Identification of Embolic Stroke Patterns by Diffusion-Weighted MRI in Clinically Defined Lacunar Stroke Syndromes

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Background—A number of clinical syndromes describing the presentation of deep brain infarcts are called lacunar syndromes resulting from small vessel occlusion (SVO). To verify the reliability of the clinical diagnosis “lacunar syndrome,” the value was investigated with diffusion-weighted MRI (DWI).

Methods and Results—A total of 73 patients (mean age 66 years; range 35 to 83 years) with sudden onset of a classical lacunar syndrome were enrolled. On the basis of the DWI findings, patients were divided into 3 groups: group 1, single subcortical lesion (<15-mm lesion; 43 patients; 59%); group 2, large (≥15 mm) or scattered lesions in 1 vascular territory (16 patients; 22%); and group 3, multiple lesions in multiple vascular territories (14 patients; 19%). A stroke mechanism other than SVO could be identified in 17 (23%) patients. Cardiac work-up revealed a cardiac embolic source in 8 patients (11%). Duplex sonography revealed symptomatic stenosis in 9 patients (12%). Based on the work-up information, 29 patients (40%) were found to have a potential cause of stroke other than SVO. A significant correlation with >1 single lesion on DWI-MRI and a clinical proven embolic source was observed (P=0.002). In 9 patients with MRI suspicious for a pathomechanism other than SVO, no embolic source was found.

Conclusions—The use of DWI-MRI improves the accuracy of the subtype diagnosis of stroke. Inaccuracy has to be expected in approximately one third if lacunar diagnosis is based on clinical and computed tomography findings. Most of these “false-positive” cases are attributable to large artery or cardiogenic embolic stroke. (Stroke. 2005;36:757-761.)

Key Words: clinical syndrome ■ lacunar stroke ■ magnetic resonance imaging ■ stroke

In the early half of the 19th century, the first postmortem reports on lacunar stroke were published.1 Fisher2,3 was the first to describe the clinical “lacunar stroke syndrome.” The term “lacunar infarction” for deep brain ischemia was coined. Following Fisher’s definition,2,3 lacunar strokes are still defined as small brain lesions (0.2 to 15 mm³) caused by occlusion of the deep brain perforating arteries and resulting in distinct clinical syndromes: dysarthria-clumsy hand syndrome (DCHS), pure motor stroke (PMS), pure sensory stroke (PSS), sensorimotor stroke (SMS), ataxic hemiparesis (AH), homolateral ataxia, and crural paresis (HACP).2 The underlying mechanism is thought to be local thrombosis caused by microatheroma and lipohyalinosis.2–6 Because of the clear clinical definition of lacunar strokes and the presumed pathophysiology, a frequently found notion is to concentrate on treatment of underlying risk factors and not to extensively search for embolic sources in these patients.

In this study, we evaluated the yield of diffusion-weighted MRI (DWI) in patients with a clinically defined acute lacunar stroke syndrome in detecting embolic stroke patterns, which might alter treatment decisions.

Patients and Methods

Over 1.5 years, 382 consecutive patients with ischemic stroke were screened and 73 patients were recruited for this study. Inclusion criterion was the presentation with an acute lacunar stroke syndrome2,5,7 (DCHS, PMS, PSS, SMS, AH, or HACP) assessed by a board-certified neurologist unaware of the imaging findings. Exclusion criteria were “cortical symptoms” such as aphasia, apraxia, and hemianopia, as well as seizures and disturbed consciousness. In all cases, the following stroke risk factors were recorded: hypertension, diabetes, hyperlipidemia, hyperhomocysteinemia, peripheral vascular disease, smoking, previous transient ischemic attack or stroke, coronary artery disease, and atrial fibrillation (AF). Criteria for AF were known history of permanent or paroxysmal AF or newly diagnosed permanent or paroxysmal AF on 24-hour Holter-ECG.

All patients received an extracranial and transcranial color-coded duplex ultrasound examination. Transesophageal echocardiography (TTE) and 24-hour Holter-ECG monitoring was obtained in every patient. Additional transesophageal echocardiography was performed if TTE, Holter-ECG and duplex sonography of the extracranial and intracranial vessels did not show evidence for cardiogenic or large artery embolism in 48 (66%) patients.

