Background and Purpose—To test the hypothesis that the National Institutes of Health Stroke Scale (NIHSS) score is associated with the findings of arteriography performed within the first hours after ischemic stroke.

Methods—We analyzed NIHSS scores on hospital admission and clinical and arteriographic findings of 226 consecutive patients (94 women, 132 men; mean age 62±12 years) who underwent arteriography within 6 hours of symptom onset in carotid stroke and within 12 hours in vertebrobasilar stroke.

Results—From stroke onset to hospital admission, 155±97 minutes elapsed, and from stroke onset to arteriography 245±100 minutes elapsed. Median NIHSS was 14 (range 3 to 38), and scores differed depending on the arteriographic findings (P<0.001). NIHSS scores in basilar, internal carotid, and middle cerebral artery M1 and M2 segment occlusions (central occlusions) were higher than in more peripherally located, nonvisible, or absent occlusions. Patients with NIHSS scores ≥10 had positive predictive values (PPVs) to show arterial occlusions in 97% of carotid and 96% of vertebrobasilar strokes. With an NIHSS score of ≥12, PPV to find a central occlusion was 91%. In a multivariate analysis, NIHSS subitems such as “level of consciousness questions,” “gaze,” “motor leg,” and “neglect” were predictors of central occlusions.

Conclusions—There is a significant association of NIHSS scores and the presence and location of a vessel occlusion. With an NIHSS score ≥10, a vessel occlusion will likely be seen on arteriography, and with a score ≥12, its location will probably be central. (Stroke. 2005;36:2121-2125.)

Key Words: angiography, digital subtraction ■ stroke, acute ■ thrombolytic therapy

The National Institutes of Health Stroke Scale (NIHSS) is widely used to assess the severity of acute ischemic stroke.1 It has been used in many trials and is a validated tool to predict stroke outcome.2–6 Specifically, it has been used in thrombolysis trials to include or exclude patients from active treatment.7–9 The NIHSS is robust for use by non-neurologists and nurses and also to scale patients retrospectively from chart records.10–13 Today, the NIHSS score is used routinely to assess stroke severity in most stroke centers.

Patients with acute stroke and without visible vessel occlusion or peripheral occlusions on intra-arterial digital subtraction arteriography (DSA) tend to have a low NIHSS score and a favorable outcome.14 Furthermore, studies of 54 patients with magnetic resonance (MR) angiography and 43 patients with DSA showed an increasing probability to find vessel occlusions with higher NIHSS scores.15,16 The presence of a symptomatic cerebral arterial occlusion may have clinical implications for treatment decisions, especially if intra-arterial thrombolysis (IAT) is considered.

The aim of the present study was to evaluate the relationship of NIHSS score and DSA findings in a large series of patients who were examined within the first hours after stroke onset.

Methods
From January 2000 to December 2003, 226 patients with acute ischemic stroke (94 women, 132 men; mean age 61.58±12.4 years) underwent DSA at our stroke unit because they had been considered for IAT. Some aspects of these patients have been reported previously.14,17–19 IAT was considered in the carotid territory up to 6 hours after stroke onset and in basilar artery (BA) occlusion up to 12 hours. They scored ≥4 points on the NIHSS or had an isolated aphasia or hemianopsia. The neurological status was assessed by a neurologist in the emergency room using the 15-item version of the NIHSS score.20 As soon as possible thereafter, all patients underwent computed tomography (CT) or MRI scans to rule out intracranial hemorrhage. All 226 patients of this study were considered to be candidates for IAT after CT or MRI and went on to arteriography. A 4-vessel diagnostic arteriography by transfemoral approach was performed in all the study patients to assess the complete vessel status and collateral circulation. Classification of collaterals from angiographic films was possible in all but 5 of the 226 study patients. Collaterals in the anterior circulation were classified into 2 groups: poor if none or minimal leptomeningial anastomoses were visualized and no or minimal filling of the occluded vessel territory was seen.
and good if leptomeningeal anastomoses filled the occluded vessel territory by more than half. Collaterals in the posterior circulation were considered good when antegrade or reversed unilateral or bilateral filling of the superior cerebellar arteries was seen and poor when such filling was absent. Within 1 or 2 days after DSA, 204 patients underwent cranial CT, MRI, or both (158 CTs, 79 MRIs, and 33 CTs and MRIs). Twenty patients had no early follow-up scans: 18 because they did not receive thrombolytics after diagnostic arteriography, 1 because of rapid clinical improvement after thrombolysis, and 1 diabetic because he died.

