Radionuclide Cerebral Blood Flow and Carotid Angiogram

Correlation in Internal Carotid Artery Disease

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SUMMARY Radionuclide cerebral blood flow (CBF) examinations of 48 patients with atherosclerosis, 18 with occlusion and 30 with stenosis of the internal carotid artery (ICA) were correlated with their respective cerebral angiograms.

The following results were obtained. Flow was visually unilaterally diminished in 29 (60%) of 48 patients, including 14 (78%) with occlusion and 15 (50%) with stenosis. Sixty-two percent of the subjects with severe stenoses and 46% of the patients with mild stenoses had a positive flow study. Diminished flow was evident in the neck in 80% of the patients, 91% of the patients with severe stenoses, and 82% of the patients with mild stenoses. In the territory. Despite perfusion pressures calculated at 110 cm H2O and less, we were unable to demonstrate profound capillary collapse, even in areas at high risk to the "no-reflow phenomenon" such as thalamus and basal ganglia. In addition, Chiang et al. probably infused their fixative against a much higher cerebrovascular resistance because, in their experiments, the cerebral vasculature had been filled with blood during ischemia, the viscosity of which was undoubtedly increased as a result of the stasis. Thus, it is highly likely that the fixative perfusions of Chiang et al. occurred at pressures and flow rates considerably less than those of the present experiments.

The possibility remains that the absence of the formed elements of the blood (red cells, white cells and platelets) from the lumina of the ischemic capillaries might have prevented the endothelial and glial changes from occurring in the current experiments. If substances released by these structures are instrumental in causing the pathology in question, they would operate equally in all areas of the brain rather than preferentially in selected areas which is the pattern of the "no-reflow phenomenon." Although the current experiments cannot relate the changes in ischemic cerebral capillaries to postischemic neurological function, we believe that they provide a more accurate picture of the structural state of the ischemic capillaries than was previously offered. Although glial swelling previously seemed to obstruct red cell passage through capillaries within 15 minutes of ischemia, we agree with others that this seems doubtful, as it is quite unlikely that the glial swelling and capillary luminal narrowing found in the present experiments would present an absolute barrier to the flow of red cells. We feel that the impaired flow noted in acute experimental ischemic models therefore must be better explained by mechanisms other than pericapillary glial swelling, such as precapillary shunting, increased blood viscosity due to red cell settling or vascular constriction.

References


Introduction

FISHER mentioned his experience with the autopsy findings in 200 cases of cerebrovascular accident clinically suspected of having middle cerebral artery (MCA) thrombosis in which he failed to find any such thrombosis. Nor was he able to locate the source of cerebral emboli in many cases with postmortem examinations. By a systematic investigation of the cervical portion of the carotid arteries at autopsy and by carrying out a thorough clinicopathological correlation, he established the role of internal carotid artery (ICA) disease as a major cause of ischemic stroke.

Brain scanning was introduced by Moore in 1948. Subsequently, the development of the scintillation camera allowed the use of dynamic evaluation of radioisotope movement.
through the carotid and cerebral arteries. Radionuclide cerebral blood flow (CBF) has been used widely since its introduction in 1966. There have been several excellent reviews of this subject which describe the radionuclide angiographic results in cerebrovascular disease.

In experiments with dogs and with square-wave electromagnetic flowmeters, critical stenosis was determined for the canine common carotid artery (CCA) with some of the cervical vessels occluded. In a similar study in conscious humans with intracranial berry aneurysms whose CCAs were to be ligated, Brice et al. determined the critical stenosis when a significant decrease in carotid blood flow occurred. Mann et al., in their experiments with dogs, estimated that the area of the arterial lumen might be reduced 90% before 50% reduction in blood flow occurred. Fischer et al. estimated that the radionuclide angiography would be abnormal if the carotid stenosis was greater than 50%.

The exact diagnosis of ICA lesions rests on the carotid angiogram or autopsy, but clinical features serve to distinguish most cases. As mentioned by Fisher, hemiplegia of unknown cause in persons in the younger age group and absence of the carotid pulse at the acute phase of stroke are highly diagnostic. However, in some cases the clinical picture is atypical and additional investigation is required to establish the diagnosis. Brain scanning frequently locates the site and estimates the size of cerebral infarct. Serial scanning sometimes can differentiate stroke from brain tumor. In many cases of cerebral infarction, the dynamic flow study is positive while the static views are still negative shortly after stroke. Animal and human experiments have demonstrated a certain correlation between the degree of ICA stenosis and decreased carotid blood flow. Many reports in the past have demonstrated the use of the radionuclide CBF technique in the diagnosis of carotid lesion. As it is easily available and noninvasive, it has been widely used in the evaluation of patients with strokes, ischemic and nonischemic, together with the static images.

In the previous English literature, there were not many large studies using this method to evaluate ICA disease.

