Prolonged Hypoperfusion and Early Stroke
After Transient Ischemic Attack

J. Bogousslavsky, MD, A. Delaloye-Bischof, MD, F. Regli, MD, and B. Delaloye, MD

Many patients suffer a stroke early after a transient ischemic attack, but the reason why is often unclear. We studied 12 patients with <75% stenosis of the internal carotid artery and a single hemispheric transient ischemic attack lasting <1 hour who had a normal neurologic examination 3-13 hours later and a normal computed tomogram 24-36 hours later. Single-photon emission computed tomography using technetium-99m HM-PAO ^50 hours after the attack showed no abnormality in eight patients, but in the other four there was an area with 30-50% reduction in perfusion ipsilateral to the transient ischemic attack. Three of these four patients developed an ipsilateral infarct 3-7 days later, but none of the eight patients with normal single-photon emission computed tomograms had a stroke during the following weeks. No difference in therapy, risk factors, severity of internal carotid artery disease, or timing of the technetium-99m study could explain these findings. We suggest that some transient ischemic attacks, though clinically identical to others, may be associated with persisting focal hypoperfusion, which predisposes to early stroke. (Stroke 1990;21:40-46)

The duration of focal cerebral hypoperfusion in so-called transient ischemic attack (TIA) is not well known because its relation to the duration of clinical symptoms and signs varies. We used single-photon emission computed tomography (SPECT) to study 12 patients with one isolated TIA lasting <1 hour and found that persisting focal hypoperfusion after resolution of TIA symptoms may be associated with early infarction in the same area.

Subjects and Methods
The aim of our study was to assess SPECT findings early after a brief and unique TIA. As most TIAs lasting >1 hour may actually correspond to true infarction (cerebral infarction with transient signs [CITS], including TIA due to lacunar infarction), entry into the study was limited by preestablished policy to patients whose symptoms lasted <1 hour and who had a normal neurologic examination ≤12 hours after the TIA. Because previous cerebrovascular events could also confuse the findings, we selected only patients with a single TIA in the carotid territory, without any history of a prior TIA or stroke. Symptoms of carotid-territory TIAs were defined as motor hemiparesis with or without hemisensory or homonymous hemianopsic impairment and aphasic disturbance with or without motor or sensory disturbances. We also excluded patients with ≥75% stenosis (internal carotid artery [ICA] systolic peak >8 KHz with spectral broadening, decreased diastolic window, and increased diastolic frequency) or occlusion of the ipsilateral ICA demonstrated by extracranial carotid and transcranial Doppler ultrasounds because ICA or middle cerebral artery (MCA) occlusion or ≥75% stenosis may in itself cause ipsilateral cerebral hypoperfusion. Brain computed tomography (CT) with or without contrast was performed at least 24 hours after the TIA to exclude patients with visible cerebral infarction. Electrocardiography (ECG) with 24-hour monitoring and two-dimensional echocardiography were also performed to rule out an undetected cardiac source of embolism. The clinical characteristics and potential risk factors for stroke (as defined in the Lausanne Stroke Registry) of the patients were also recorded for subsequent analysis. SPECT using technetium-99m HM-PAO (10 mCi; dual Rota camera at 6° steps of 30 seconds each) was performed just before or just after CT. For the SPECT studies, the patients were examined in a lying position with their heads slightly retroflexed and untilted to obtain slices parallel to the orbitomeatal line, and images were obtained 10 minutes after injection of HM-PAO in sequential slices every 1 cm parallel to and above the orbitomeatal line. Regions of interest (ROI) 4-9 cm² were drawn on four different sections at the level of the presumed symptomatic cerebral region for comparison with images from the asymptomatic hemisphere. The differences in total count rate in the ROI...
between the hemispheres were computed and expressed as a percentage of the values from the asymptomatic hemisphere. Interhemispheric differences of >20±5% were considered to be significant with reference to previous experience in this laboratory.

Results

We selected 12 consecutive patients for the study, who were immediately admitted to the hospital. The characteristics of their TIAs and their concomitant risk factors for stroke are summarized in Tables 1 and 2, respectively.

