Silent Stroke in Patients With Transient Ischemic Attack or Minor Ischemic Stroke

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Background and Purpose: We studied silent stroke (i.e., infarcts on computed tomographic scan not related to later symptoms) in patients after transient ischemic attack or minor ischemic stroke.

Methods: Ours is a cross-sectional study of 2,329 patients who were randomized in a secondary prevention trial after transient ischemic attack or minor ischemic stroke and had no residual deficit after the qualifying event.

Results: Silent stroke was observed in 13% of the 2,329 patients. Lacunes formed 79%, cortical lesions 14%, and border zone lesions 7% of all silent strokes. Silent lacunes were most often located in the basal ganglia and symptomatic lacunes most often in the corona radiata. Age, hypertension, and current cigarette smoking were related to the presence of silent stroke. Silent stroke was equally common in different types of transient ischemic attack, including transient monocular blindness. Residual symptoms of any kind were more common in patients with silent stroke than in those without.

Conclusions: Because only the sites of silent stroke infarcts differed slightly from those of symptomatic infarcts and the frequency of vascular risk factors was similar to that of symptomatic infarcts, silent stroke may have the same bearing on future risk as known prior stroke. (Stroke 1992;23:1220-1224)

KEY WORDS • cerebral ischemia, transient • risk factors • tomography, x-ray computed
Clinical Data

The symptoms of the qualifying event (with or without residual deficit) were recorded on a standard questionnaire in plain language. We distinguished transient monocular blindness, cortical TIA (presence of any of the following: visual field defects; spatial neglect; or disorders of language, writing, reading, memory, or orientation), supratentorial lacunar syndrome (pure motor symptoms, pure sensory symptoms, or sensorimotor symptoms), and vertebrobasilar infratentorial TIA (no hemianopia, aphasia, alexia, or agraphia, but at least two of the following: rotatory dizziness, diplopia, dysphagia, disturbance of balance, or ataxia). The occurrence of similar or different attacks over the preceding year was specifically requested. In addition, the following baseline items from the medical history were recorded: age; current cigarette smoking; and history of diabetes, hypertension (known high blood pressure in the past, treated or not), or cardiovascular disease (angina pectoris, myocardial infarction, or intermittent claudication). Laboratory studies included tests for hematocrit and fibrinogen.

CT Scan

Except in patients with transient monocular blindness, a CT scan was mandatory to exclude causes other than ischemia and to establish a baseline in case of subsequent events. All scans were reviewed independently and in a blinded fashion by at least two neurologists. On the basis of clinical information subsequently taken into account, a hypodense lesion was judged relevant or not for the event. Infarcts were defined as hypodense lesions within a recognized arterial territory. We distinguished among cortical infarcts (when the lesion included a part of the cerebral cortex), lacunar infarcts (in cases of small, deep lesions less than 1.5 cm in diameter), and border zone infarcts (in cases of hypodensities between arterial territories). The locations of the lacunar infarcts were described as the anterior limb of the internal capsule, the genu, the posterior limb of the internal capsule, the corona radiata, the basal ganglia, the thalamus, the brain stem, or other. In cases of lacunes in the internal capsule with involvement of adjacent areas, the location in the internal capsule was designated as the main site.

Data Analysis

The relation of the different variables to the presence of silent stroke was studied in all patients and also in the group of patients with symptomatic lesions. Dichotomies of age, hematocrit, and fibrinogen were chosen at median values of all patients in the trial. In a univariate analysis, relations between variables were determined by means of the odds ratio. The precision of the estimates was described by means of the 95% confidence interval (CI). For multivariate analysis, we used logistic regression analysis with the EGRRET statistical package (Statistics and Epidemiology Research Corporation, Seattle, Wash.).

Results

Of the 2,329 patients studied, 206 patients (9%) had only silent stroke, 108 patients (5%) had both symptomatic infarcts and silent stroke, 507 patients (22%) had only symptomatic infarcts, and 1,508 patients (65%) had a normal CT scan (Figure 1). Of all silent strokes, lacunes represented 79%, cortical lesions 14%, and border zone lesions 7%.

