Evaluation of Cerebral Vascular Disease With Radionuclide Angiography

BY RONALD J. FISCHER, M.D., AND AUGUST MIALE, JR., M.D.

Experience with radionuclide angiography (RA) utilizing radiosodium pertechnetate and the scintillation camera as a practical means of evaluating cerebral vascular disease (CVD) is presented. The normal RA patterns were established in more than 500 patients without clinical evidence of CVD. Detailed study of the arterial and venous perfusion patterns in cases of CVD showed that certain discrete changes can be classified. The RA patterns were evaluated in 143 patients with strokes and in 120 patients with transient ischemic attacks (TIA) and correlated with symptomatology, clinical hospital course and cerebral angiograms. Although static brain scanning in patients with strokes is reportedly positive in approximately 42%, such scans are rarely positive (3%) in patients with TIA. However, by using the RA in combination with static camera imaging, in those patients with documented stroke, positive studies were obtained in more than 80%, a twofold increase compared to previous experience. In patients with TIA, a tenfold (33%) increase in positive studies was found related to CVD and, in addition, another 7% were positive as mass lesions. The data presented stress the importance of establishing specific criteria for analysis of RA as well as the greatly enhanced sensitivity of this combined approach in detecting CVD.

ADDITIONAL KEY WORDS cerebral contrast angiography
brain scanning completed stroke transient ischemic attack
radiosodium pertechnetate scintillation camera scintiphotography

Introduction

The diagnostic approach to elderly patients with suspected cerebral vascular disease (CVD) has been based primarily on clinical findings. The large elderly population affected by CVD, estimated at nearly one and one-half to two million persons annually in the United States, comes to the attention of physicians usually in one of two ways.1 The largest portion presents with brief recurrent nonspecific neurological deficits regarded as transient ischemic attacks (TIA). The other group has well-defined persistent clinical signs indicating
serious intracranial disease, of which completed stroke is the major diagnostic possibility. In recent years, increased stress has been placed on the use of cerebral contrast angiography (CCA) to demonstrate characteristic vascular changes or to discover other lesions such as primary or metastatic tumor, subdural hematoma, or vascular anomalies which may mimic or mask the signs and symptoms of CVD.

Another approach consisting of static radionuclide brain scanning with the rectilinear scanner has been used on patients with CVD because of simplicity and absence of morbidity. The reported data indicate that patients with TIA rarely (3%) have positive studies and patients with completed stroke have a low yield of positive results within the first few days after an ischemic infarction or hemorrhage. However, on the average the positive findings can be found in about 42% of the cases. The yield can be as high as 72% three weeks later.

CVD has also been studied with rapid sequential imaging of a radionuclide bolus passing through the brain vasculature (radionuclide angiography). This technique utilizes for isotope imaging an Anger scintillation camera, which is uniquely designed to permit high-speed or rapid sequential imaging of radioactivity. In an extensive review of the subject of intravenous and intracarotid radionuclide angiography (RA), Rosenthal describes five perfusion patterns found in patients with intracranial disease. Four of these five patterns refer to changes produced by intracerebral tumors, whereas only one, namely "reduced" perfusion to the afflicted hemisphere, corresponds to cerebral vascular disease. No data were presented regarding the relative statistical accuracy of the detection of documented intracerebral vascular disease in patients with TIA or with completed stroke using RA alone. In another detailed analysis of RA, Handa et al. stress the importance of this procedure in detecting AV malformations or brain tumors but do not describe findings with respect to CVD. Meschan et al. correlated information provided by the RA studies and rectilinear static scans with CCA findings and pneumograms in a wide variety of neurological disorders including CVD. Correlation of RA with CCA was regarded as extremely promising especially in cases of cerebral artery thromboses, but the correlation was less in the group called "aortocranial vessel disease" and this was not adequately explained. In none of the previously reported studies were the criteria for analysis and interpretation of the RA defined specifically with respect to CVD.

The present study reports our experience in the development of the RA as a practical means of evaluating suspected CVD in a symptomatic population. An approach to the analysis of RA's has been developed, and criteria for interpretation are delineated. The numerical information derived from this study indicates that RA is a far more sensitive means of detecting evidence of intracerebral disease in patients with CVD than static scan alone and, when combined with static brain scanning, the RA represents a valid laboratory diagnostic approach which adds significant new information to the findings from the history and physical examination in the patient with CVD.

