Deteriorating Ischemic Stroke in 4 Clinical Categories Classified by the Oxfordshire Community Stroke Project

Hideaki Tei, MD; Shinichiro Uchiyama, MD; Kuniko Ohara, MD; Michiko Kobayashi, MD; Yumiko Uchiyama, MD; Megumi Fukuzawa, MD

Background and Purpose — The aim of this study was to investigate the frequency, possible predictive factors, and prognosis of deteriorating ischemic stroke in 4 clinical categories according to the classification of the Oxfordshire Community Stroke Project (OCSP).

Methods — A total of 350 patients with first-ever ischemic stroke who presented within 24 hours of onset were enrolled. Based on the OCSP criteria, cerebral infarctions were divided into the following 4 clinical categories: total anterior circulation infarcts (TACI), partial anterior circulation infarcts (PACI), lacunar infarcts (LACI), and posterior circulation infarcts (POCI). Clinical deterioration was defined as a decrease of ≥1 points in the Canadian Neurological Scale (CNS) (in TACI, PACI, and LACI) or Rankin Scale (RS) (in POCI) during 7 days from the onset. In each clinical category, deteriorating (D) and nondeteriorating (ND) patients were compared in terms of their background characteristics, risk factors, vital signs, laboratory data, and cranial CT at the time of hospitalization. The acute-phase mortality and functional outcome were also compared.

Results — The subjects comprised 86 patients (24.6%) with TACI, 63 (18.0%) with PACI, 141 (40.3%) with LACI, and 60 (17.1%) with POCI. Overall, 90 patients (25.7%) deteriorated. The frequency was very high in TACI (41.9%), followed by LACI (26.2%) and PACI (21.7%), whereas it was very low in PACI (6.3%). There were some clinical variables that differed significantly between D and ND groups. In the patients with TACI, early abnormalities of the cranial CT and significant stenoses in corresponding arteries were more frequent in the D than the ND group. In those with LACI, the CNS and hematocrit were lower in the D than the ND group. In those with POCI, cerebral atrophy was more severe and significant stenoses in vertebrobasilar arteries were more frequent in the D than ND group. The mortality of the D groups of patients with TACI and POCI exceeded 35%, and the functional outcome was worse in the D group than in the ND group of patients with TACI, LACI, and POCI.

Conclusions — The frequency of deterioration in acute ischemic stroke significantly differed among the OCSP subgroups, and deterioration worsened the prognosis. There were some factors that could predict deterioration: early CT findings in TACI, large-artery atherosclerosis in TACI and POCI, and stroke severity in LACI. Further research to find sophisticated radiological and chemical markers appears to be needed. (Stroke. 2000;31:2049-2054.)

Key Words: cerebral infarction ■ stroke classification ■ stroke outcome

Neurological progression or deterioration during the first hours to days of cerebral infarction is common and produces serious clinical problems. The frequency of deterioration varies, ranging from 12% up to 42% among several reports, and the underlying mechanism has yet to be unanimously defined.

Diagnostic criteria and the time from onset of symptoms to the first evaluation are the major factors of the variation of the frequency of worsening. Although most studies have enrolled all patients with various degrees of severity into a nonstratified group and analyzed them with respect to deterioration or progression, different subgroups in symptoms and severity apparently exist at onset in patients with cerebral infarction. It has been suggested that the mechanism of worsening and its outcome differ between subgroups with different symptoms and severity.

In 1991, the Oxfordshire Community Stroke Project (OCSP) proposed 4 easily defined subgroups of cerebral infarction. These definitions are based solely on presenting symptoms and signs and have been estimated as easy to apply, having good interobserver reliability, ability to predict the prognosis, and good correspondence to the underlying pattern of vascular origin and cranial CT. We have recently reported the frequency, possible predictive factors, and prognosis of clinical progression in 4 clinical subgroups according to the OCSP in 250 patients with acute ischemic stroke. It is available at http://www.strokeaha.org

Received March 6, 2000; final revision received May 23, 2000; accepted May 30, 2000.

From the Department of Neurology, Toda Central General Hospital, Saitama, Japan (H.T., M.F.); Department of Neurology, Neurological Institute, Tokyo Women’s Medical University, Tokyo, Japan (S.U., K.O., Y.U.); and Department of Neurology, Teikyo University Hospital, Tokyo, Japan (M.K.).

Correspondence to Hideaki Tei, Department of Neurology, Toda Central General Hospital, 1-19-3 Hon-cho, Toda City, Saitama 3350023, Japan.

© 2000 American Heart Association, Inc.

