling, 1 = poor incomplete filling, 2 = good filling of all major branches, 3 = excellent filling identical with the nonobstructed side.

In one series this score was applied to the three largest carotid collaterals, i.e., to the cross flow into the middle cerebral artery, to the cross flow into the anterior cerebral artery, and to the ophthalmic collateral. In view of the minor importance of the latter connection, no differentiation...
was made between the filling of only one or both arteries. The sum of these scores established the collateral flow index ($I_c$) with a theoretical maximum of 9.

In another series collateral circulation demonstrated by vertebral angiography was included into the score, thus increasing the maximum $I_c$ to 12; however, it never reached more than 7. This series then was evaluated separately.

**CBF Measurements**

Cerebral blood flow studies were performed in all patients one to four weeks after the onset of the cerebrovascular event, i.e., in a subacute to chronic stage of the clinical course. No measurements were performed in the acute phase. The intra-arterial inert gas isotope clearance technique, as introduced by Ingvar and Lassen, was used. After direct puncture of the respective artery (internal carotid artery, vertebral artery) under local anesthesia, 5 to 10 mc $^{133}$Xenon in saline solution (2 to 4 cc) were injected within one to two seconds using a lead-shielded syringe.

The artery to be punctured in each case was chosen according to the angiographically demonstrable collateral circulation. In the case of cross filling of most parts of the obstructed hemisphere from the patent carotid, this vessel was punctured (42 patients); in case of predominating collateral circulation via the posterior communicating artery, or in case of an obstruction of both carotid arteries, the vertebral artery was chosen (eight patients). In all cases injection of Evans blue dye and scintiphotos of the initial Xenon distribution proved the proper intra-arterial injection.

Time activity curves were registered over the head by means of a scintillation camera (Pho/Gamma III, Nuclear Chicago) connected to a double countrate meter potentiometer-writer, on the one hand, and to a Dual-ADC-1,600 channel core memory with data transfer to a digital incremental magnetic tape store, on the other hand. Details and theoretical considerations on this equipment are presented elsewhere. The patient's head was placed in front of the scintillation camera, with the vertex touching the center of the collimator, thus allocating each hemisphere to one-half of the crystal. Thereby clearance curves from each hemisphere could be registered separately. From these curves hemispheric blood flow ($F_h$) was computed by hand using the stochastic and bicompartmental calculations (for details, see reference 27). The $F_h$ values were in the ranges of 20 ml/100 gm per minute to 43 ml/100 gm per minute. A further index ($F_h + F_c$) was computed by adding hemispheric and contralateral hemispheric blood flow (fig. 1). This index includes into the evaluation the diminished blood flow of the obstructed hemisphere, the possible hemodynamic affection of the other hemisphere by basal steal, and the possibly detrimental factor of general arteriosclerosis of the cerebral vessels.

The ADC core memory magnetic tape store unit permitted the computer calculation (IBM 1,800) of rCBF maps, which present the rCBF values of contiguous square areas of 12 mm lateral length over all parts of the brain containing Xenon activity. Details of the mode of data acquisition, storage and correction for background, count loss, shunt peaks, etc., have been discussed elsewhere. Both the stochastic and the bicompartmental rCBF maps were used for evaluation.

The rCBF maps were examined for the presence of areas of ischemia and hyperemia. For this evaluation areas of at least 2 cm in diameter were shaped by hand comprising rCBF values which differed at least 20% from the surrounding hemispheric background values ($\bar{T}$). A difference of 20% between rCBF values of such areas is well above the level of statistical fluctuation and inherent errors of the measurement. Average regional flow values of these areas were computed. A region was considered to be ischemic if this average regional flow value ($\bar{f}$) was at least 20% below $\bar{T}$, on the other hand, average regional flow values of at least 20% above $\bar{T}$ were considered to be hyperemic ($\bar{f}$) (fig. 1).