Demographic patient data, vascular risk factors, intervals from symptom onset to admission and from symptom onset to arteriography (when vessel status was recorded), and modified Rankin Scale (mRS) scores 3 months after stroke were recorded. Stroke cause was determined using ancillary investigations as necessary and classified according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) categories. Outcome was assessed using the mRS score 3 months after the ictus by clinical examination in 164 patients.22 A total of 56 patients who were not able or willing to return for a control visit were contacted by phone to determine their mRS score. Six patients were lost for follow-up at 3 months: 3 of them did not receive thrombolytic agents, and 2 of the 3 remaining patients could be contacted later.

Arteriograms were used to divide patients into 8 groups according to the location of their arterial occlusion: (1) internal carotid artery (ICA) group, (2) main stem of the middle cerebral artery (MCA; M1) group, (3) main branch of MCA (M2) group, (4) branches of MCA (M3/4) group, (5) anterior cerebral artery (ACA) group, (6) posterior cerebral artery (PCA) group, (7) BA group, and (8) no visible occlusion (no occlusion) group. If a patient showed ≥2 occluded arteries, the patient was placed into the larger artery group (eg, if the ICA and the ipsilateral M1 segment were occluded, the patient was allocated to the ICA group). Ischemic lesions as seen on MRI or CT scans and clinical findings were used to divide patients into a group with carotid territory (ICA, ACA, and MCA) and another with vertebrobasilar territory (BA and PCA) strokes.

Statistical analysis was performed with the SPSS 10 statistical software package (SPSS Inc). Categorical clinical characteristics and outcome were compared using χ² tests. Comparisons of stroke severity (NIHSS), time intervals, and outcome (mRS score) were analyzed using the Kruskal–Wallis Test. P<0.05 was considered significant. To distinguish patients with and without arterial occlusion on DSA, a sensitivity–specificity analysis was performed and curves were plotted. Such an analysis was also performed for patients with ICA, M1, M2, or BA occlusions (central occlusion group) versus patients without visible occlusions or occlusions of the MCA (M3 or M4), ACA, or PCA (peripheral occlusion group). To find associations with central vessel occlusion, logistic regression analyses were performed. Explanatory variables were tested one by one against the dependent variable “occlusion,” and variables without association (P>0.05) were removed from the model. Regression analysis was then performed by using a stepwise forward approach. We analyzed the data using a logistic regression model in which central vessel occlusion in early arteriography was used as the dependent and demographic factors and individual NIHSS scores as independent variables. For this, all NIHSS subitem scores were dichotomized into a group with 0 and a group with ≥1 points. The groups “motor function of arm” and “motor function of the leg” were given points irrespective of right or left side.

Results
A total of 156 (69%) of the 226 patients enrolled in this study underwent IAT. A total of 189 strokes were in the carotid territory, and 37 were in the vertebrobasilar territory. Risk factors were hypertension in 125 patients (55%), diabetes mellitus in 38 (17%), hyperlipidemia in 78 (35%), smoking in 45 (20%), and personal history of stroke or myocardial infarction in 25 (11%). They were equally distributed in the subgroups (P>0.05). Stroke etiologies were 44 (19%) large artery disease, 6 (3%) small artery disease, 94 (42%) cardio-embolic, and 23 (10%) others, such as dissections and other rare causes. In 58 (26%) patients, stroke etiology remained unclear. Intervals from stroke onset to arrival at the hospital were 142±73 minutes for patients with carotid territory stroke and 206±166 minutes for vertebrobasilar territory stroke (P=0.073); intervals from stroke onset to DSA were 226±69 and 312±179 minutes (P=0.009; Mann–Whitney test). A total of 200 (88.5%) of the 226 patients showed an occluded artery on DSA, whereas 26 patients (11.5%), 19 with carotid and 7 with vertebrobasilar strokes, had no visible occlusion. A total of 171 (75.7%) occlusions were central and 29 (12.8%) peripheral. Strokes were located 189 times in the carotid territory and 37 times in the vertebrobasilar territory.