Stroke is available at http://www.strokeaha.org
stroke. In the present study, we added 100 patients and analyzed those aspects in deteriorating ischemic stroke.

Subjects and Methods

We investigated 350 patients with first-ever acute ischemic stroke within 24 hours of their symptoms, which lasted until entry, and who were admitted to the Department of Neurology, Toda Central General Hospital, from May 1994 to August 1999. There were 206 men and 144 women, aged 32 to 92 years (average 67 years). These patients were prospectively studied. All the patients underwent a cranial CT at the time of entry to rule out cerebral hemorrhage. The entry time was defined as the time when the first CT was performed. According to the definition of OCSP, patients were classified into the following 4 clinical subgroups: total anterior circulation infarcts (TACI), partial anterior circulation infarcts (PACI), lacunar infarcts (LACI), and posterior circulation infarcts (POCI) by 1 neurologist (H.T.). Patients whose symptoms were hard to classify into any of the subgroups (uncertain cases) were excluded (there were 20 such patients during the study period). Each patient was examined daily by the same neurologist during the first 7 days, and the clinical deterioration was defined as a decrease of ≥1 point in the Canadian Neurological Scale (CNS) in patients with TACI, PACI, and LACI, or a worsening of ≥1 point on the Rankin Scale (RS) in patients with POCI during the 7 days compared with the scores at entry. We applied the CNS, which has been used most frequently in the assessment of deteriorating stroke to patients with TACI, PACI, and LACI. Many symptoms such as sensory deficit or ataxia are systematically neglected in most established neurological scales, and these domains affect most prominently cases of posterior circulation syndrome. We considered that the RS, which is an assessment scale of disability, is more suitable for evaluating the deterioration in patients with POCI. We followed up each patient until 2 months later or hospital discharge. Patients who had recurrent cerebral infarction in another vascular territory during observation period were excluded. Standard blood and coagulation tests were performed in all patients. Patients underwent cardiac and large-artery investigations as follows: 12-lead ECG in all patients (100%), transthoracic echocardiography in 340 patients (97.1%), 24-hour Holter ECG in 108 (30.9%), 3-D MR angiography (phase contrast, extracranial, and intracranial) in 279 (79.7%), conventional angiography in 3 (0.9%), and carotid ultrasonography (B-mode) together with 3-D CT angiography (intracranial) in 31 patients (8.7%).

In each clinical subgroup, deteriorating (D) and nondeteriorating (ND) patients were compared in terms of the following variables: background characteristics (age, gender, time from onset, CNS or RS at entry, antithrombotic therapy before onset); vital signs at entry (systolic blood pressure, diastolic blood pressure, body temperature); risk factors (hypertension [past use of antihypertensive agents or blood pressure >140/90 mm Hg at least twice before onset], diabetes mellitus [use of insulin or oral hypoglycemic agents, fasting blood glucose ≥140 mg/dL, or random blood glucose ≥200 mg/dL], current cigarette smoking, transient ischemic attack); laboratory data (C-reactive protein, blood glucose, glycosylated hemoglobin, hematocrit, fibrinogen, total cholesterol, triglyceride, high-density lipoprotein; cranial CT at entry [early abnormality [early infarction, early parenchymatous signs], leukoaraisoage score [according to the method of van Swieten et al.], atrial arrhythmia [mean of the bifrontal, bicaudate, and biparietal indices], silent infarctions [patchy, low-density areas that are sharply demarcated from the surrounding tissue, irrelevant to the current symptoms]; cardiac evaluation (≥1mm depression of ST segment on ECG, potential cardiac sources of embolism); large-artery disease (≥50% stenosis or occlusion of the corresponding artery); and prognosis (acute-phase mortality [within 1 month], RS at discharge or 2 months from the onset [patients who died were excluded]).

The only difference between D and ND groups was the CNS score at entry in LACI, which was more severe in D group. No other differences were detected between D and ND groups of TACI, LACI, and POCI in the background characteristics or risk factors.

Table 2 describes background characteristics and risk factors in each D and ND group of the 4 clinical categories. The only difference between D and ND groups was the CNS score at entry in LACI, which was more severe in D group. No other differences were detected between D and ND groups of TACI, LACI, and POCI in the background characteristics or risk factors.