From these basic data different rCBF parameters were computed, using either the quantitative information or a qualitative transformation in scoring the presence of homogenous rCBF (fig. 2), or of ischemic patches, or of hyperemic patches, or of both simultaneously. Furthermore, certain borderlines of rCBF derangements were sought by correlating empirically chosen levels of rCBF to the clinical deficiencies. These parameters were in detail:

1. $fH + fC$: Represented by $f_H$ in case of homogenous rCBF values the index was calculated from: $f_H + f_C$.
2. $fH + fC$: Represented by $f_H$ in case of homogenous rCBF values the index was calculated from: $f_H + f_C$.
3. $fH + fC$: Represented by $f_H$ in case of homogenous rCBF values the index was calculated from: $f_H + f_C$.

In case of homogenous rCBF values the index was calculated from: $f_H + f_C$. This index takes the degree of regionally altered blood flow ($f_H$ or $f_C$) and the blood flow of the hemispheric background ($\bar{T}$) into account. It should provide information as to whether side by side with regional disturbances a well-perfused hemisphere provides a better collateral background for the ischemic lesions and thus a better clinical outcome than a badly perfused hemisphere.
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**FIGURE 2**

Stenosis of the right internal carotid artery, left-sided transient ischemic attacks, dementia. No significant changes in CBF. The right middle cerebral artery territory is suspected of developing an ischemic focus on the background of reduced hemispheric CBF

\[ f_h = 39 \text{ ml/100 g.min} \]

\[ f_h = 34 \text{ ml/100 g.min} \]

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4. **reguation**: The score was:

- 0 = rCBF values homogenously and regionally above 30 ml/100 gm per minute;
- 1 = rCBF values homogenously or regionally reduced down to 25 ml/100 gm per minute, accompanied by hyperemic patches;
- 2 = rCBF values homogenously or regionally reduced down to 25 ml/100 gm per minute without hyperemia, and rCBF values regionally reduced below 25 ml/100 gm per minute accompanied by hyperemia;
- 3 = rCBF values homogenously or regionally below 25 ml/100 gm per minute without hyperemic patches.

To give a short definition of 4. **reguation**: It is assumed that emergency borderlines lie at 30 and 25 ml/100 gm per minute, respectively, and that hyperemic phenomena improve the score by one point.

\[ \text{Paco}_2 \] was determined from the carotid blood just before Xenon injection, using an Eschweiler blood gas analyzer. Most of the \[ \text{Paco}_2 \] values were around the mean value of 37 mm Hg; a few values were scattered down to 30 mm Hg and up to 45 mm Hg. The CBF values were not corrected for a standard \[ \text{Paco}_2 \].

**STATISTICAL EVALUATION**

The correlation of the clinical deficiency index with the various parameters was performed by using the parameter-free rank correlation test according to Spearman:

\[ r_s = 1 - \frac{6 \sum D^2}{n(n^2 - 1)} \]

**Results**

The results of the correlation of the clinical deficiency index (\( I_D \)) with the various other parameters are presented in table 1.

Age and angiographically demonstrable collateral circulation had no correlation with the neurological deficiencies. When the results of vertebral angiography were added to the collateral flow index, the correlation improved only unsubstantially, and not to a level of significance. This amounted to a correction only in cases which did clinically well but had a very poor carotid collateral flow. They had an excellent flow via the posterior communicating artery. However, cases with severe neurological disturbances but excellent collateral flow still predominated and prevented a better correlation.

Correlation starts getting significant with \( F_h \), and the more the indices express purely regional flow values, the tighter the correlation becomes. The highest correlations exist between clinical picture and

**TABLE 1**

<table>
<thead>
<tr>
<th>Correlation of Clinical Deficiency (( I_D )) With Other Parameters</th>
<th>( N )</th>
<th>( r_s )</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( I_D ) versus age</td>
<td>52</td>
<td>0.042</td>
<td>N.S.</td>
</tr>
<tr>
<td>( I_D ) versus collateral circulation ( I_C )</td>
<td>52</td>
<td>0.118</td>
<td>N.S.</td>
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<td>( I_D ) versus ( F_h )</td>
<td>45</td>
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<tr>
<td>( I_D ) versus ( F_h )</td>
<td>52</td>
<td>0.347</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>( I_D ) versus ( regr )</td>
<td>33</td>
<td>0.450</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>( I_D ) versus ( regr_{min-max} )</td>
<td>33</td>
<td>0.475</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>( I_D ) versus ( regr_{min} )</td>
<td>33</td>
<td>0.6304</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>( I_D ) versus ( regr_{max} )</td>
<td>33</td>
<td>0.686</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Discussion

