Silent Stroke and Carotid Stenosis

J.W. Norris, MD, FRCP, and C.Z. Zhu, MD

Background and Purpose: Silent cerebral infarction is often found on computed tomographic scan in patients with asymptomatic carotid stenosis, but its relation to the arterial stenosis is uncertain.

Methods: We compared computed tomographic scans and carotid Doppler in 115 patients with asymptomatic carotid stenosis, 203 with carotid transient ischemic attacks and carotid stenosis, and 63 with transient ischemic attacks but without carotid stenosis. There was no group with normal carotid arteries for comparison.

Results: Lesions seen on CT scan were most common in the transient ischemic attack with carotid stenosis group (47%) compared with the other groups (30%, 19%) (p<0.001). Cerebral infarcts ipsilateral to the carotid stenosis were found in 10% of patients with mild (35–50%) stenosis, 17% in moderate (50–75%) stenosis, and 30% with severe (>75%) carotid stenosis (p<0.001). In patients with asymptomatic carotid stenosis, 68% of infarcts were ipsilateral to the stenosis; in those with transient ischemic attacks and carotid stenosis, 86% of infarcts were ipsilateral to the stenosis.

Conclusions: The more severe the carotid stenosis, the higher the incidence of cerebral infarction ipsilateral to the stenosis. This finding applied to central infarcts as well as to peripheral infarcts in both symptomatic and asymptomatic patients. Silent cerebral infarction may be an indication for carotid endarterectomy in asymptomatic patients. (Stroke 1992;23:483–485)

KEY WORDS • cerebral infarction • carotid artery diseases • ultrasonics

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oon after the advent of computed tomography, it became evident that the reversible clinical deficits seen in transient ischemic attacks (TIAs) were often accompanied by irreversible structural cerebral lesions; 12–70% of computed tomographic (CT) scans in these patients revealed small cerebral infarctions.1 In the National Institute of Neurological and Communicative Disorders and Stroke Data Bank Study,2 11% of patients with clinical signs of stroke but without any history of stroke had CT lesions unrelated to the presenting stroke. Also, approximately 20% of patients with asymptomatic carotid stenosis have infarcts confirmed on CT scan,3 while multiple small infarcts without any accompanying symptoms sometimes appear after carotid endarterectomy.4 Because stroke is a clinical phenomenon, these asymptomatic lesions are better termed “silent infarctions” than “silent strokes.”

The dilemma presented by transient clinical deficits with permanent structural cerebral lesions caused Waxman and Toole5 to propose a new term, “cerebral infarction with transient signs,” a separate and presumably more serious syndrome than TIAs with normal appearance on CT scan. However, just as silent infarcts cannot be equated with silent strokes, TIAs remain clinical observations independent of CT scan or other laboratory findings.

Because we have often observed a variety of small cerebral infarcts in patients with asymptomatic carotid stenosis, we decided to investigate this observation further to evaluate the clinical significance of the lesions and to decide whether other factors such as the severity of the carotid stenosis relate to the appearance of infarction on CT scan.

Subjects and Methods

We compared the CT findings of three groups of patients. First, 115 patients with asymptomatic stenosis in one or both carotid arteries were referred to the carotid Doppler laboratory because of asymptomatic neck bruits. These patients had undergone previous CT scanning and were prospectively followed up in a special outpatient clinic at 6-month intervals.6

Second, in the neurology outpatient department 63 patients with TIAs had normal carotid arteries on Doppler ultrasound examination. Patients in this group were eligible for inclusion in the study only if they had both CT scanning and carotid Doppler examination. Hence, although these patients were consecutively enrolled, those with only one test result were not included.

Finally, 203 patients with TIAs and evidence of carotid stenosis in one or both arteries on Doppler examination (obtained from the medical records) were initially gathered for enrollment in a carotid surgery study. Because this is a retrospective review of prospectively gathered data, the timing of the CT scanning was random in the asymptomatic patients. However, all the symptomatic patients were investigated acutely, so all CT scans were performed within days or weeks of the clinical event.