**Methods**

The study is based on the evaluation of 143 patients with completed stroke and 120 other patients with transient ischemic attacks. These patients were evaluated at Jackson Memorial Hospital, Miami, Florida, and selected on the basis of well-established clinical evidence for the diagnosis of either TIA or completed stroke. The age range was 35 to 87 years. Many of the patients also had CCA's, EEG's, skull films, lumbar puncture, ophthalmodynamometry, pneumoencephalography, and other studies. The majority were referred for radionuclide brain study by the Neurology Service. All patients were studied with the Anger scintillation camera following intravenous bolus injection of radiosodium pertechnetate in doses ranging from 15 to 20 mCi. The frontal projection of the patient's head was studied in all instances and included the area from the bifurcation of the common carotid vessels to the superior aspect of the sagittal sinus. Following antecubital vein injection of the radionuclide, serial photographs were obtained at 2.5-second intervals in a cine fashion with a Nikon 35 mm rapid sequence motor drive camera attached to the B-oscilloscope of the scintillation camera. Kodak High Contrast Copy Film HC 710 developed in a 90-second x-ray processor was used in all cases. In technically adequate studies, a peak count rate between 12.00 to 15,000 counts

EVALUATION OF CVD WITH RADIONUCLIDE ANGIOGRAPHY

per each two and one-half-second interval in the maximal arterial phase was obtained. In all cases static camera studies in five projections were obtained one and one-half to two hours after the RA.

Results

Certain characteristic perfusion or RA patterns appeared repetitively and careful observation of specific phases of the perfusion could be observed reproducibly in patients free of cerebral vascular disease and in patients with clinical manifestations of cerebral vascular disease.

Criteria for Interpretation

A. NORMAL PERFUSION PATTERN (UNRELATED TO CEREBRAL VASCULAR DISEASE)

The following criteria were established on the basis of analysis of RA’s in patients without clinically suspected or subsequently demonstrated cerebral vascular disease. These were derived from 500 patients predominantly below the age of 50, with metabolic disorders, alcoholic brain syndromes, suspected mass lesions, psychiatric disorders, or head trauma without sequelae.

1. Figure 1a demonstrates prompt appearance of activity in both proximal carotid and internal carotid areas. The importance of this “promptness” reflects mainly the adequacy of the injection and the cardiac output of the patient. When both are optimal, activity is clearly defined in both carotid areas five to eight seconds following the injection.

2. Figure 1b shows equal progressive blushing of activity over the perfusion bed of the middle and anterior cerebral arteries bilaterally, with a transit of radioactivity from the region of the middle cerebral artery peripherally to the small vessels of the superior cortex. This blush represents the perfusion of the small vessels extending upward from the lenticulostriate area and perfusion of multiple small branches of the middle cerebral artery and anterior cerebral arteries.

3. In figure 1c the area of the sagittal sinus is seen in the venous phase of the study, along with a symmetrical and homogeneous rapid fading of activity over the middle cerebral area, with only a faintly visible background remaining.

B. ABNORMAL PERFUSION PATTERN (RELATED TO CEREBRAL VASCULAR DISEASE)

Analysis of 134 abnormal RA’s revealed four distinct characteristics which could be iden-

![Figure 1](http://stroke.ahajournals.org/)

(a) Normal carotid phase, (b) normal anterior and middle cerebral phase, (c) normal venous phase, (d) right carotid deficit, (e) delayed right middle cerebral activity, (f) amputated middle cerebral with lack of peripheral filling (arrow), (g) focal retention late arterial phase (arrow), (h) arterial demonstration of vascular tumor (meningioma).
TABLE 1
Transient Ischemic Attacks (120 Cases)

<table>
<thead>
<tr>
<th>Carotid vessel symptomatology</th>
<th>64%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases studied: 77</td>
<td></td>
</tr>
<tr>
<td>Abnormal flow pattern</td>
<td>23</td>
</tr>
<tr>
<td>Abnormal static scan (mass lesion)*</td>
<td>4</td>
</tr>
<tr>
<td>Total†</td>
<td>27  (35%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vertebral basilar symptomatology</th>
<th>36%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases studied: 43</td>
<td></td>
</tr>
<tr>
<td>Abnormal flow pattern</td>
<td>8</td>
</tr>
<tr>
<td>Abnormal static scan (mass lesion)*</td>
<td>5</td>
</tr>
<tr>
<td>Total†</td>
<td>13  (30%)</td>
</tr>
</tbody>
</table>

*Unsuspected mass lesions (9/120) or 7%.
†Total cases studied (both groups) positive (40/120) or 33%

Seventy-seven, or 64%, presented with predominantly carotid vessel symptomatology, while 43, or 36%, presented with predominantly vertebral basilar artery symptomatology. The latter group referred to patients with transient lesions yielding signs and symptoms such as syncope, vertigo or diplopia. Headache, when present, was mostly occipital in location. The carotid group included patients in whom transient hemispheric symptoms such as limb paresis, seizures, and unilateral headaches with or without visual disturbances were more prominent. Some patients had symptoms of both groups. Analysis of carotid artery cases revealed that 35% who presented with symptoms suggestive of TIA had abnormal nuclide studies. In this group of patients with TIA's the incidence of mass lesions which were not previously suspected was nine in 120 cases or about 7%.