In experimental animals occlusion of one internal carotid artery does not affect CBF. This also may be true in man, provided that the occlusion is proximal to the siphon, other alterations of vessels are absent, and the circle of Willis is patent. Unfortunately, some or all of these conditions are usually missing in the elderly sclerotic patient. In these patients the extent of a cerebral infarction depends exclusively on the collateral circulation within the first minutes or probably the first hour. Nobody is in a position to detect these regulations and compensations during such an early stage in man. Trial clamping of the internal carotid artery before therapeutic occlusion permits some conclusions as to the compensatory mechanisms and the early signs of inadequate collateral circulation.

Due to the fact that collateral pathways may develop gradually within hours and that emboli, frequently found in cerebral vessels in cases of internal carotid artery occlusion, may disappear after hours, one cannot necessarily expect a relationship between angiographically demonstrable collateral circulation and the extent of infarction. Under these circumstances the angiogram of an infarcted area may show excellent filling due to sufficient collateral flow, which nevertheless came too late (fig. 3). On the other hand, the assumption seems reasonable that good collateral flow in a subacute phase (later than two hours) would suggest good compensatory capability in the moment of occlusion. However, all such reflections require the knowledge of the entire collateral circulation obtained by selective angiography of all neck vessels. Almost no investigator has such complete material at hand.

The angiographical material of the present study has not been selected to fulfill these requirements. The aim, however, was to find out whether the angiographical material accessible to a nonresearch neuroradiological laboratory provides sufficient information to go beyond the simple, although important, statement as to the presence or absence of occlusion. Since we did not find any correlation between collateral circulation and motor deficiencies, we came to the conclusion that evaluation of collateral circulation in the angiogram does not provide information on the degree of threatening or already developed infarction. This is in agreement with some critical authors, but not with all of them.

The good correlation of motor deficiencies with hemispheric blood flow (Fh) as well as with the regional flow index (reg) indicates that diminished blood supply to the whole hemisphere represents one factor in the development of local flow derangements in carotid occlusion. The fact that the correlation factor decreases when the collateral hemispheric blood flow (Fh+C) also is taken into account leads to the conclusion that general cerebral arteriosclerosis seems not to be of decisive importance. The tight correlation of the other three regional flow parameters to the motor deficiency index indicates that tissue damage is reflected in respective CBF alterations even several weeks after onset of the stroke. The evaluation of these CBF alterations provides some prognostic information.

An earlier paper has postulated that hyperperfusion may represent a beneficial sign. This is supported further by the present results, insofar as reg and reg, both factors comprising incidence and degree of hyperperfusion, show excellent correlation with the motor deficiency index (fig. 4).

The limits of 25 and 30 ml/100 gm per minute, respectively, used in the index reg, were chosen arbitrarily but are based on experience with rCBF measurements. Although no evidence has been presented until now as to which lower limit of cerebral perfusion constitutes a threat to the tissue and which degree of perfusion reduction is incompatible with intact tissue function, it is generally agreed that such limits must lie under 30 ml/100 gm per minute. The suggested limits of 30 ml/100 gm per minute for assuming an ischemic threat to the tissue, and of 25 ml/100 gm per minute for dangerous tissue ischemia, are strongly supported by the good correlation between reg and IOP.

Thus, a stroke patient showing no area with CBF values below 25 ml/100 gm per minute but hyperperfused areas can be expected to dispose of a remaining capacity of recovery and compensation, which might give him a good chance for the future. However, long-term follow-up studies on a larger patient material than presented in the earlier paper would be necessary to confirm this conclusion deduced from the present cross-sectional study.

Stenoses

Methods

The material consists of 40 patients admitted with cerebrovascular accidents to the Neurological University Hospital and to the Neurological Hospital of the City of Vienna Rosenhiigel (Austria) under the same conditions as the patients with neck vessel occlusions.