The median NIHSS score was 14 (range 3 to 38) and differed among the 8 subgroups (P<0.001; Figure 1). Median NIHSS was highest in the BA group and lowest in the no occlusion group. There was no association between collaterals and NIHSS score on admission. Sensitivity–specificity curves to predict arterial occlusions in carotid and vertebrobasilar artery territories are shown in Figure 2. The sensitivity and specificity curves intersect between NIHSS scores 10 and 11 in the carotid territory and between NIHSS scores 9 and 10 in the vertebrobasilar territory. Figure 3 contains sensitivity and specificity curves for central versus peripheral or no occlusions, which intersect between NIHSS scores 12 and 13. According to logistic regression analyses, demographics or risk factors did not predict central occlusions on DSA; however, several items of the NIHSS score such as “level of consciousness questions,” “gaze,” “motor leg,” and “neglect” were significant predictors (Table). Right and left hemispheric strokes after defined arterial occlusions (ICA, M1, M2, or M3/4) as seen on arteriography did not differ with their median NIHSS scores (P>0.05; Mann–Whitney test).

Discussion
This study analyzed arteriographic findings in the first hours after stroke onset. Approximately 7 of 8 patients showed an occlusion on DSA, which is in the same order as in previous
studies. Fieschi et al found 76% occlusions in a series of 80 patients. When the clinical findings on admission expressed as NIHSS score are compared with the arteriograms, a total of 10 points make the chances to find an occluded artery considerable. The positive predictive value (PPV) of an NIHSS score of 10 is 97% to find an occluded artery on angiography in the carotid and 96% in the vertebrobasilar territory. When the NIHSS score rises to 12, the chances to find a central occlusion are substantial with a PPV of 91%. This is the main message of the analysis of our 226 patients. Overall, patients with BA thrombosis and ICA occlusions showed the highest NIHSS scores. The more peripheral that occlusions were located, the lower NIHSS scores tended to be. The lowest scores were found in patients without visible occlusions. Nakajima et al found similar associations in 43 patients with carotid territory strokes who had undergone DSA.

The next arising question is whether demographic factors or single items of the NIHSS can predict vessel occlusion on arteriography. In a logistic regression analysis, demographic factors did not forecast occlusions on DSA; however, several single items of the NIHSS score such as “level of consciousness questions,” “gaze,” “motor leg,” and “neglect” were predictors to find a central occlusion on arteriography. These single items are probably most significantly associated with large hemisphere or brain stem lesions, which result only from central occlusions but, for anatomical reasons, not from peripheral arterial occlusions.

Left hemisphere lesions tend to result in higher NIHSS scores compared with right-sided lesions of equal anatomical size. Therefore, the question arises whether given types of vessel occlusions on the right side result in NIHSS scores that are different from the scores of left-sided occlusions. This was not the case with any of the occluded arteries or arterial segments.