Computed Tomography Imaging

In all cases, intracranial hemorrhage was excluded by a computed tomography (CT) scan on admission. Brain CT scans (performed on

Received October 20, 2004; final revision received December 22, 2004; accepted January 10, 2005.
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Stroke is available at http://www.strokeaha.org DOI: 10.1161/01.STR.0000158908.48022.47

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a Somatom Plus CT system; Siemens) were evaluated for cerebral infarction and leukoaraiosis. The finding of leukoaraiosis in 7 brain regions was graded by CT: absent, mild (in at least 1 of 7 brain regions), or severe (present in all 7 brain regions), as suggested by van Swieten et al.8

**Magnetic Resonance Imaging**

MRI was performed within 48 hours of symptom onset on a 1.5-Tesla whole body scanner (General Electrics) equipped with echo planar imaging data capability designed to obtain rapid diffusion images (repetition time 4657 ms; echo time 118 ms; matrix 128×128; gradients of b-values 0, 500, and 1000 s/mm²). The apparent diffusion coefficients (ADCs) were calculated for each pixel and composed to an ADC map. Time-of-flight magnetic resonance (MR) angiography was performed with a spoiled gradient echo sequence (2D TOF; flip angle 50°; bandwidth 15.63; slice thickness 1.5 mm; field of view 26 cm). Images were reconstructed 3-dimensionally using a maximum intensity projection. All MRI scans were assessed by a neuroradiologist and a neurologist unaware of the clinical findings. On the basis of the DWI findings, the patients were divided into 3 groups: (1) single subcortical lesion (diameter ≤15 mm); (2) large and scattered lesions in 1 vascular territory (≥15 mm); scattered small lesions ≤15 mm or confluent scattered lesions ≥15 mm); and (3) multiple lesions in multiple vascular territories as defined in recent studies.9,10

The leukoaraiosis in 7 brain regions was graded by T2 MRI: absent, mild (in ≥1 of 7 brain regions) or severe (present in all 7 brain regions), as suggested by van Swieten et al.8

**Stroke Subtype**

To determine the stroke subtype, Trial of Org 10172 in Acute Stroke Treatment (TOAST)11 classification criteria were used. The stroke subtype diagnosis was based on clinical, laboratory and imaging data.

**Statistical Analysis**

All numerical variables were expressed as mean±SD. The χ² test and Fisher’s exact tests, if appropriate, were used to analyze the differences between patients with and without more than a single lesion on DWI-MRI. The Fisher exact test was used to compare the frequency of an identifiable mechanism between the patients with a lesion on DWI-MRI. The positive predictive value for the finding of a cortical lesion and an etiology other than SVO resulted in a moderate value of 0.69. The number of large artery arteriosclerosis and cardioembolism as underlying stroke reasons did not differ significantly among these patients.

Agreement of 2 blinded and independent observers for classification for the actual presence of a lacunar stroke (ICC, 0.95; 95% CI, 0.76 to 0.99). Sensitivity of the initial clinical classification for the actual presence of a lacunar stroke on DWI was low (0.58). The presence of leukoaraiosis on initial CT (mild 0.75; severe 0.65) as well as T2-weighted MRI (mild 0.76; severe 0.65) had low positive predictive values for lacunar stroke (<15-mm subcortical ischemia) on DWI.

**CT and MRI**

No clearly symptomatic acute lesions were identified on admission CT scan. CT showed no (18 patients; 25%), mild (37 patients; 50%), and severe leukoaraiosis (18 patients; 25%). On DWI, 34 of the 51 patients (67%) had a single hyperintense subcortical lesion with a diameter of ≤15 mm, consistent with the clinically assumed lacunar stroke; and in 9 patients (17%), a pontine infarct was found (group 1). Eight patients (16%) showed a subcortical single lesion of ≥15-mm diameter (group 2). In groups 1 and 2, all DWI lesions were located in a region appropriate for the clinical symptoms. Based on the work-up information in 86% of all patients in group 1, the assumed cause of stroke was small vessel occlusive disease (P<0.0001).

Group 3 consisted of 14 patients (Table; Figures 1 and 2). DWI discovered multiple hyperintense lesions in 1 vascular territory in 7 (10%; group 2), and in >1 territory in 14 patients (21%; group 3), consistent with an embolic stroke pattern. In 13 patients (groups 2 and 3), a single cortical lesion (4 patients; 5%) and scattered or multiple lesion patterns (9 patients; 12%) containing a cortical lesion were observed on DWI. The positive predictive value for the finding of a cortical lesion and an etiology other than SVO resulted in a moderate value of 0.69. The number of large artery arteriosclerosis and cardioembolism as underlying stroke reasons did not differ significantly among these patients.

Agreement of 2 blinded and independent observers for classification of the DWI pattern was excellent (ICC, 0.95; 95% CI, 0.76 to 0.99). Sensitivity of the initial clinical classification for the actual presence of a lacunar stroke on DWI was low (0.58). The presence of leukoaraiosis on initial CT (mild 0.75; severe 0.65) as well as T2-weighted MRI (mild 0.76; severe 0.65) had low positive predictive values for lacunar stroke (<15-mm subcortical ischemia) on DWI.

**TOAST Classification**

Based on the work-up information, 7 patients in group 1 (18%) were found to have a potential cause of stroke other than small vessel occlusive disease. In 6 patients, cardiac embolism and large artery disease were the assumed underlying etiology.