The ages ranged from 40 to 79 years, with a mean age of 62 years. Fourteen patients were females and 26 were males. All patients had stenotic or tortuous processes of the internal carotid artery.

The etiology of the occlusive vascular process was, in all cases of stenosis, arteriosclerosis; no indication of another pathogenesis was detectable.

All patients underwent the same routine examinations as were performed in the group with occlusions of the internal carotid artery and were treated in the same manner.

The score for defining the neurological deficiencies was confined to motor deficiencies, similar to the thrombotic group, in order to keep it as simple and unequivocal as possible. In this stenotic group a considerable part of the patients reported typical transient ischemic attacks (TIAs) without longer-lasting disturbances, so that the score was established as follows: 0 = no motor deficiencies, TIA = short-lasting motor deficiencies, 1 = motor function disturbed, but still useful, and 2 = not useful, plegic.

This score was applied to the cranial nerves and the upper...
Occlusion of the left internal carotid artery. Excellent collateral circulation with filling of all branches in the angiogram. Hemiparesis, hemihypesthesia and sensory aphasia. In the rCBF map ischemic strip across the left hemisphere corresponding to the watershed between anterior, posterior, and middle cerebral arteries.

per and lower extremities, thus resulting in a clinical deficiency index ($I_P$) of 6 in hemiplegic patients (0 = seven patients, TIA = nine patients, 1 = eight patients, 2 = three patients, 3 = nine patients, 4 = two patients, 5 = two patients, 6 = one patient. Totally, measured 41 hemispheres in 40 patients).

Bilateral carotid angiography was performed in 25 patients; in 15 patients only the stenotic carotid was ex-
CBF MEASUREMENTS AND ANGIOGRAPHY

FIGURE 4
Occlusion of the left internal carotid artery. Note the ischemic and hyperemic patches in the central region. Further ischemic patches in occipital and frontal regions of both hemispheres suggest bad perfusion of the entire brain. Three previous attacks of right-sided hemiparesis and parietal symptoms. At the CBF investigation only slight hemiparesis, severe amnestic aphasia, alexia, agraphia, etc. Two months later death occurred after a new attack. At autopsy, extensive softening of the parietal occipital lobe was noted.

£amine. In cases with multiple occlusive processes aortic arch angiography was performed (seven patients).

The angiograms were evaluated according to the following criteria:

(1) Localization and type of vascular abnormality: It was determined whether the stenosis was localized at the bifurcation (18 patients) or at the siphon (ten patients), or whether it affected the internal carotid artery in its full length (15 patients). Multiple stenoses are included in these figures. Furthermore, the existence of tortuosity, coiling or kinking was registered.

(2) Condition of the other vessels (neck vessels and intracranial vessels): It was determined whether there existed a stenosis (one patient) or occlusion (seven patients, included also in the occlusive group) of the other internal carotid artery, of the vertebral or of the subclavian artery. In three cases an occlusion of the middle cerebral artery, a stenosis of the middle cerebral artery, and an occlusion of the anterior cerebral artery, respectively, were detected additionally.

(3) Degree of stenosis: The diameter of the open lumen at the narrowest point of the stenosis was measured in millimeters. Maximum attention was directed toward avoiding false measurements caused by overlapping of bone and vessel shadows and tortuous course of the vessel itself. In most cases it was possible to measure the stenosis both in the anteroposterior and the lateral views. In case of deviating results of both measurements a mean value was used. Patients with mere tortuosity of the internal carotid artery without stenosis were not included in this series. Kinking and coiling as defined by Weibel and Fields, Metz et al. and Herrschaft without demonstrable stenosis were included as a separate group. Kinking with stenosis of 5 mm and smaller was treated like a stenosis of a straight vessel.

The following score was used to define the degree of vascular lesion and abnormality, respectively: 1 = 0.5 to 1 mm, 2 = 1.1 to 2 mm, 3 = 2.1 to 3 mm, 4 = 3.1 to 4 mm, 5 = 4.1 to 5 mm, and 6 = coiling and kinking without stenosis.

