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, leading to the differentiation between major and minor ICA stenoses. Positive radionuclide angiograms always pointed to the side with occlusion or the greater degree of stenosis even though the middle cerebral artery was occluded intracranially in 20%. Positive radionuclide angiograms always pointed to the side with occlusion or the greater degree of stenosis even though bilateral internal carotid disease was frequently found (54%). The data leading to the differentiation between major and minor ICA stenoses are not sufficient to justify any conclusion.

Introduction  FISHER 1, 2 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 angiographical 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>
<thead>
<tr>
<th>Table 1</th>
<th>Number of Cases Not Included in This Study</th>
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<tbody>
<tr>
<td>(1) 93 cases of carotid angiograms</td>
<td></td>
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<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>3</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>
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<tr>
<td>ICA stenosis with equivocal radionuclide study</td>
<td>2</td>
</tr>
<tr>
<td>&gt;5 months between nuclear and contrast angiograms</td>
<td>8</td>
</tr>
<tr>
<td>(2) 16 cases of radionuclide flow studies</td>
<td></td>
</tr>
<tr>
<td>Equivocal asymmetry of radionuclide flow</td>
<td>2</td>
</tr>
<tr>
<td>ICA stenoses with poor flow</td>
<td>4</td>
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<tr>
<td>&gt;5 months between nuclear and contrast angiograms</td>
<td>8</td>
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*For 1976, please see Methods of text.

Hjingga et al., Griepp et al., and Bell found a high correlation between ICA occlusion and the result of the radionuclide study. However, apart from the study by Griepp et al., few reports compare the results of radionuclide studies with the degree of ICA stenosis.

Some authors did not find any significant correlation between the site of obstruction of the ICA and the site of the diminished activity in the radionuclide CBF. However, there was no large study of this sort of comparison. Many of the reviewed studies were only case reports. In addition, bilateral carotid artery disease is quite frequent. The role of the radionuclide study in bilateral ICA lesions has not been adequately evaluated as well apart from bilateral ICA occlusion in which the isotope study is usually poor.

The purpose of this study is to correlate the radionuclide CBF with the findings at bilateral carotid angiography in ICA lesions limited to the cervical region only. Attempts were made to (1) compare the result of the radionuclide study between ICA occlusion and stenosis of varying severity, (2) correlate the site of ICA lesion proved at cerebral angiography and the site of diminished activity in the radionuclide study, and (3) evaluate the role of the radionuclide study in bilateral ICA lesions.

Methods

Bilateral carotid angiograms performed at the Minneapolis Veterans Administration Hospital in the last five-year period were reviewed. During the period 1971 to 1974, only stenoses greater than 25% were consistently recorded in the radiology files. During 1975, ICA stenoses of all degrees of severity were recorded. Therefore, those cerebral angiograms with ICA stenosis less than 25% were not selected. A total of 141 bilateral carotid angiograms were reviewed. Of these, 48 were selected because the ICA lesion was limited to the cervical region and the corresponding dynamic flow studies of the brain scan were available. In these 48 cases, there were no significant lesions in the CCA, MCA, ACA or other portions of the internal carotid artery beyond the cervical region. Bilateral ICA occlusions were also excluded. The other 93 studies were not considered (table 1), including 52 ICA lesions without available radionuclide blood flow examinations, three bilateral ICA occlusions, three CCA occlusions, two ICA lesions in the intracavernous portion of the vessel, three mainstem MCA occlusions and one ICA occlusion with additional severe external carotid artery disease on the opposite side. In eight cases, the time interval between the carotid angiogram and radionuclide study was greater than five months. These cases were also excluded. Another six subjects with ICA stenoses were excluded because of poor radionuclide flow or equivocal asymmetry of flow.

In this study, the terms "radionuclide cerebral blood flow," "dynamic flow study" and "radionuclide angiogram" are used interchangeably.

ICA stenosis was defined as narrowing of the arterial lumen less than 100%. The degree of the ICA stenosis was graded in accordance with the criteria in the article on cerebral infarction by Alter et al. Lesions were classified as severe with 90% to 99% stenosis, moderate with 50% to 89% stenosis, and mild with 25% to 49% stenosis. ICA occlusion...
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 et al. 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 the radioactivity in the neck and in the head in the distribution of the MCA and distinct asymmetry between the activity bilaterally. The side with diminished activity was considered abnormal or positive. This asymmetry was found most strikingly on the first scintiphoto following the appearance of tracer. Therefore, only the first scintiphotos of the anterior flow images following appearance of radioactivity was examined for asymmetry 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 30 cases, and greater than two weeks in five cases. Neurosurgical records confirmed that no patients underwent endarterectomy between the radionuclide and contrast angiogram. The carotid angiograms were reviewed independent of the radionuclide study.

No attempt was made to correlate the degree of angiographically proved stenosis with the quantitative diminution in radionuclide flow. Our visual analysis was considered too insensitive for such a quantification and comparison.

In the Minneapolis VA Hospital, an Anger camera (Pho-Gamma III; Serle) was used with a low-energy, high-sensitivity collimator and a 25% window centered over the 140 kev ⁹⁹ᵐTc photopake. With the patient facing the camera, 20 mCi of ⁹⁹ᵐTc-pertechnate in less than 1 cc of saline were injected as a bolus into an antecubital vein. Serial 70-mm images of flow in the neck and head were obtained every three seconds following completion of injection. Incapacitated patients were examined in the supine position.

Results

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 results of the radionuclide flow study in these patients with angiographically proved ICA lesions were tabulated (table 2). Unilateral diminished radioactivity was observed in 14 (78%) of the 18 subjects with ICA occlusion, 15 (50%) of the 30 subjects with ICA stenosis, and 29 (60%) of the 48 subjects with ICA occlusion or stenosis.

Table 3 shows that the degree of ICA stenosis in the 30 subjects of Group 2 was severe in 13, moderate in 4, and mild in 13. Diminished radionuclide flow was observed in eight (62%) of the 13 subjects with severe stenosis, one (25%) of the four subjects with moderate stenosis, and six (46%) of the 13 subjects with mild stenosis.

The site of the diminished activity in the radionuclide examinations was correlated with the level of the ICA lesion identified angiographically (table 4). Radioactivity was diminished in the neck in 23 (80%) of the 29 patients with a positive radionuclide study. In the other 20%, the diminished activity was seen in the head in the region of the MCA. In 10 (71%) cases of ICA occlusion and 13 (87%) cases of ICA stenosis, the diminished radioactivity was observed in the neck.

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

Bell noted 100% correlation between 99mTc CBF studies and bilateral carotid angiograms in 13 cases with ICA occlusion. Jhingram et al. 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. 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. noted in 11 of 15 subjects with aortoocoronary 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. 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%. In our study, 71% or 14 of 18 subjects with unilateral ICA occlusion had a positive radionuclide study (table 7).

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. 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., 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 evaluation. 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. 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.\textsuperscript{9} 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 the ICA, ACA and anterior MCA were easily identified, vertebrobasilar and posterior MCA branches were less visible. Collateral flow, both intracranial and extracranial, is frequent, especially in cerebrovascular atherosclerotic disease.\textsuperscript{5,6} Developmental aorticcranial 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.\textsuperscript{10} 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\textsuperscript{11} noted diminished flow in the MCA in a patient with left ICA occlusion. Powell et al.\textsuperscript{12} 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\textsuperscript{13} 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.\textsuperscript{14} 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 stenosis and 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

Radionuclide cerebral blood flow and carotid angiogram. Correlation in internal carotid artery disease.
D Foo and L Henrickson

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