Of the 120 cases in the group a total of 40 (33%) had positive or abnormal RA's. A smaller sample of this larger group representing the last 30 consecutive cases with TIA symptoms was studied in more detail (table 2). Of these, 11 had abnormal RA's; six of these 11 cases had CCA's that were abnormal and showed positive correlation with the RA. There were 19 normal RA's and the CCA was...
EVALUATION OF CVD WITH RADIONUCLIDE ANGIOGRAPHY

TABLE 2
Analysis of 30 Cases With Transient Ischemic Attacks

<table>
<thead>
<tr>
<th>Analysis of 30 Cases With Transient Ischemic Attacks</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal radionuclide angiograms:</td>
<td></td>
</tr>
<tr>
<td>Abnormal findings (CCA) in TIA patients</td>
<td>6</td>
</tr>
<tr>
<td>(Diagnostic information complements RA)</td>
<td></td>
</tr>
<tr>
<td>Not studied with CCA</td>
<td>5</td>
</tr>
<tr>
<td>Normal radionuclide angiograms:</td>
<td></td>
</tr>
<tr>
<td>Not studied with CCA</td>
<td>19</td>
</tr>
<tr>
<td>Abnormal CCA</td>
<td></td>
</tr>
<tr>
<td>1. Partial internal carotid stenosis</td>
<td>2</td>
</tr>
<tr>
<td>2. Partial basilar artery stenosis</td>
<td></td>
</tr>
<tr>
<td>Normal CCA</td>
<td>2</td>
</tr>
</tbody>
</table>

TABLE 3
Static Scans and Radionuclide Angiograms in 143 Cases of Clinical Stroke

<table>
<thead>
<tr>
<th>Static Scans and Radionuclide Angiograms in 143 Cases of Clinical Stroke</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>A. CVD diagnosis on nuclide study</td>
<td></td>
</tr>
<tr>
<td>1. Static lesions alone</td>
<td>20</td>
</tr>
<tr>
<td>2. Flow pattern lesions alone</td>
<td>54</td>
</tr>
<tr>
<td>Carotid</td>
<td>0</td>
</tr>
<tr>
<td>Middle cerebral</td>
<td>27</td>
</tr>
<tr>
<td>Carotid and middle cerebral</td>
<td>13</td>
</tr>
<tr>
<td>Hemispheric retention</td>
<td>14</td>
</tr>
<tr>
<td>3. Flow and static abnormalities combined</td>
<td>40</td>
</tr>
<tr>
<td>4. Total abnormal diagnosis on RA</td>
<td>94</td>
</tr>
<tr>
<td>B. No CVD diagnosis on nuclide study</td>
<td>29</td>
</tr>
<tr>
<td>Total cases</td>
<td>143</td>
</tr>
</tbody>
</table>

94/114 (83%) abnormal diagnosis on RA alone.
114/143 (80%) abnormal static and RA studies in clinical CVD (stroke).

done in four of these cases. Two of the four were normal and two showed abnormalities, which were reported as minimal unilateral internal carotid stenosis and minimal basilar artery stenosis, respectively.

Completed Stroke
A group of 143 cases of clinically completed stroke was studied. Of these 114 had abnormal static brain studies and/or abnormal RA’s, representing the combined yield of abnormal studies at 80%. In this group, the diagnosis could be made on the RA alone in 94/114 or 83%. The static brain study alone was positive in only 20/114. The abnormal observations are categorized in table 3.

Of this group of 143 cases, 43 who had CCA’s were studied in further detail (table 4). Twenty-nine of these cases had findings on the RA which corresponded directly with the CCA in respect to the information content as described below (fig. 2).

1. A major lesion seen in the middle cerebral artery on the angiogram corresponded to a major lesion in the perfusion of the middle cerebral artery area on the RA (figs. 2a, b, and c).

2. When the CCA reported an infarction represented by early filling veins, delayed arterial flow, or an avascular area, the static study demonstrated either a positive infarct pattern, usually irregular or patchy in nature, or a focal persistence in the venous perfusion phase on the RA (figs. 2d, e, and f).