### Table 1  Number of Cases Not Included in This Study

<table>
<thead>
<tr>
<th>(1) 52 cases of carotid angiograms</th>
<th></th>
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<tbody>
<tr>
<td>ICA stenosis &lt;25%*</td>
<td>15</td>
</tr>
<tr>
<td>ICA stenosis without available radionuclide flow study</td>
<td>23</td>
</tr>
<tr>
<td>ICA occlusion without available radionuclide study</td>
<td>29</td>
</tr>
<tr>
<td>Bilateral ICA occlusion with poor flow study</td>
<td>3</td>
</tr>
<tr>
<td>CCA occlusion</td>
<td>3</td>
</tr>
<tr>
<td>Occlusion of cavernous ICA with cervical stenosis</td>
<td>1</td>
</tr>
<tr>
<td>Stenosis of cavernous ICA with cervical stenosis</td>
<td>1</td>
</tr>
<tr>
<td>MCA occlusion with cervical stenosis of ICA</td>
<td>1</td>
</tr>
<tr>
<td>ICA occlusion with severe stenosis of contralateral ICA</td>
<td>1</td>
</tr>
<tr>
<td>ICA stenosis with poor radionuclide study</td>
<td>4</td>
</tr>
<tr>
<td>ICA stenosis with equivocal radionuclide study &gt;5 months between nuclear and contrast angiograms</td>
<td>8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(2) 13 cases of radionuclide flow studies</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Equivocal asymmetry of radionuclide flow</td>
<td>2</td>
</tr>
<tr>
<td>ICA stenoses with poor flow</td>
<td>4</td>
</tr>
<tr>
<td>&gt;5 months between nuclear and contrast angiograms</td>
<td>8</td>
</tr>
</tbody>
</table>

*For 1976, please see Methods of text.
was defined as obliteration of the lumen of the artery. The authors examined the dynamic flow studies of the brain scan together for evidence of unilaterally decreased radioisotope activity in the region of the neck or the head in the distribution of the MCA. Rosenthal defined five patterns of perfusion in the radionuclide cerebral angiogram in patients with intracranial disease. Four of these patterns referred to changes resulting from brain tumors and the remaining pattern to diminished perfusion of the afflicted cerebral hemisphere. Strauss et al. stated that asymmetry of the distribution of the tracer was the most important criterion in the interpretation of the nuclear angiogram. In this study only anterior images were examined. A normal radionuclide study meant that the radioactivity in the distribution of the major cerebral blood vessels was equal bilaterally. The study was positive or abnormal if there was definite asymmetry of radioactivity. If visualization of radioactivity in the neck and head was unsatisfactory, the study was designated poor and was excluded.

No attempt was made to quantify the degree of diminished radioisotope activity in the abnormal studies as our analysis was only visual. Undoubtedly, the quantitative analysis of the radionuclide angiogram increases its sensitivity in detecting ICA lesions by comparing the slope of activity with time over the cervical carotid region. Similarly, the activity or time differential of radioisotope activity and the "hemispheric retention phenomenon" from delayed arterial or venous visualization were not chosen as criteria in our study. Criteria used in our study were clear visualization of radioactivity in the neck and head. In none of the 48 patients were there significant lesions beyond the cervical carotid or within the external carotid artery.

Incapacitated patients were examined in the supine position. Subjects were divided into two groups: (1) 18 with unilateral ICA occlusion, and (2) 30 with unilateral or bilateral ICA stenoses.

All ICA occlusions were situated at the carotid sinus or close to its origin. In none of the 48 patients were there significant lesions beyond the cervical carotid or within the external carotid artery.

The site of the diminished activity in the radionuclide examination was considered abnormal if there was disparity between the activity in the neck and head. Two cases with equivocal asymmetry, four with poor flow and eight with a greater than five-month interval between contrast and radionuclide angiograms were excluded (table 1, part 2).

Forty-eight cases were eventually selected. The time interval between all the radionuclide and carotid angiograms was within six weeks, i.e., within one week in 23 cases, two weeks in 23 cases, and three weeks in two cases.

### Table 2: Radionuclide CBF in 48 Cases of Angiographically Proved ICA Lesions

<table>
<thead>
<tr>
<th>Type of ICA lesion</th>
<th>Normal</th>
<th>Abnormal*</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occlusion</td>
<td>4 (22%)</td>
<td>14 (78%)</td>
<td>18</td>
</tr>
<tr>
<td>Stenosis</td>
<td>15 (56%)</td>
<td>13 (44%)</td>
<td>28</td>
</tr>
<tr>
<td>Total</td>
<td>19 (50%)</td>
<td>27 (50%)</td>
<td>46</td>
</tr>
</tbody>
</table>

*Diminished radioisotope perfusion on one side.