Table 3 shows the comparisons of laboratory data, cranial CT, cardiac, and large-vessel evaluation in the D and ND groups of each subclassification. Among TACI patients, early abnormalities of the cranial CT and significant stenoses on corresponding arteries were more frequent in the D group than in the ND group. In the LACI patients, a difference was observed only in hematocrit, which was lower in the D group than in the ND group. In POCI patients, cerebral atrophy was more severe and significant stenoses in vertebrobasilar arteries were more frequent in the D group than in the ND group. Other variables were not different among the D and ND groups of patients with TACI, LACI, and POCI.
Table 4 shows the prognosis in D and ND groups of the 4 clinical categories. The mortality of the D group of patients with TACI and POCI exceeded 35%, and the functional outcome was worse in the D group than in the ND group of patients with TACI, LACI, and POCI.

### Discussion

The frequency of deterioration in acute ischemic stroke differs among several reports, ranging from 12% up to 42%.1 The main factor for this difference appears to be the time from the onset of symptoms to the first evaluation. Worsening of the neurological deficits are probably more frequently detected when the patients are assessed earlier.2 Recent studies that used 24 hours from onset as the inclusion criterion reported that the worsening rate was from 27.0% to 33.6%,6,21–24 values that are comparable with our results. Another factor might be the diagnostic criteria of deterioration. Although most studies have applied established neuro-

### TABLE 2. Background Characteristics and Risk Factors in D and ND Groups, by OCSP Category

<table>
<thead>
<tr>
<th>TACI</th>
<th>LACI</th>
<th>POCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>D (n=36)</td>
<td>ND (n=50)</td>
<td>PACI (n=63)</td>
</tr>
<tr>
<td>Age</td>
<td>72.7 (13.4)</td>
<td>71.3 (9.8)</td>
</tr>
<tr>
<td>Time from onset, h</td>
<td>6.4 (6.8)</td>
<td>3.9 (3.9)</td>
</tr>
<tr>
<td>CNS or RS at entry</td>
<td>5.5 (5.3)</td>
<td>4.8 (1.5)</td>
</tr>
<tr>
<td>Prethrombotic therapy, %</td>
<td>11.1</td>
<td>18.0</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>167.7 (39.3)</td>
<td>158.4 (27.4)</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>91.1 (17.8)</td>
<td>88.5 (17.4)</td>
</tr>
<tr>
<td>Body temperature, °C</td>
<td>36.0 (0.9)</td>
<td>36.3 (0.7)</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>61.1</td>
<td>48.0</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>19.4</td>
<td>10.0</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>33.3</td>
<td>32.0</td>
</tr>
<tr>
<td>Transient ischemic attack, %</td>
<td>31.6</td>
<td>30.0</td>
</tr>
</tbody>
</table>

Values in parentheses are SD.

*P<0.05; †P<0.01.

### TABLE 3. Comparisons of Laboratory Data, Cranial CT, Cardiac, and Large-Vessel Evaluation in D and ND Groups, by OCSP Category

<table>
<thead>
<tr>
<th>TACI</th>
<th>LACI</th>
<th>POCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>D (n=36)</td>
<td>ND (n=50)</td>
<td>PACI (n=63)</td>
</tr>
<tr>
<td>C-reactive protein, mg/dL</td>
<td>1.3 (2.1)</td>
<td>0.7 (1.3)</td>
</tr>
<tr>
<td>Blood glucose, mg/dL</td>
<td>163.9 (79.0)</td>
<td>136.0 (38.0)</td>
</tr>
<tr>
<td>HbA1c, %</td>
<td>5.9 (1.5)</td>
<td>5.5 (1.0)</td>
</tr>
<tr>
<td>Hematocrit, %</td>
<td>39.9 (4.7)</td>
<td>40.3 (4.5)</td>
</tr>
<tr>
<td>Fibrinogen, mg/dL</td>
<td>388.6 (124.9)</td>
<td>346.1 (99.4)</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>180.4 (45.0)</td>
<td>189.3 (40.4)</td>
</tr>
<tr>
<td>Triglyceride, mg/dL</td>
<td>109.9 (60.1)</td>
<td>97.4 (50.4)</td>
</tr>
<tr>
<td>HDL, mg/dL</td>
<td>52.6 (16.5)</td>
<td>51.3 (13.0)</td>
</tr>
<tr>
<td>ST depression on ECG, %</td>
<td>30.6</td>
<td>30.0</td>
</tr>
<tr>
<td>Cardioembolic source, %</td>
<td>50.0</td>
<td>66.0</td>
</tr>
<tr>
<td>Cranial CT, %</td>
<td>86.1†</td>
<td>18.4</td>
</tr>
<tr>
<td>Leukoaraiosis</td>
<td>1.2 (1.1)</td>
<td>1.3 (1.1)</td>
</tr>
<tr>
<td>Atrophy</td>
<td>0.34 (0.03)</td>
<td>0.33 (0.03)</td>
</tr>
<tr>
<td>Silent infarction</td>
<td>27.8</td>
<td>26.0</td>
</tr>
<tr>
<td>Significant stenosis on corresponding artery, %</td>
<td>68.4*</td>
<td>34.9</td>
</tr>
</tbody>
</table>

Values in parentheses are SD. HbA1c indicates glycosylated hemoglobin; HDL, high-density lipoprotein.