The National Institute of Neurological Disorders and Stroke (NINDS) recombinant tissue-type plasminogen activator (rtPA) Stroke Trial showed that patients with all stroke subtypes derived a clinical benefit from intravenous thrombolytic treatment, including patients with small artery disease. On the other hand, the Prolyse in Acute Cerebral Thromboembolism (PROACT) Trial II, which studied IAT with recombinant pro-urokinase (r-proUK) in stroke attributable to M1 or M2 occlusion, did not show a benefit for all patients. The benefit was limited to those with an NIHSS score of ≥11. It was most noticeable when the baseline NIHSS score was between 11 and 20, and IAT was useless with an NIHSS score of ≤10. In patients with M1 or M2 MCA occlusions, the spontaneous recanalization rate was 18%, as assessed by arteriography in PROACT II. In a study using MR angiography as assessment tool, 24% of the M1
and M2 segments recanalized spontaneously and 48% after intravenous rtPA. In PROACT II, which used intra-arterial r-proUK, 66% of the corresponding vessels recanalized, and in own series, 79%. Because recanalization is a powerful predictor of clinical outcome, recanalization rates give an indirect measure of the efficacy of IAT and intravenous thrombolysis (IVT). It is likely that IAT with urokinase is at least as efficacious as IVT with rtPA in central arterial occlusions. Furthermore, combined IVT and IAT thrombolysis or mechanical recanalization, alone or combined with IAT, achieves better recanalization than IVT alone.

All together, these randomized trials and open series have shown that it will be worthwhile to pursue IAT, and that randomized trials to compare IVT and IAT and the combination of IVT and IAT are needed. Because all studies of IAT or mechanical recanalization have been performed in patients with central occlusions, it becomes crucial to identify those who will likely be candidates for such treatments already at the emergency ward. The results of the present study will help the clinician to select such patients, but the NIHSS does not substitute for vascular imaging. With an NIHSS score ≥12, there is a good chance that a central vessel occlusion will be seen on arteriography in patients with acute stroke of carotid and vertebrobasilar ischemia.

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References

### NIHSS Items at Baseline and ORs for ICA, M1, M2, or BA Occlusions on DSA

<table>
<thead>
<tr>
<th>NIHSS Items</th>
<th>ORs for Vessel Occlusion</th>
<th>P Value (univariate model)</th>
<th>ORs for Vessel Occlusion</th>
<th>P Value (multivariate model)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOC</td>
<td>3.3 (1.7–6.5)</td>
<td>0.001</td>
<td>4.0 (1.9–8.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LOC alertness</td>
<td>3.0 (1.50–5.7)</td>
<td>0.001</td>
<td>2.9 (1.4–6.2)</td>
<td>&lt;0.001</td>
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<td>LOC questions</td>
<td>2.7 (1.5–5.1)</td>
<td>0.002</td>
<td>2.9 (1.4–6.2)</td>
<td>&lt;0.001</td>
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<td>LOC commands</td>
<td>2.7 (1.4–5.4)</td>
<td>0.005</td>
<td></td>
<td></td>
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<tr>
<td>Gaze</td>
<td>4.6 (2.3–8.9)</td>
<td>&lt;0.001</td>
<td>2.9 (1.4–6.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Visual fields</td>
<td>2.8 (1.2–6.5)</td>
<td>0.021</td>
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<tr>
<td>Facial palsy</td>
<td>2.1 (0.8–5.3)</td>
<td>0.129</td>
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<tr>
<td>Motor arm</td>
<td>4.5 (1.8–11.5)</td>
<td>0.002</td>
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<td>Motor leg</td>
<td>5.2 (2.5–10.9)</td>
<td>&lt;0.001</td>
<td>4.2 (1.8–9.6)</td>
<td>0.001</td>
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<td>Ataxia</td>
<td>0.4 (0.2–1.2)</td>
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<tr>
<td>Sensation</td>
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<tr>
<td>Language</td>
<td>1.7 (0.9–3.2)</td>
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<td>Dysarthria</td>
<td>1.3 (0.7–2.5)</td>
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<tr>
<td>Neglect</td>
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<td>0.002</td>
<td>3.2 (1.3–8.1)</td>
<td>0.013</td>
</tr>
</tbody>
</table>

Figures in parentheses indicate 95% CI. OR indicates odds ratio; LOC, level of consciousness.
NIHSS Score and Arteriographic Findings in Acute Ischemic Stroke
Urs Fischer, Marcel Arnold, Krassen Nedeltchev, Caspar Brekenfeld, Pietro Ballinari, Luca Remonda, Gerhard Schroth and Heinrich P. Mattle

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