According to Gabrielsen and Greitz the diameter of the normal internal carotid artery at the level of the atlas is $5.9 \pm 0.73$ mm and is 1 to 2 mm larger near the bifurcation, where most of the stenoses had to be measured. Thus, the point where it is justified to speak of a beginning stenosis seems to be 5 mm.

(4) Collateral circulation: In the 25 patients in which bilateral angiography had been performed the existence of a cross flow into the anterior cerebral artery and the middle cerebral artery was determined. No case showed an ophthalmic anastomosis. In seven patients with contralateral internal carotid artery occlusion the cross flow was inverse to the stenosis, i.e., the stenotic internal carotid artery substantially contributed to the blood flow of the other hemisphere, a situation which constitutes a double risk.
for the stenotic hemisphere. There also was collateral circulation via the communicating posterior artery (one case). The degree of collateral circulation was scored as present (+) or absent (−). In general, collateral circulation was less pronounced in the stenotic group than in the occlusive group.

CBF studies
CBF studies were performed in all 40 patients in a subacute to chronic stage, i.e., one to four weeks after the cerebrovascular accident. The same technique (intravascular 133Xenon clearance, scintillation camera, 1,600 channel core memory, digital incremental magnetic tape store) as used in the occlusive group was applied to the stenotic group.

The artery to be punctured was chosen according to the collateral flow, i.e., in cases with no collateral circulation the stenotic artery was directly punctured, mostly above the stenosis, and CBF was registered from the lateral view (21 patients); in cases with high-grade stenosis and with collateral flow at least into the anterior cerebral artery of the stenotic side, the unaffected side was punctured and CBF of both hemispheres was registered from above (19 patients).

Hemispheric and regional blood flows were assessed as already described at the beginning of this article. The hemispheric CBF values ranged from 21.0 ml/100 gm per minute to 50.9 ml/100 gm per minute. Evaluation of rCBF maps and the parameters deduced were the same as in the occlusive group.

The mean \( P_{\text{aco}} \) amounted to 37.4 mm Hg, the lowest value was 29 mm Hg, and the highest value was 51 mm Hg; most values were closely around the mean value. The statistical evaluation was carried out by the Spearman rank correlation test as in the occlusive group.

**Results**

The results of the rank correlation of the clinical deficiency indices (Id) with the various other parameters are presented in table 2.

There was definitely no correlation of the clinical deficiency index with age, degree of stenosis, hemispheric blood flow \( (F_h) \) and bihemispheric blood flow \( (F_{h+e}) \). The correlation coefficient increases slowly with the regional parameters and reaches a level of significance with \( \text{reg}_{\text{min}} \) and \( \text{reg}_{\text{qual}} \). This sequence of increasing correlation coefficients corresponds completely with the results of the occlusive group, whereas the level of significance is somewhat lower in all correlations in the stenotic group than it is in the occlusive group.

In order to find out whether a stenosis was hemodynamically active and at what degree of stenosis this influence starts to occur, the degree of stenosis was correlated to presence or absence of collateral circulation in 25 patients in whom bilateral carotid angiography had been performed (table 3).

From this table it is clear that in patients with a stenosis of 3 mm and less collateral circulation was present, while it was lacking in all patients with a stenosis of 4 mm and more. The mean hemispheric blood flow values in the two groups indicate that the carotid flow, which was impeded by the increasing stenosis, was compensated substantially although not completely by the collateral circulation, which was initiated by the rising pressure gradient.

**Discussion**

There are two theories about the pathogenetic impact of stenotic processes of the internal carotid artery on CBF. The first theory, mainly advocated in the past decade, favors the hemodynamic effect of the narrowed vessel, resulting in diminished hemispheric CBF and critically lowered rCBF in areas which incline to infarction due to a fall in systemic blood pressure and watershed localization. The other theory considers the stenosis as a source of emboli causing recurrent ischemic attacks. Recent studies strongly support this latter theory but do not decide the controversy.