SPECT showed no significant abnormality in eight patients, but in the other four patients there was an area with 30–50% reduction in perfusion ipsilateral to the TIA (Table 3). No differences in duration of the TIA, treatment received after admission (20% dextran-40 in 500 ml of 0.9% saline every 12 hours and 500 mg acetylsalicylic acid per day), time from TIA to SPECT, associated carotid artery disease, and risk factors listed in Table 2 explained these findings.

During follow-up in the hospital, three of the four patients with focal hypoperfusion developed an infarct in the same area 3–7 days after the TIA (see below); in one patient, the infarct was concomitant with drug-induced hypotension. On the other hand, none of the eight patients without hypoperfusion on SPECT developed an infarct while in the hospital or after discharge (follow-up 1.5–8 months).

Case Reports

Patient 1. A 74-year-old housewife was in good health until she suddenly experienced tingling in her face, head, and leg on the right side. These paresthesias were immediately followed by weakness in her right upper limb. She also reported word-finding difficulty during the same time. These symptoms lasted half an hour, with complete resolution within 5 minutes. On admission 3 hours later, her general and neurologic examinations were normal. Her blood pressure was 150/90 mm Hg. Results of an ECG as well as standard blood tests were normal. Doppler ultrasounds with B-mode echography showed 25% stenosis of the left ICA. Transcranial Doppler ultrasound was unremarkable. Brain CT 36 hours after her TIA was normal (Figure 1, left), but SPECT done ≤2 hours after the CT showed a 30% decrease of perfusion in the frontoparietal region of the left hemisphere compared with the right (Figure 1, bottom). Two days later, patient 1 was found with a severe right hemiplegia and aphasia on awakening. CT 1 day after the stroke showed a large left MCA-territory infarct (Figure 1, right). No change was seen on ECG and Doppler examination.

Patient 2. This 60-year-old man was a smoker and was known to have untreated hypertension for at least 1 year. He suddenly experienced severe weakness in his left arm, which resolved completely within 10 minutes. His wife noted that during this episode his face was asymmetrical and did not move as usual on the left side. Patient 2 was admitted to the hospital within 4 hours. His general and neurologic examinations were normal. His blood pressure was 160/90 mm Hg. Results of ECG and standard blood tests were normal. Doppler ultrasounds and B-mode echography of the carotid arteries showed small plaques on both sides. Transcranial Doppler ultrasound was normal. SPECT 36 hours after the TIA showed decreased perfusion (50%) in the right hemisphere compared with the left (Figure 2, top). Brain CT 3 hours later was normal (Figure 2, left). Four days after his TIA, after lunch, Patient 2 complained of weakness in the left side of his body. On neurologic examination, he had a pure left hemiparesis with faciobrachial predominance. CT 18 hours later showed an infarct in the territory of the right MCA deep perforators (Figure 2, right). Cerebral angiography 2 days later showed no significant abnormality.

Patient 3. A 69-year-old man with untreated hypertension diagnosed 6 months earlier suddenly experienced weakness in his left leg, which was immediately followed by weakness in his left arm and face and dysarthria. These symptoms lasted 20 minutes,
complete recovery. On admission half an hour later, he had a normal neurologic examination. His blood pressure was 160/90 mm Hg, and he had a regular pulse. Results of ECG and carotid and transcranial Doppler ultrasound were normal, as were standard blood tests. CT (Figure 3, left) and bilateral carotid pulse. Results of ECG and carotid and transcranial Doppler ultrasounds were normal, as were standard two-dimensional echocardiography, EC, extracranial carotid; TC, transcranial (ipsilateral middle cerebral artery stem); SPECT, single-photon emission computed tomography; ROI, % difference (ipsilateral–contralateral); R, right; L, left; F, face; Ul, upper limb; LJ, lower limb; HT, hypertension; CS, cigarette smoking; DM, diabetes mellitus; HC, hypercholesterolemia; N, normal; SVE, supraventricular extrasystoles; RBBB, right bundle branch block; IAVB, first-degree atioventricular block; AS, aortic sclerosis; LVH, left ventricular hypertrophy; B, bilateral; ICA, internal carotid artery.