*P<0.05; †P<0.01.
TABLE 4. Prognosis for D and ND Groups, by OCSP Category

<table>
<thead>
<tr>
<th></th>
<th>TACI</th>
<th></th>
<th>PACI</th>
<th></th>
<th>LACI</th>
<th></th>
<th>POCI</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>D</td>
<td>ND</td>
<td></td>
<td>D</td>
<td>ND</td>
<td></td>
<td>D</td>
<td>ND</td>
</tr>
<tr>
<td>(n=36)</td>
<td>(n=50)</td>
<td></td>
<td></td>
<td>(n=63)</td>
<td></td>
<td></td>
<td>(n=13)</td>
<td>(n=47)</td>
</tr>
<tr>
<td>Acute phase mortality, %</td>
<td>47.2*</td>
<td>0.0</td>
<td>1.6</td>
<td>2.7</td>
<td>0.0</td>
<td>38.5*</td>
<td>0.0</td>
<td></td>
</tr>
<tr>
<td>Rankin Scale score at 2 months</td>
<td>4.7 (1.0)*</td>
<td>3.9 (1.2)</td>
<td>1.9 (0.9)</td>
<td>2.7 (1.1)†</td>
<td>1.8 (0.9)</td>
<td>2.8 (1.0)*</td>
<td>1.7 (1.0)</td>
<td></td>
</tr>
</tbody>
</table>

Values in parentheses are SD.
*P<0.01; †P < 0.05.

logical scales such as the CNS, the National Institutes of Health Stroke Scale (NIHSS), or the Scandinavian Neurological Scale; some studies did not use these scales.1,14 We applied the CNS and RS because of the reasons detailed in the Subjects and Methods section.

Except for a few studies, any patients with various degrees of severity have been enrolled into a nonstratified group and analyzed in the studies of deteriorating or progressing stroke.6 We sought to analyze the deteriorating ischemic stroke by subdividing patients into 4 groups according to the criteria of the OCSP. Yamamoto et al14 analyzed the clinical worsening in cerebral infarction resulting from different causes (ie, cardioembolic, large-artery atherosclerosis, small-artery disease, or other causes), whereas the precise diagnosis of these subtypes is very difficult in the early phase.11,18 Therefore, we analyzed deteriorating ischemic stroke by the symptomatic subgroups of the OCSP criteria.

The frequency of deterioration was very high in TACI, followed by LACI, and then PACI, whereas it was very low in PACI. We previously reported11 that the mechanism of infarction in PACI was either cardioembolic or large-artery atherosclerosis in equal numbers, whereas in TACI >60% of cases were caused by cardioembolism and only 20% caused by large-artery atherosclerosis. It has been suggested that the thrombus from the heart is generally larger than that from the large vessel.25,26 The low frequency of deterioration in PACI could be explained by relatively small emboli from the heart or from the large artery. Favorable short-term prognosis in PACI patients was described by the first report of the OCSP,8 and Pinto at al27 also reported a low frequency of worsening in PACI (4%). However, Dahl et al28 reported that, among the 4 OCSP groups, the progression was most frequent in the PACI group. Further studies are warranted. It has been suggested that the early progression and final outcome were dependent on the initial stroke severity.6,13,29 DeGraba et al6 recently reported that only 14.8% of patients with the NIHSS score of ≤7 experienced progression, whereas 65.9% of patients with an NIHSS score of >7 experienced progression. According to the NIHSS, the majority of patients with TACI would be scored >7 and the majority of those with PACI would be scored ≤7. The high frequency of worsening in TACI and the low frequency of worsening in PACI in our results were consistent with those reported by DeGraba et al.6

The fact that the CNS at entry was significantly lower in the D than in the ND group of patients with LACI again implies the importance of initial stroke severity as a determinant of the worsening in acute ischemic stroke. According to the NIHSS, LACI patients with mild severity would be scored ≤7, whereas those with dense severity would be scored >7. The intermediate frequency of worsening of LACI between TACI and PACI in our study is consistent with the suggestion of DeGraba et al.6

With respect to the comparison of the D and ND groups in each category, early abnormalities of the cranial CT were more frequent in the D group than in the ND group of patients with TACI. It has been reported that early abnormalities on CT, such as hypodensity, hyperdense middle cerebral artery sign, or mass effect are important predictors of deterioration.1,3,5,29–31 Given that it was the case only in TACI group, it could be speculated that edema (cytotoxic and vasogenic) is the important mechanism of clinical deterioration in TACI.5 Another difference between the D and ND groups in TACI patients was that the significant stenosis of the large artery was more frequent in the former group. Thrombus propagation or insufficient collateral blood supply might be another important mechanism in the worsening of TACI.4,5 However, because not all the patients in our study could undergo large-artery evaluation, this speculation must be reevaluated in future studies.