The results of the present study produced neither a correlation between motor deficiencies and degree of stenosis, nor between motor deficiencies and hemispheric blood flow. Therefore, it must be concluded that the simple hemodynamic concept did not hold true in our material. The reason for this can be deduced from further results: with increasing stenosis hemispheric CBF decreased only unsubstantially (stenosis 3 to 5 mm and kinking: \( F_h = 34.5 \); stenosis 1 to 3 mm: \( F_h = 31.5 \)) and hemispheric CBF was not correlated to the degree of stenosis. This is mainly due to the activation of collateral circulation, which was present in all patients with stenosis under 3 mm in diameter. From the fact that none of the patients with stenosis over 3 mm in diameter had developed collateral circulation it can be deduced that the reduced patency of the internal carotid artery starts affecting intracranial hemodynamics only when the lumen is narrowed to 3 mm and less. This finding corresponds well with the results obtained by other investigators.

The good correlation between \( I_d \) and the rCBF parameters used indicates that the neurological deficits are reflected in regional blood flow disturbances (fig. 5). While in carotid occlusion the good correlation between hemispheric blood flow \( (F_h) \) and

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**TABLE 2**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>( r )</th>
<th>( P )</th>
</tr>
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<tbody>
<tr>
<td>( I_d ) versus age</td>
<td>0.122</td>
<td>N.S.</td>
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<tr>
<td>( I_d ) versus degree of stenosis</td>
<td>0.087</td>
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<tr>
<td>( I_d ) versus ( F_h )</td>
<td>0.130</td>
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<td>( I_d ) versus ( F_{h+e} )</td>
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<td>( I_d ) versus ( \text{reg}_\text{min} )</td>
<td>0.265</td>
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<tr>
<td>( I_d ) versus ( \text{reg}_\text{min+max} )</td>
<td>0.331</td>
<td>&lt;0.05</td>
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<tr>
<td>( I_d ) versus ( \text{reg}_\text{min} )</td>
<td>0.422</td>
<td>&lt;0.01</td>
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<tr>
<td>( I_d ) versus ( \text{reg}_\text{qual} )</td>
<td>0.447</td>
<td>&lt;0.01</td>
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**TABLE 3**

<table>
<thead>
<tr>
<th>Correlation of Degree of Stenosis to Collateral Circulation</th>
</tr>
</thead>
<tbody>
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<td>Degree of stenosis</td>
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<tr>
<td>---------------------</td>
</tr>
<tr>
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K = kinking and coiling.

*Expressed in millimeters.

**motor deficiency index (I_D) points toward a hemodynamic pathogenetic factor of these rCBF alterations, this correlation does not exist in carotid stenosis. Here another pathogenetic factor must be effective, independent of degree of stenosis, of hemispheric CBF, of age and of general cerebral arteriosclerosis. This suggests thromboembolism as the main cause of the rCBF alterations and of infarction in carotid stenosis.**

The results also provide some comments on the diagnostic significance of angiographical findings and of rCBF measurements in patients with internal
carotid artery stenosis. We may consider the angiographical demonstration of a stenosis to be the detection of the probable cause of recurrent stroke and the localization of the point of operation. In our opinion it does not furnish information as to the extent to which brain circulation is endangered by the stenosis and as to the urgency of surgical intervention. rCBF measurements may provide such information. Patients with TIAs showed, with some exceptions, no focal blood flow disturbances in this subacute stage. This is in agreement with other authors. Thus, rCBF measurement does not suggest urgent operation in this group. Hyperperfused patches seem to represent, similar to the occlusive group, an important beneficial factor, as can be interpreted from the highest correlation coefficient for reg\textsubscript{qual}, which

![Diagram](image-url)

**Figure 6**

Occlusion of internal carotid artery on the left side, high-grade stenosis on the right side. The right hemisphere is supplied both from the stenotic internal carotid artery and from the vertebral artery. Note patches of ischemia and relative hyperemia of very similar shape, location and level of perfusion in both rCBF maps registered by carotid and vertebral Xenon injection, respectively.
parameter expresses also the presence of hyperperfusion.