### Table 4: Correlation Between Site of Abnormal Radionuclide CBF and Angiographically Proved ICA Lesion in 29 Cases

<table>
<thead>
<tr>
<th>Type of ICA lesion</th>
<th>Neck*</th>
<th>Head†</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occlusion</td>
<td>10 (71%)</td>
<td>4 (29%)</td>
<td>14</td>
</tr>
<tr>
<td>Stenosis</td>
<td>13 (57%)</td>
<td>2 (13%)</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td>23 (80%)</td>
<td>6 (20%)</td>
<td>29</td>
</tr>
</tbody>
</table>

*Diminished radioisotope perfusion in the carotid area.
†Diminished radioisotope perfusion in the MCA area.

The prevalence of bilateral ICA lesions proved angiographically was also assessed (table 5). In 26 (54%) of the 48 patients, bilateral ICA lesions were present. Ten (56%) of
the 18 subjects with ICA occlusion and 16 (53%) of the 30 subjects with ICA stenosis had bilateral ICA lesions. The distribution of the bilateral ICA abnormalities in both groups was also tabulated (table 6). There were three bilateral ICA occlusions which were excluded from this study because of poor radionuclide flow study. It was noticed that the radioactivity was always diminished on the side of the occluded ICA irrespective of the severity of the associated stenosis on the contralateral ICA. Diminished flow was also on the same side as the stenosis if the stenosis was unilateral (except for one patient with unilateral mild stenosis and diminished flow on the opposite side). If the ICA stenoses were bilateral, flow was always diminished on the side with the greater stenosis. Six subjects were found with mild bilateral ICA stenoses. Four of these had normal radionuclide examinations. Two others had diminished flow corresponding to the symptomatic side.

The abnormal radionuclide cerebral flow between unilateral and bilateral ICA lesions was also compared (table 7). The radionuclide study was abnormal in 16 (62%) of the 26 subjects with bilateral ICA lesions and normal in the other ten subjects. In unilateral ICA lesions, 13 (60%) of 22 subjects had an abnormal radionuclide flow, the other nine (40%) being normal. Therefore, the results of the radionuclide study were similar between unilateral and bilateral ICA lesions.

Discussion

Bell16 noted 100% correlation between 99m Tc CBF studies and bilateral carotid angiograms in 13 cases with ICA occlusion. Jhingram et al.3 compared the contrast cerebral angiogram with the radionuclide angiogram. He found that in 24 subjects with angiographically proved unilateral carotid occlusion, 23 had a positive radionuclide study. Jhingram also found that if there was stenosis of the ICA, four of seven subjects had a positive radionuclide study. Fischer et al.13 noted that in 29 subjects with completed stroke, the cerebral angiogram corresponded with the radionuclide angiogram, but he did not mention the various types of carotid artery lesions. Meschan et al.7 noted that in 11 of 15 subjects with aortocranial atherosclerosis proved angiographically, the dynamic flow on the brain scan was abnormal. In another 39 subjects, the dynamic study was normal in 18. Again, he failed to quantify or qualify the lesion in the aortocranial vessels. Griep et al.4 also noted that 11 of 14 subjects with unilateral ICA occlusion had abnormal radioisotope angiography. From the above studies, the correlation between ICA occlusion and the results of radionuclide flow examination is strong ranging from 79% to 100%.14 In our study, 78% or 14 of 18 subjects with unilateral ICA occlusion had a positive radionuclide study (table 2).

Few large studies in the English literature compare the results of radionuclide angiography between patients with various degrees of narrowing of the ICA lumen. Griep et al.4 noted a significant difference in the radionuclide angiograms between subjects with ICA occlusion and stenosis of varying severity. Eleven of 14 of his subjects with unilateral ICA occlusion, three of six subjects with 50% to 80% stenosis and three of 29 subjects with ICA stenosis less than 50% had a positive study. In our study, while 78% or 14 of 18 subjects with unilateral ICA occlusion had a positive radionuclide study, it was observed only in 50% or 15 of 30 patients with unilateral or bilateral ICA stenoses. Thirteen of these had severe stenoses, eight with positive radionuclide study. Of 13 subjects with mild ICA stenoses, six had a positive radionuclide examination. The percent variation in positive flow between severe and mild stenoses is not significant, 62% versus 46% (table 3). This contrasts with the study of Griep et al. However, the system for grading ICA stenoses in our study is different from Griep’s and stenoses less than 25% were excluded from our analysis. The following phenomena may account for the lack of discrepancy in radionuclide angiograms between patients with high-grade and low-grade stenoses.

(1) Our examination of the anterior flow images was visual. Weissman et al.,21 by a quantitative analysis of the slope of radioactivity with time over the entire cerebral region in dogs, found that surgically produced high-grade stenosis and occlusion could be differentiated from controls. Definitely, a quantitative analysis is superior to a visual examination. With the improved technique of Weissman et al., probably the radionuclide flow in ICA stenosis can be quantified and severe ICA stenoses may be differentiated from mild.