The anatomic distribution of all 280 silent lacunes was as follows: anterior limb of the internal capsule, 18%; genu, 5%; posterior limb, 17%; corona radiata, 20%; basal ganglia, 21%; thalamus, 6%; brain stem, 2%; and other, 15%. This distribution differed from that of the 402 symptomatic lacunes in that more (27%) of symptomatic lacunes were in the corona radiata and fewer (11%) were in the basal ganglia. Another difference between symptomatic and silent lacunes was that symptomatic lacunes tended to include more than one anatomic structure (30%) more often than silent lacunes (13%). Symptomatic and silent border zone infarcts were usually situated between the territories of the middle and posterior cerebral arteries (60%). There was a slight difference in vascular territory between silent and symptomatic cortical infarcts, with 52% of silent infarcts in the middle and 40% in the posterior cerebral artery territory versus 67% and 30%, respectively, of the symptomatic infarcts. Symptomatic cortical infarcts were more often on the left side than silent infarcts. A symptomatic lacunar infarct was more commonly accompanied by a silent stroke than was a symptomatic cortical infarct (odds ratio, 4.0; 95% CI 2.0–8.3) or a symptomatic border zone infarct (odds ratio, 2.5; 95% CI 1.1–6.3) (Figure 1).

Type of TIA

In Table 1, the type of TIA is listed in relation to the presence of silent stroke. Patients with cortical, vertebrobasilar, and lacunar TIAs had a slightly higher frequency of silent stroke than those with transient monocular blindness. Patients with multiple TIAs be-
### TABLE 1. Type of Transient Ischemic Attack and Silent Stroke

<table>
<thead>
<tr>
<th>Type of TIA</th>
<th>Silent stroke (yes/no)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transient monocular blindness</td>
<td>9/81</td>
<td>...</td>
</tr>
<tr>
<td>Cortical*</td>
<td>84/580</td>
<td>1.3 (0.6-2.9)</td>
</tr>
<tr>
<td>Vertebrobasilar (infratentorial*)</td>
<td>25/180</td>
<td>1.3 (0.5-3.0)</td>
</tr>
<tr>
<td>Lacunar syndrome (supratentorial*)</td>
<td>196/1,174</td>
<td>1.5 (0.7-3.4)</td>
</tr>
</tbody>
</table>

Odds ratio (95% confidence interval [CI]) represents odds that patients with a certain type of TIA has silent stroke compared with patients who entered study with attacks of transient monocular blindness.

*For definitions of transient ischemic attack (TIA) types, see "Subjects and Methods."

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fore randomization (similar or different) had as many silent strokes as those without such a history.

### Risk Factors for Vascular Disease

Univariate analyses for the presence of silent stroke in all patients and in patients with a symptomatic infarct are shown in Figure 2. In all patients age 65 or older, current cigarette smoking, a history of hypertension, and a blood fibrinogen level of 3 mg/l or over were significantly related to silent stroke. In a multivariate analysis, these predictive factors proved to be independent, with the exception of the blood fibrinogen level. In patients who also had a symptomatic infarct, only current cigarette smoking remained just significant at the \( p < 0.05 \) level.

### Rankin Scale Grade

The relation between Rankin scale grade and infarcts on the CT scan is summarized in Table 2. The proportion of patients classified as Rankin scale grade 1 (rather than 0) was higher in patients with silent stroke than in those with a normal CT scan (odds ratio, 1.5; 95% CI, 1.2–1.9). This was particularly the case for patients with silent stroke only. Not unexpectedly, patients with a symptomatic infarct were relatively often classified as Rankin scale grade 1, but an additional silent infarct made no difference.

### Discussion

We found that 13% of the 2,329 patients who were randomized in the Dutch TIA trial with a Rankin scale grade not higher than 1 had silent stroke on their first CT scan. This frequency is similar to the findings from the National Institute of Neurological and Communicative Diseases and Stroke (NINCDS) Stroke Data Bank\(^4\) (11%) and the Framingham study\(^5\) (10%). The definition of silent stroke in these studies included the absence of a compatible history but not necessarily a normal neurological examination, whereas the disability status of patients was undefined, and all causes of stroke were considered.\(^4\,^5\) In the present study, we specifically studied the frequency of silent stroke in patients with focal cerebral ischemia that left no residual disability and was presumably caused by atherosclerosis.

Lacunar infarcts were prevalent among symptomatic lesions. This can be explained by selection of patients with no handicap or only a minor handicap after the qualifying event, which favors small infarcts. Of all silent strokes, 78% were lacunes. In concordance with

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![Figure 2. Diagram of 95% confidence interval (CI) of odds ratio that patient with silent stroke will possess risk factor compared with patient without silent stroke. If odds ratio is 1, frequency of risk factor is equal in both groups; if larger, frequency is higher in silent stroke.](http://stroke.ahajournals.org/)