In patients with patches of ischemia down to 25 ml/100 gm per minute the compensatory mechanisms at the level of macrocirculation and microcirculation can be assumed to be exhausted, and one can hardly expect the present attack to be fully reversible. This also may hold for the next possible attack. According to Millikan (quoted in reference 50), the once infarcted area will be, with a high probability, the place where the next embolus will be carried with the blood stream — a phenomenon which is due to laminar blood flow. In these patients surgical intervention must be urgently recommended.

**Conclusion**

One problem of measuring CBF in patients with collateral circulation is choosing the proper vessel for the Xenon injection. In some instances of internal carotid artery occlusion, the contralateral internal carotid artery supplies most of the occlusive hemisphere; sometimes a vertebral injection must be used to bring out parietal and frontal regions. In the case of an extensive ophthalmic or other extra-
cranial collateral flow correct CBF measurement is totally impossible, because this way of input goes along with extracerebral contamination (fig. 6).

No error arises from the condition of mixed blood supply to the brain tissue via different channels. Once Xenon activity, high enough to get reasonable clearance curves, has been brought to the tissue by any of these channels, the clearance curve is a function of the entire tissue perfusion, thus including every collateral supply (fig. 7).

In internal carotid artery stenosis the homolateral internal carotid artery was punctured only in cases showing no cross flow. In general, a filling via cross flow was preferred in order to minimize the patient's risk and to get the comparison between the stenotic and the nonstenotic hemispheric flow. However, due to the much lesser developed cross flow in internal carotid artery stenosis than in occlusion, one sometimes must accept as a minimum requirement for rCBF evaluation a good filling of the anterior cerebral artery of the stenotic hemisphere. Thus, the most common region of infarction, the middle cerebral arterial territory, was not or was only partially included in the measurement.

A further problem arises if the chosen way of Xenon input brings only low activity to the part of the hemisphere which is supplied by this collateral channel. Extracerebral recirculation and increasing background depend on the entire Xenon dose administered via the contralateral internal carotid artery, thus affecting the low activity clearance curves of the obstructed hemisphere more than the curves of the nonobstructed hemisphere. Although cases with insufficient activity in the obstructed hemisphere were abandoned, this error cannot be ruled out completely in the remaining cases.

Considering these limitations and difficulties it is remarkable that such relatively high correlation coefficients were found. The generally lower r in the stenotic group can be explained by the greater influence of the above-mentioned disturbing factors in this group.

It is furthermore remarkable that the relatively long interval (several weeks) between infarction and CBF measurements did not prevent the detection of respective rCBF alterations. At such a late time one must already assume a leveling off of the acute compensatory mechanisms and a demarcation of irreversibly damaged tissue. In this region of reduced or almost extinguished metabolism rCBF is low because of reduced demand. Thus the expression used in this study “ischemic area” might not be correct in the common sense of “ischemia” as a demand for but lack of blood supply. In the same sense “hyperperfused areas” of this study might not represent the “luxury perfusion syndrome” of Lassen or the “hyperperfusion syndrome” of Prosenz, which are considered to be acute alterations of microcirculation. This subacute “hyperperfusion” could be caused by intensive collateral circulation at the arteriolar level, washing the Xenon out of this region via arterial channels. A similar observation has been made in arteriovenous aneurysms.

In summary, one main point of this study should be stressed: the awareness of the complexity of the processes and factors involved in the clinical picture of obstructive neck vessel disease. This complexity rules out simple diagnostic measures and pathogenetic conceptions, although there is a great demand for it. Especially, the vascular surgeon needs, in addition to his clinical experience, objective and quantitative data to decide the indication and urgency of a reconstructive operation on the carotid artery. Angiography is still essential in carotid processes; its application should even be extended to a three-vessel investigation. However, one also must be aware of its limitations. rCBF measurements complement the angiographical findings by information which can be essential for this decision and cannot be provided by any other method.

References

Stroke, Vol. 5, January-February 1974
rCBF MEASUREMENTS AND ANGIOGRAPHY


The Value of Regional Cerebral Blood Flow Measurements Compared to Angiography in the Assessment of Obstructive Neck Vessel Disease

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Stroke. 1974;5:19-31
doi: 10.1161/01.STR.5.1.19

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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