Discussion

Cerebral blood flow after one or more TIA(s) has been assessed in several studies, but with variable findings, such as focal or diffuse hypoperfusion, hyperperfusion, or no abnormality. A persisting focal hypoperfusion in the area corresponding to the TIA has been correlated with a longer TIA and an increased severity of ipsilateral carotid artery disease. However, many of these findings may be difficult to interpret because of methodologic problems, such as the absence of systematic assessment of the carotid and intracranial arteries (hemodynamically significant stenoses and occlusions were not excluded), the absence of brain CT (CITS were not excluded), and the absence of mention of the time from TIA to cerebral blood flow measurement. Our patients formed a very homogeneous group as all had a single brief TIA, a normal neurologic examination, and a normal CT and none had hemodynamically significant ICA disease. Though SPECT was performed during the same period (<50 hours after the TIA) in all 12 patients, we found normal results in eight but a significant focal hypoperfusion in the area of the TIA in the other four. The origin of this asymptomatic persisting focal hypoperfusion is not clear in the absence of clinical and CT evidence for an underlying infarct and significant ipsilateral carotid artery disease. A cortical diaschisis phenomenon, due to an undetected small subcortical infarct, seems unlikely because of the extent of the hemispheric hypoperfusion. Other hypotheses, such as “partial emolliement” with “incomplete infarction” may explain symptomatic persisting hypoperfusion, but these concepts remain controversial.

Table 3. Characteristics of 12 Consecutive Patients With a Single Brief Carotid-Territory TIA

<table>
<thead>
<tr>
<th>Pt/sex/age</th>
<th>Symptoms</th>
<th>Duration (min)</th>
<th>Risk factors</th>
<th>Heart disease</th>
<th>Doppler ultrasonography</th>
<th>TC</th>
<th>SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F/74</td>
<td>R F, Ul, LJ tingling; Ul weakness; aphasia</td>
<td>30</td>
<td>None</td>
<td>None</td>
<td>N</td>
<td>N</td>
<td>25% L ICA stenosis</td>
</tr>
<tr>
<td>2/M/60</td>
<td>L F, Ul weakness</td>
<td>10</td>
<td>HT, CS</td>
<td>None</td>
<td>N</td>
<td>N</td>
<td>B ICA plaques</td>
</tr>
<tr>
<td>3/M/69</td>
<td>L F, Ul, L ICA weakness; dysarthria</td>
<td>20</td>
<td>HT</td>
<td>None</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>4/M/60</td>
<td>R F, Ul weakness</td>
<td>40</td>
<td>CS</td>
<td>None</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>5/F/59</td>
<td>L F, Ul tingling and weakness</td>
<td>2</td>
<td>None</td>
<td>None</td>
<td>N</td>
<td>N</td>
<td>B ICA plaques</td>
</tr>
<tr>
<td>6/M/52</td>
<td>R F weakness; aphasia</td>
<td>10</td>
<td>CS</td>
<td>None</td>
<td>N</td>
<td>N</td>
<td>B ICA plaques</td>
</tr>
<tr>
<td>7/M/52</td>
<td>R F, Ul, L ICA weakness</td>
<td>50</td>
<td>DM</td>
<td>None</td>
<td>N</td>
<td>N</td>
<td>R ICA plaques</td>
</tr>
<tr>
<td>8/M/75</td>
<td>R F, Ul weakness</td>
<td>30</td>
<td>HT</td>
<td>Angina</td>
<td>SVE</td>
<td>AS</td>
<td>50% L ICA stenosis</td>
</tr>
<tr>
<td>9/F/65</td>
<td>R F, Ul weakness; dysarthria</td>
<td>10</td>
<td>DM, HC</td>
<td>Angina</td>
<td>RBBB</td>
<td>N</td>
<td>25% L ICA stenosis</td>
</tr>
<tr>
<td>10/M/59</td>
<td>L F, Ul, weakness and numbness</td>
<td>20</td>
<td>HT, CS</td>
<td>None</td>
<td>N</td>
<td>N</td>
<td>50% R ICA stenosis</td>
</tr>
<tr>
<td>11/F/64</td>
<td>R F, Ul, L ICA weakness and tingling; aphasia</td>
<td>20</td>
<td>HT, CS</td>
<td>None</td>
<td>IAVB</td>
<td>LVH</td>
<td>25% L ICA stenosis</td>
</tr>
<tr>
<td>12/M/58</td>
<td>L F, Ul weakness</td>
<td>2</td>
<td>CS</td>
<td>None</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>