3. When unilateral carotid obstruction seen on the CCA was greater than 50%, an extensive reduction of perfusion on the same side was also seen on the RA (figs. 2g, h, and i).

Bilateral carotid disease, which occurred infrequently with greater than 50% obstruction, was not always appreciated in the original RA. However, on retrospective analysis, when technical factors, such as poor injection and low cardiac output secondary to arrhythmias or congestive heart failure, were excluded, then
<table>
<thead>
<tr>
<th>Case frequency</th>
<th>CCA</th>
<th>RA</th>
</tr>
</thead>
<tbody>
<tr>
<td>29</td>
<td>Abnormal (see text)</td>
<td>Abnormal (see text)</td>
</tr>
<tr>
<td>3</td>
<td>Technically unsatisfactory</td>
<td>Abnormal</td>
</tr>
<tr>
<td>1</td>
<td>Ventricular dilatation</td>
<td>Normal</td>
</tr>
<tr>
<td>2</td>
<td>Subdural hematomas</td>
<td>Abnormal</td>
</tr>
<tr>
<td>2</td>
<td>Mass lesions (hematomas)</td>
<td>Normal</td>
</tr>
<tr>
<td>1</td>
<td>Normal</td>
<td>Metastatic lesions</td>
</tr>
<tr>
<td>1</td>
<td>Cerebral contusion</td>
<td>Normal</td>
</tr>
<tr>
<td>1</td>
<td>Small aneurysm</td>
<td>Abnormal</td>
</tr>
<tr>
<td>3</td>
<td>Small plaques</td>
<td>Normal</td>
</tr>
</tbody>
</table>

**FIGURE 2**

(a) Middle cerebral deficit, (b) composite anterior angiogram with absent middle cerebral (arrow) (c) lateral view, (d) focal retention (arrow), (e) and (f) early draining vein and avascular area (arrows), (g) absent internal carotid, (h) and (i) anterior and lateral angiograms showing occluded internal carotid (arrow).
bilateral obstruction of carotid vessels greater than 50% could be suspected. In the other 14 cases, the findings were indirectly related to the CCA for a variety of reasons explained in table 4.

Of 143 patients studied with clinical stroke, 29 had no CVD diagnosis made on the basis of RA or static brain study (table 3). Of these, 13 were diagnosed by radionuclide study as lesions other than CVD.

The remaining 16 cases with normal RA’s were analyzed as follows (table 5): eight cases had no CCA or pneumoencephalogram. One CCA was read as normal without perfusion deficits, but the pneumoencephalogram revealed atrophy and ventricular dilatation, consistent with hydrocephalus. Two cases were interpreted as minor atherosclerotic changes in the carotid vessels, but no flow deficits or definite diagnosis of infarction was made on CCA. In one case the CCA was considered technically inadequate, while in another case the CCA was abnormal with a left posterior cerebral infarct. On retrospective review, the static scan in the same case was also considered abnormal. The CCA in another case revealed a small posterior rightsided infarction, but both the RA and CCA had a normal vascular pattern in the middle cerebral artery area. In two cases pneumoencephalography was performed without CCA. One (a) was normal and the other (b) indicated communicating hydrocephalus secondary to toxoplasmosis.

Discussion

TRANSMISSIVE ATTACK

In a recently reported review series, the findings of abnormalities in TIA patients by static rectilinear brain scan alone was extremely low (3%), and this was found to be a stroke. Nevertheless, because of the possibility that mass lesions may be responsible for TIA symptoms, nine of 120 patients with TIA in our series had mass lesions discernible on the static study (7%). Consequently, a procedure such as a static brain study is extremely valuable in these patients.

Completed Stroke

Unlike other workers who have documented completed stroke on the temporal average in 42% of the cases using rectilinear scan
discerned by brain scanning include pituitary
adenomas, craniopharyngiomas, and acoustic
 tumors. The RA was positive in 60/114 cases (53%)
and complemented the RA in the diagnosis of stroke.
There were 13 lesions in addition diagnosed by
static studies which were not CVD but mass
lesions; the static camera study therefore was valuable
in this differentiation. An initial diagnosis of CVD in patients who
actually have brain tumors is not an uncommon
clinical occurrence resulting in delay of surgical or radiotherapeutic treatment. If the
RA and static brain study are used as the
initial examination, the presence or absence of
metastatic disease, meningioma, the more
undifferentiated astrocytomas, brain abscess,
and AVM's are for practical purposes eliminated in the differential diagnosis. The high
accuracy approaching 90% in detecting intracerebral tumors by static rectilinear brain
study is of great value in this situation and, in
our laboratory, the static scintillation camera
studies duplicate this frequency of detection.
Other tumors near the large blood pools or at
the base of the brain which are less likely to be
discerned by brain scanning include pituitary
adenomas, craniopharyngiomas, and acoustic
neuromas; however, these are seldom implicated in the usual patient evaluated neurologically for CVD.