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Risk factors

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;65 years</td>
<td></td>
</tr>
<tr>
<td>Diabetes present</td>
<td></td>
</tr>
<tr>
<td>Hypertension present</td>
<td></td>
</tr>
<tr>
<td>Current smoking</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular disease present</td>
<td></td>
</tr>
<tr>
<td>Hematocrit &gt;45</td>
<td></td>
</tr>
<tr>
<td>Fibrinogen &gt;3 mg/liter</td>
<td></td>
</tr>
</tbody>
</table>

**More common in no-silent-stroke.**

**More common in silent stroke.**

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*By guest on September 2, 2017 http://stroke.ahajournals.org/*
the NINCDS study, we found that if patients had a symptomatic and a silent infarct, they were usually both of the lacunar type; the finding of two cortical or two border zone infarcts (one symptomatic and one silent) in a single patient was comparatively rare. The distribution of the silent and symptomatic lacunae was different; there were relatively more silent infarcts in the basal ganglia, which are less often clinically manifest. There was a large overlap in location, however. The finding of small silent lacunes in the white matter tracts of the internal capsule and even in the genu and the posterior limb, where the corticobulbar and the corticospinal tracts are situated, has been described before.\(^5\)\(^6\) Another difference was that symptomatic lacunes tended to be larger than the silent ones.

Risk factors for TIA and small stroke were found to be similar in a population study.\(^6\) In this study, patients with silent stroke determined by CT scan more often had hypertension, were older, had a history of current cigarette smoking, and had higher fibrinogen levels than patients with normal CT scans. In a secondary analysis of patients with only a symptomatic lesion (507) versus patients with an additional silent stroke (108), only current smoking of cigarettes \((p<0.05)\) remained significantly related to silent stroke; this is difficult to explain. In the Framingham study, the frequency of hypertension, cigarette smoking, and atrial fibrillation did not differ between patients with a normal CT scan, a scan that showed a symptomatic lesion, and one that showed a symptomatic infarct and additional silent stroke. Only diabetes occurred more often in patients with silent stroke, but the numbers were small. Silent stroke has been previously studied in atrial fibrillation,\(^17\)\(^18\) although the criteria for defining infarcts were not always adequate\(^19\); atrial fibrillation, however, was an exclusion criterion for randomization in the trial that formed the basis for this study. Age as a risk factor for silent stroke in patients with cerebrovascular disease can be explained by a longer period available for accrual of these lesions if they occur randomly. In the NINCDS study, only age emerged as a statistically significant risk indicator of silent stroke. The presence of silent stroke in the NINCDS study was related to TIAs, but in our series a history of previous attacks (similar or dissimilar) in the preceding year was not associated with silent stroke. There was no significant difference in frequency of silent stroke in different types of TIA compared with that in transient monocular blindness.

The proportion of patients with some degree of handicap (Rankin scale grade 1 or symptoms only) was greater in patients with silent stroke than in those with a normal CT scan. The occurrence of symptoms in the presence of a silent lesion may be explained by the silent stroke itself or by a concomitant and symptomatic lesion that was not (yet) visible on the CT scan. On the other hand, a Rankin scale grade of 1 may represent not only neurological symptoms but handicap in general as a result of depression, difficulty in concentration, and problems in returning to previous work, which may all occur after a TIA.\(^9\)\(^10\)

### Acknowledgments

The indispensable help of Paul Grob with the computer data is gratefully acknowledged. The participants of the Dutch TIA trial have been listed elsewhere.\(^9\)

### References

1. NINCDS Ad Hoc Committee on Cerebrovascular Diseases: A classification and outline of Cerebrovascular Disease II. *Stroke* 1975;6:564–566


### Table 2. Rankin Scale Grade and Symptomatic or Silent Stroke on Computed Tomographic Scan

<table>
<thead>
<tr>
<th>CT scan</th>
<th>Rankin scale grade</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No lesion</td>
<td>485/1,023</td>
<td>(\ldots)</td>
</tr>
<tr>
<td>Only silent stroke</td>
<td>89/117</td>
<td>1.6 (1.2–2.2)</td>
</tr>
<tr>
<td>Only symptomatic lesion</td>
<td>298/209</td>
<td>3.0 (2.5–3.7)</td>
</tr>
<tr>
<td>Symptomatic lesion and silent stroke</td>
<td>64/44</td>
<td>3.1 (2.1–4.6)</td>
</tr>
</tbody>
</table>

Odds ratio (95% confidence interval [CI]) represents odds that patients with Rankin scale grade of 1 have a certain type of computed tomographic (CT) scan lesion compared with patients with Rankin grade of 0. If odds ratio is 1, frequency is equal to that of patients with a normal CT scan.
Silent stroke in patients with transient ischemic attack or minor ischemic stroke. The Dutch TIA Trial Study Group.
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