Carotid Doppler studies were performed on a Carolina Medical Electronic Dopsca 1060, a duplex scanning device with a 5-MHz probe. In our laboratory, this...
technique has a specificity of 95% and sensitivity of 96% compared with cerebral angiography.7

The severity of carotid stenosis of the internal carotid artery was classified as mild (35–50%), moderate (50–75%), and severe (>75%). We performed CT scans with a GE 9800 scanner. Statistical analysis was performed by comparing groups using $\chi^2$ test. Mantel-Haenszel $\chi^2$ was used to test the association between severity of carotid stenosis and frequency of ipsilateral lesions on CT scans in symptomatic and asymptomatic groups.

### Results

There were no significant age or sex differences in the three groups (Table 1). Of the 381 patients evaluated, 137 had “positive” scans (i.e., showing evidence of cerebral infarction). All lesions shown on CT scan were small (<15 mm) and were of two types. Deep, centrally located infarcts and peripheral (cortical) infarcts, while 61% (83) were peripheral infarcts located in the cortex or immediate subcortical regions.

In the asymptomatic group, 19% had lesions confirmed on CT scan compared with 30% in patients with TIA+ and no carotid stenosis and 47% in those with TIA+ and stenosis (Table 1). In 16 cases, the lesions were bilateral and multiple. Patients with TIA+ and carotid stenosis had significantly more lesions than the other groups ($p<0.0001$).

When the CT lesions were divided into deep, centrally located infarcts and peripheral (cortical) infarcts, patients with TIAs and carotid stenosis had significantly more infarcts of both types ($p<0.0001$, Table 1).

The severity of carotid stenosis (mild, moderate, or severe) in the two groups with carotid stenosis was also compared for the frequency of ipsilateral lesions shown on CT scan (Table 2). The frequency of lesions increased with the severity of carotid stenosis in both symptomatic and asymptomatic groups ($p<0.0001$). There were significantly more peripheral infarcts in the severe stenosis group compared with the mild and moderate carotid stenosis groups ($p<0.0001$). Hence, the more severe the carotid stenosis, the higher the frequency of both central and peripheral lesions in the ipsilateral cerebral hemisphere.

The incidence of lesions ipsilateral to the most stenosed carotid artery were compared in the symptomatic and asymptomatic groups with carotid artery stenosis. In the patients with asymptomatic carotid artery stenosis, 68% (15 of 22) of lesions on CT scan were ipsilateral to the most stenosed carotid artery compared with 86% (83 of 96) in the patients with TIAs and carotid artery stenosis. However, this difference was not significant.

### Discussion

Silent as well as symptomatic cerebral infarcts were uniformly small, which is the finding of virtually all similar reports.1,2,8–10 This may reflect the suggested pathogenesis of these lesions, that showers of small microemboli composed of platelet aggregates or cholesterol crystals are shed from the surface of carotid plaques but, because of their size, do not produce symptoms.1 It has even been argued that these tiny infarcts are therefore markers of active carotid plaque ulceration, based on the correlation of postoperative examination of carotid plaques and the CT findings in the same patients.10 Recent transcranial Doppler monitoring observations in patients undergoing cardiothoracic and carotid surgery confirm that streams of microemboli bombard the brain during and after the surgical procedure.11

Apart from the small size of these infarcts, there may be other reasons for their silent appearance. Patients experiencing cerebral microembolization during sleep may be unaware of transient symptoms which would otherwise alarm them during waking hours. We were unable to distinguish any specific localization of the lesions to silent areas of the brain, and this has been the experience of others.8 Dismissal of fleeting and minor symptoms by either patient or physician might also explain the apparent absence of symptoms.