A recent extensive study reviews the
prognosis following early surgical treatment of
acute stroke due to lesions in the carotid
arteries. An important finding of this study was that a patient with acute stroke had a
relatively high mortality or serious permanent
morbidity following early surgery. It was
suggested that surgery for extracranial arterial
obstruction should be delayed for periods from
one week to three months. Other data stress
that when CCA's were done on patients with
an altered level of consciousness associated
with acute stroke, not only were the minor
complications as high as 14%, but also the
more grave complications, including death and
permanent hemiparesis, occurred in 1.2%. These
data would indicate strongly that if surgery is to be delayed a few weeks, then there
is no reason or rationale for an immediate
CCA as long as the RA and static study are
available to contribute information about the
presence, degree, and location of the cerebral
disorder and to screen out lesions requiring
immediate attention.

There remains some controversy with
respect to the detection of obstructive lesions in
carotid vessels by the RA. One study reported six patients who had 50% to 80%
carotid lumen obstruction demonstrated on the
CCA, three of whom were found to have
abnormal studies on the RA. In one of these,
with an apparently normal RA of the carotid
vessels, there was only a 20-mm systolic
pressure drop across the stenotic lesion found
at carotid endarterectomy. This indicated a
borderline significance with respect to
decreased blood flow. In another patient with a
60% right internal carotid artery stenosis,
while the radioactivity over the carotids
appeared to be relatively equal, there was a
diminished pattern of perfusion over the right
middle cerebral artery area, indicating vascular
disease in the smaller intracranial vessels. This
type of perfusion deficit in our study was more
important clinically than the cervical carotid
lesions. In another group of 14 patients in the
same study, total carotid artery occlusion seen
by CCA procedures was detected by the RA in
all but three patients. In each one of the three,
there appeared to be some explanation based
on either dilated vertebral arteries which mimic
the appearance of normal carotid vessels, or
instances where the diagnostic problem was
complicated and the correlation could not be
made. In short, there is a relatively high yield of abnormality seen over the carotid vessels
when the disease is unilateral and the areas are
carefully studied. Our experience in a similar
study of carotid vessels in 14 patients with the
RA technique indicates that where the degree of
unilateral carotid vessel lumen obstruction
as measured by CCA is 50% or more, some
evidence of abnormality in the RA pattern over
the carotid arteries occurred in all cases. It has
EVALUATION OF CVD WITH RADIONUCLIDE ANGIOGRAPHY

been estimated that about 80% occlusion of a carotid vessel is required to produce flow impairment sufficient to render the patient symptomatic by decreased blood flow alone. If 80% unilateral stenosis is present, the discovery of such a lesion should be made easily with RA.

Cerebral thrombosis and embolism occur in about 70% of the cases with CVD. Twenty percent more have subarachnoid hemorrhage or intracerebral hemorrhage, and the remaining 10% are made up of a variety of ill-defined vascular lesions including arterial spasm and arteriovenous malformation. The diagnostic problem in intracerebral hemorrhage or subarachnoid hemorrhage is not usually difficult, since the diagnosis can be made by a history which includes hypertension, physical examination, lumbar puncture, and other routine studies. The main difficulty appears to lie in the large number of patients who have cerebral thrombosis or cerebral ischemia and in those who have TIA, which may later develop into completed strokes. In both, the major etiological factor appears to be atherosclerosis involving not only extracranial vessels but small intracranial vessels as well. Our data indicate that the diagnosis of cerebral vascular disease can be approached in a practical way from the radiographical viewpoint by a simple, noninvasive, high-yield diagnostic test free of morbidity.

The initial development and establishment of the technical reliability of the RA and recognition of the significance of various patterns in cerebral vascular disease can be difficult. However, once such a capability is established, it appears to be a reliable clinical tool.

References

Evaluation of Cerebral Vascular Disease With Radionuclide Angiography
Ronald J. Fischer and August Miale, JR.

Stroke. 1972;3:1-9
doi: 10.1161/01.STR.3.1.1

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1972 American Heart Association, Inc. All rights reserved.
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:
http://stroke.ahajournals.org/content/3/1/1