For group 2, SVO was the stroke etiology for 7 patients (44%), cardiac embolism was diagnosed in 3 patients (18%), and large artery disease in 1 patient (7%). In 4 patients (25%) with scattered lesion patterns, no other stroke risk factor than hypertension was found. As recommended by the guidelines,11 these patients were not classified as SVO because of the lesion pattern. Based on the work-up information, 11 patients of the group with more than a single lesion (69%) were found to have a proven cause of stroke other than small vessel occlusive disease (P<0.0001).
For group 3, a stroke mechanism could be identified in 9 (65%) of these patients. Cardiac work-up (echocardiography; 24-hour Holter-ECG) revealed a cardiac embolic source in 4 patients (29%). AF was diagnosed as the causal mechanism in 3 patients (21%), and in 1 patient, a ventricular thrombus was found. Duplex sonography of the extracranial and intracranial vessels revealed symptomatic internal carotid artery stenosis in 5 patients (36%). Altogether, in 9 patients of group 3 (65%), a cause of stroke other than small vessel occlusive disease was diagnosed based on the extensive work-up (P<0.0001). Further significant differences in clinical presentation among the 3 subgroups were not observed.

Discussion
In this study of 73 patients presenting with a classical lacunar syndrome, 21 patients had embolic stroke patterns with more than a single lesion on DWI, and 14 patients showed multiple infarcts in different vascular territories. This highlights that the clinical presentation alone has a low predictive value for evaluation of the actual stroke type.

The clinical management and therapy decisions are influenced by stroke subtype and etiology. Therefore, early classification is of substantial clinical value. Long-term therapy and prevention differ significantly among distinct stroke subtypes. DWI is a highly sensitive and specific technique for use in the early diagnosis of acute stroke. DWI provides improved information about embolic lesion pattern compared with CT scan. This is supported by recent studies using DWI that have shown that patients with assumed subcortical infarcts on DWI may have cortical lesions and multiple small deep brain infarcts, indicating an embolic source. Multiple lesions on DWI support an embolic etiology. Those patients with multiple infarctions on DWI were more likely to harbor an identifiable stroke mechanism than those with a single lacunar infarction. However, whether multiple DWI lesions in different vascular territories occurring simultaneously are caused by embolic showers or recurrent emboli remains unknown. Other possible explanations are diffuse thrombotic or inflammatory processes that lead to
multiple SVOs. Chowdhury et al investigated 10 patients with multiple subcortical lesions in a recent study. A definite embolic source was identified in only 1 patient. The authors assumed a generalized intrinsic process affecting many small cerebral vessels contemporaneously, causing multiple acute small subcortical infarcts.22

In a number of studies, different rates for the detection of embolic sources in patients with multiple DWI lesions were identified.9,19,21 Symptomatic extracranial arteriosclerosis or major cardioembolic sources were found in patients with lacunar infarctions, but 2 to 3 times less frequently than among patients with cortical infarctions.19,23 This is supported by our findings in which large artery embolism was found as the underlying stroke mechanism in 6 of 22 patients (27%) with more than a single infarct but only in 3 of 51 patients (6%) with a single lesion on DWI. The importance of aortic arch emboli for a combined finding of subcortical and cortical lesions was confirmed by autopic studies.24,25 Soloway and Aronson described in 1964 the finding of cholesterol crystals within the leptomeningeal cortical and cerebellar branches and in the deep brain perforating arteries. Vessels with a diameter of 14 μm were loaded with cholesterol emboli. These autopsy findings suggest that if a deep brain artery is occluded by a small embolus, more of such emboli may be expected in different brain vascular territories. The infarction in the territory of a penetrating artery can be explained by its lack of leptomeningeal collateral pathways and a greater susceptibility to ischemia. The finding of multiple acute infarcts in different vascular territories strongly indicates embolism. However, whether DWI lesions are caused by recurrent emboli or embolic showers is still unclear. Using well-accepted criteria for grading of leukoaraiosis by CT scan and T2 MRI does not result in acceptable positive predictive values for the presence of a small, single lesion on DWI.

Our data and the results of other studies18,19,23 indicate that relying entirely on the clinical presentation as lacunar syndrome may put patients at risk when search of embolic sources is omitted. Inaccuracy has to be expected in about one third if lacunar diagnosis is based on clinical and CT findings. Most of these false-positive cases are attributable to large artery or cardiogenic embolic stroke. Of course, on the other hand, coexisting lacunar infarctions in patients with atherosclerotic or cardiogenic embolic sources are possible. For patients with lacunar syndromes, DWI may be an important modality to obtain the accurate diagnosis and stroke subtype and should prompt the physician to search for an underlying embolic source.

References


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Stroke. 2005;36:757-761; originally published online March 3, 2005;
doi: 10.1161/01.STR.0000158908.48022.d7

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