(2) Maynard et al.11 stated that occasionally it was apparent that decreased vascularity in an area during radioisotope angiography was not due to decreased perfusion but to displacement of the major blood vessel groups. They added that perhaps with more attention to the positioning of the patient and added experience, displacement of the vessels could be more easily detected. Probably this is a factor accounting for the lack of difference in radionuclide flow in patients with severe and minor stenoses in our study.

(3) The sensitivity of radionuclide angiography in detec-
tion of cerebral flow abnormalities remains unknown. Strauss et al.28 has estimated that at peak activity of 10,000 counts per second in the head, at least a 10% to 20% difference in flow is needed to be detected.

(4) We only assessed anterior flow images. While theICA, ACA and anterior MCA were easily identified, verteobasilar and posterior MCA branches were less visible. Collateral flow, both intracranial and extracranial, is frequent, especially in cerebrovascular atherosclerotic disease.25,26 Developmental aortocerebral vascular anomalies also could give false results. A large vertebral artery also may mimic the normal carotid artery.

Our sample size was not large. Further observation is required to compare the radionuclide flow between severe and mild ICA stenosis.

While the incidence of positive radionuclide study is 78% for ICA occlusion and 50% for ICA stenoses (table 2), the average percent falls to 60%. Nevertheless, in the absence of carotid angiography, an abnormal radionuclide flow cannot predict whether the ICA is occluded or stenosed, although the probability of finding an occlusion is higher.

No large studies in the English literature attempt to correlate the site of diminished radioactivity and the ICA obstruction visualized angiographically. Fischer et al. observed that the radionuclide flow was diminished in the MCA area in 27 cases of completed strokes, and in the area of the ICA and MCA in another 13 cases, not including the ones with “hemispheric retention.” Their sample of cases was not a homogenous one like the subjects in this study. Rosenthal stated that noted diminished flow in the MCA in a patient with left ICA occlusion. Powell et al. also noted decreased flow in the MCA in a case of proved left ICA occlusion. In another case with right CCA ligation, the decreased flow was seen in the neck. Rosenthal stated that there was little relationship between the site of obstruction and the appearance of the isotope flow pattern in the positive study. However, the relationship is significantly high in our subjects. In 80% of 29 angiographically demonstrated ICA lesions, the diminished activity was seen in the neck in the abnormal radionuclide studies (table 4). Therefore, in the presence of diminished radioisotope activity in the neck, an ICA lesion is more likely present than an MCA lesion. Small vessel occlusions, developmental vascular anomalies and collateral cerebral circulation may be present and, in ICA disease with diminished isotope activity in the MCA area, these factors may be partly responsible.

Angiographically or autopsy-demonstrated ICA lesions are frequently bilateral. Bauer et al. found bilateral involvement in 72% of 172 patients with strokes studied angiographically. A little more than 50% of our subjects had bilateral ICA disease (table 5). The radioisotope flow is nearly always unsatisfactory in bilateral ICA occlusion. Poor injection technique, increased intracranial pressure and decreased cardiac output also give poor radionuclide study. Probably, the radioisotope evaluation of bilateral ICA occlusion can rarely be satisfactory. When the ICA lesion was unilateral, diminished isotope activity was noted on the involved side. With bilateral ICA lesions, excluding bilateral ICA occlusion, a positive radionuclide study pointed to the side of occlusion or greater stenosis. Our limited experience with the two cases of bilaterally equally mild ICA stenosis does not justify us to make a correlation between the radionuclide study and the symptomatic side if the stenosis on both sides is the same. Besides, the results of the radionuclide flow were similar in unilateral and bilateral ICA disease (table 7).

In summary, the radionuclide CBF examination plays a role in the assessment of ICA lesions, but its limitations have to be appreciated. Carotid occlusion or stenosis may be clinically asymptomatic. Similarly, symptomatic stenoses may not always be detected by the isotope method. The presence of a unilaterally decreased flow in a patient with clinically suspected ischemic stroke shows the side of ICA disease if unilateral and the side of greater stenosis if the disease is present on both sides. Our study suggests that a positive flow examination is more often found in occlusion than that diminished flow in the MCA area may point to ICA disease. Bilateral cerebral contrast angiography is still mandatory for complete evaluation of the degree of stenosis and presence of associated ulceration. The data leading to the differentiation between major and minor ICA stenosis are not sufficient to justify any conclusion. Further observation is advisable and necessary.

References

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Radionuclide cerebral blood flow and carotid angiogram. Correlation in internal carotid artery disease.
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Stroke. 1977;8:39-43
doi: 10.1161/01.STR.8.1.39

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