Except for the difference in the CNS score at entry, hematocrit was significantly lower in the D than the ND group of LACI patients. This was an unexpected result. There has been no such report previously in the study of deteriorating stroke. Because mean hematocrit was 40.0 ± 4.3 in the D group and 41.8 ± 4.0 in the ND group, which were both within normal range, it is hard to find the significance of this difference in LACI patients. There were no other variables that significantly differed between the D and ND groups of patients with LACI. The mechanism of worsening in LACI patients is unclear. Nakamura et al24 recently analyzed progressive motor deficits in 92 patients with lacunar infarction within 24 hours of onset in the internal capsule or the corona radiata. They found that the frequency of progression was 27%, similar to our finding, and that the blood glucose was higher, the motor deficits at entry were more severe, and the lesion volume on CT was larger in the progressing group than in stable group; some of these results are consistent but others are inconsistent with our results. Because the frequency of significant stenosis of large artery did not differ between the D and ND groups, the macrovascular mechanism in deterioration in LACI is unlikely, although a microvascular mechanism4 or branch atheromatous disease52,33 may play an important role in the LACI patients.

In the patients with POCI, cerebral atrophy was more severe and significant stenosis in vertebrobasilar arteries was more frequent in the D than in the ND group. These results...
imply that unlike in LACI, macrovascular mechanisms play an important role in the clinical worsening in POCI patients. We speculate that cerebral atrophy caused by longstanding hypoperfusion due to large-artery atherosclerosis might underlie the worsening in POCI patients. It has been suggested that large-artery atherosclerosis of extracranial or intracranial vertebrobasilar arteries is more frequent in posterior circulation infarcts than previously thought.34–36

Other reported variables concerning the neurological progression, such as body temperature,23,37 fibrinogen,23 blood glucose,24,38,39 diabetes mellitus,22 blood pressure,4,22,39 transglutamate concentration increases in progressing stroke. In their improvement and deterioration of ischemic stroke. Recently analysis by transcranial Doppler ultrasonography can predict the ischemic stroke for future studies. There are some candidates for markers might be needed to predict deterioration in acute ND group in TACI, LACI, and POCI. More sophisticated but we did not perform such an analysis because we aimed to study the deteriorating ischemic stroke by stratifying patients into the 4 subgroups of the OCSP.

As expected, the prognosis was worse in the D group than the ND group in TACI, LACI, and POCI. More sophisticated markers might be needed to predict deterioration in acute ischemic stroke for future studies. There are some candidates for the predictable markers. Dávalos and Castillo and their coworkers21-41,42 have indicated that the blood and cerebrospinal fluid glutamate concentration increases in progressing stroke. In their neuroimaging recent study, Toni et al43 reported that flow analysis by transcranial Doppler ultrasonography can predict the improvement and deterioration of ischemic stroke. Recently developed diffusion-weighted and perfusion-weighted MRI44 and cerebral blood flow analysis with single-photon emission CT40 or xenon-enhanced CT46 will be useful in the study of deteriorating ischemic stroke as well.

In conclusion, the frequency of deterioration in acute ischemic stroke significantly differed among the OCSP subgroups, and it worsened the prognosis. Some factors could predict deterioration: early CT findings in TACI, large-artery atherosclerosis in TACI and POCI, and stroke severity in LACI. Future research to find more sophisticated markers appears to be needed.

Acknowledgments

We would like to thank Drs Hirohiko Murakami, Kenji Koshimizu, Masatomi Ikusaka, Yuko Shimizu, Mutsumi Iijima, Mika Ueda, Yuko Sakamoto, and Hiromi Suzuki for their clinical assistance.

References

Deteriorating Ischemic Stroke in 4 Clinical Categories Classified by the Oxfordshire Community Stroke Project
Hideaki Tei, Shinichiro Uchiyama, Kuniko Ohara, Michiko Kobayashi, Yumiko Uchiyama and Megumi Fukuzawa

Stroke. 2000;31:2049-2054
doi: 10.1161/01.STR.31.9.2049

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/31/9/2049

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/