TIA, transient ischemic attack; Pt, patient; F, female; M, male; ECG, electrocardiography (including 24-hour monitoring); Echo, two-dimensional echocardiography; EC, extracranial carotid; TC, transcranial (ipsilateral middle cerebral artery stem); SPECT, single-photon emission computed tomography; ROI, % difference (ipsilateral–contralateral); R, right; L, left; F, face; Ul, upper limb; LJ, lower limb; HT, hypertension; CS, cigarette smoking; DM, diabetes mellitus; HC, hypercholesterolemia; N, normal; SVE, supraventricular extrasystoles; RBBB, right bundle branch block; IAVB, first-degree atioventricular block; AS, aortic sclerosis; LVH, left ventricular hypertrophy; B, bilateral; ICA, internal carotid artery.
Because two of our three patients with persisting hypoperfusion and subsequent stroke had hypertension and a small deep infarct, the possibility of small-artery disease must be raised; however, this would not explain the SPECT findings, except in the case of widespread small-artery disease with severely impaired vasoreactivity.

Another possibility is that our patients with persisting hypoperfusion had a fluctuating stroke onset due to symptomatic and asymptomatic recurrent embolism to the brain. Recurrent asymptomatic embolism may explain persisting hypoperfusion in the absence of neurologic dysfunction, and recurrent symptomatic embolism may explain the first (TIA) and second (stroke) events. In the Lausanne Stroke Registry, 6.6% of 1,000 first-ever stroke patients had a fluctuating stroke onset, which evolved during >24 hours in more than half of them. Atherothrombotic stroke was the main cause.
of them. Atherothrombotic stroke was the main cause.

Since three of our four patients with persisting focal hypoperfusion developed an infarct 3-7 days after the TIA while none of our eight patients with normal SPECT did, we suggest that persisting focal hypoperfusion may be an indicator of a greater risk of subsequent stroke. However, we must emphasize that in patients with previous cerebrovascular events, severe ICA disease, or another cause of hypoperfusion, the evaluation of this risk will be obscured. Gautier et al.\textsuperscript{23} suggested that up to one half of the patients with a TIA may develop an infarct during the following 24 hours. In many
instances, the underlying cause of the TIA (carotid disease, cardioembolism, etc.) may explain why some patients have a high risk of infarction early after their TIA. However, our findings in patients without severe carotid artery disease or a cardiac source of embolism suggest that uncommon forms of TIA, though brief and clinically identical to other forms, may be associated with persisting focal hypoperfusion, which predisposes the patient to early stroke. By detecting this persisting hypoperfusion, SPECT may identify those unstable patients who are at high risk for early infarction.

**FIGURE 3.** Patient 3. Left: Computed tomogram (CT) 48 hours after transient ischemic attack (TIA). Bottom: Single-photon emission computed tomogram at same level as left 50 hours after TIA shows 40% decrease of perfusion in right hemisphere. Right: CT 2 days after stroke.
Acknowledgments

We thank P.A. Despland, MD, and A. Uske, MD, for their help in the evaluation of Doppler and CT studies.

References


KEY WORDS • cerebrovascular disorders • cerebral ischemia, transient • tomography, emission computed
Prolonged hypoperfusion and early stroke after transient ischemic attack.
J Bogousslavsky, A Delaloye-Bischof, F Regli and B Delaloye

Stroke. 1990;21:40-46
doi: 10.1161/01.STR.21.1.40

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/21/1/40