### Table 1. Frequency of Central and Peripheral Infarction in Symptomatic and Asymptomatic Patients

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Mean age</th>
<th>Men:Women</th>
<th>Peripheral infarcts</th>
<th>Central infarcts</th>
<th>Positive CT (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACS</td>
<td>115</td>
<td>69</td>
<td>66:49</td>
<td>12</td>
<td>10</td>
<td>19</td>
</tr>
<tr>
<td>TIA−</td>
<td>63</td>
<td>66</td>
<td>33:30</td>
<td>11</td>
<td>8</td>
<td>30</td>
</tr>
<tr>
<td>TIA+</td>
<td>203</td>
<td>66</td>
<td>135:68</td>
<td>60</td>
<td>36</td>
<td>47</td>
</tr>
</tbody>
</table>

ACS, patients with asymptomatic carotid stenosis; TIA−, transient ischemic attack patients without carotid stenosis; TIA+, TIA patients with carotid stenosis.

### Table 2. Frequency of Central and Peripheral Infarctions According to Degree of Carotid Stenosis

<table>
<thead>
<tr>
<th>Stenosis</th>
<th>n</th>
<th>Peripheral infarcts</th>
<th>Central infarcts</th>
<th>Positive CT scan (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (35–50%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>41</td>
<td>7</td>
<td>3</td>
<td>24</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>193</td>
<td>7</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>234</td>
<td>14</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Moderate (50–75%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>34</td>
<td>6</td>
<td>6</td>
<td>35</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>84</td>
<td>2</td>
<td>6</td>
<td>9.5</td>
</tr>
<tr>
<td>Total</td>
<td>118</td>
<td>8</td>
<td>12</td>
<td>17</td>
</tr>
<tr>
<td>Severe (&gt;75%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>128</td>
<td>40</td>
<td>17</td>
<td>52</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>156</td>
<td>18</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>284</td>
<td>58</td>
<td>27</td>
<td>30</td>
</tr>
</tbody>
</table>

n, Number of stenosed carotid arteries.
There was a disproportionately high incidence of central infarctions (39%) in the present study compared with that in our hospital stroke register (10%) and in other series. This may simply represent a bias of small lesions in asymptomatic patients. We do not have enough data on concomitant hypertension in these patients to comment on this as a risk factor. To determine the effect of carotid stenosis alone on the associated lesions shown on CT, a control group with identical risk factors but with normal carotid arteries would be ideal. However, there is no practical way to assemble such a group without an enormous study population with matching variables.

The incidence of these lesions rose significantly the higher the degree of carotid stenosis, and there was a high degree of ipsilaterality of the infarcts to the stenosis. This suggests that central infarcts may be produced by carotid stenosis as well as by hypertension and by the hemodynamic effects of carotid occlusion. Small central infarcts may be considered as lacunes. In an autopsy review of nearly 3,000 patients, 81% of lacunes were asymptomatic, most did not present clinically with classical lacunar syndromes, and the spectrum of pathogenesis was wide and included hemodynamic and embolic etiologies.

We did not perform CT scans on all patients, so a potential bias of the study is that they were more likely to be ordered in patients with severe carotid stenosis. However, we compared proportions and not absolute numbers, so this is unlikely to introduce significant error.

In surgical series, in which patients have preoperative CT scanning before carotid endarterectomy, positive scans are reported in 12–48% of patients with TIAs and 17–21% in those without symptoms. Although some authors suggest that microemboli from active carotid ulceration produce these tiny infarcts, the lesions are often contralateral to the stenosed or ulcerated artery, in some cases as frequently as 50%. Therefore, it seems more likely that an additional factor, such as associated hypertension, is responsible, but no studies with such prospective data have been performed. If silent infarctions can be equated with unrecognized symptoms, we agree with the suggestion that surgery might be justified by the presence of these preoperative silent infarcts as much as by symptoms. Similarly, the 6% incidence of silent infarcts after carotid surgery might be regarded as perioperative complications in the same light as minor strokes.

We see no justification in devising a new terminology to incorporate the results of CT scanning in established clinical terms such as TIAs or resolving ischemic neurological deficit, even if there is evidence that these findings confer a less favorable prognosis. The clinical spectrum from asymptomatic patients, through TIAs to stroke, is a distinct and separate dimension which intersects that of laboratory investigations such as CT scanning. The advent of magnetic resonance imaging may bring an even newer and more refined dimension that hopefully will aid further understanding and management of acute cerebrovascular disease.

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References
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