Status Epilepticus After Stroke

Sibel K. Velioglu, MD; Mehmet Ozmenoglu, MD; Cavit Boz, MD; Zekeriya Alioglu, MD

Background and Purpose—The main objective of our study was to determine the risk and predictive factors of status epilepticus (SE) after stroke.

Methods—From 1988 to 2000, 1174 patients were admitted to the Department of Neurology at the Karadeniz Technical University Farabi Hospital with first-time strokes. Of these, 180 patients had poststroke first-time seizures (PFSs). We followed these 180 PFS patients for an average of 3.7 years or until death to determine the occurrence rate of SE. By comparing these data with those of PFS patients without SE, we investigated whether there were significant differences.

Results—A total of 17 of the 180 PFS patients (9%) had SE. There was no relationship between the occurrence of SE and stroke risk factors, stroke type (ischemic or hemorrhagic stroke), stroke topography and cause, cortical involvement, size of lesion, seizure type, or electroencephalographic findings. SE occurred more frequently among patients with a higher disability rating (Rankin scale >3; odds ratio, 4.36). Recurrent SE was identified in 5 of 17 patients with SE. In all 5 of these patients, the first episode of SE occurred within the first 7 days after stroke (early-onset SE). Statistical analysis demonstrated that early-onset SE was associated with a higher risk for SE recurrence (P=0.003) and a higher mortality rate (P=0.04).

Conclusions—SE was not associated with a higher mortality rate but with higher functional disability. We also found that early-onset SE (within the first 7 days after stroke) was associated with a higher risk for SE recurrence and a higher mortality rate than late-onset SE (after 7 days after stroke). (Stroke. 2001;32:1169-1172.)

Key Words: epilepsy ■ seizures ■ stroke outcome ■ stroke, acute

Status epilepticus (SE) is defined as a seizure or a series of repetitive seizures without recovery between episodes that lasts >30 minutes. The role of stroke as an etiologic factor for SE is accepted.1,2 Although the occurrence of epileptic seizures complicating acute stroke is well recognized, SE has received little attention.3–6 Few studies on epilepsy complicating acute stroke are available.2,7,8

Using a hospital-based stroke cohort, we studied a series of patients with poststroke first-time seizure (PFS) to find out which factors may be associated with SE.

Subjects and Methods

Included in this study were 1676 stroke patients without an accompanying diagnosis of brain tumor or arteriovenous malformation who were admitted consecutively to the Department of Neurology of Karadeniz Technical University Farabi Hospital (an acute-care, 492-bed hospital in Trabzon, Turkey) between February 1988 and January 2000. A retrospective chart review was performed. We excluded patients with a history of seizure, subarachnoid hemorrhage, head injury, hypertensive encephalopathy, and cerebrovenous thrombosis. We included only patients with first-time ischemic strokes and primary intracerebral hemorrhages. After these restrictions, a study population of 1174 patients with first-time stroke was defined. All patients were admitted to the hospital within the first 3 days of onset of symptoms. There were 161 patients with transient ischemic attack who had no seizures. One hundred eighty patients had a PFS; 17 of these patients had SE.

All patients with PFS had a cerebral computed tomography (CT) scan and electroencephalography (EEG). The patients with lesions that could not be identified from CT as cortical or subcortical also had magnetic resonance imaging (MRI). In all patients, plasma urea, creatinine, electrolyte, and plasma glucose levels were measured on admission. Overall, 72% of patients were studied by MRI. Other investigations included arterial digital subtraction angiography in 24%, duplex ultrasound of the carotid arteries in 42%, and echocardiography in 82%. The degree of functional disability at the end of the acute phase was graded by a modified Rankin scale.9 Seizures were diagnosed and classified according to the definitions of the International League Against Epilepsy.10,11 SE was defined as a seizure or a series of continuing seizures lasting >30 minutes without full recovery between seizures.12 Unprovoked seizures refer to seizures that occurred without identifiable acute precipitants. “Early” referred to seizures and SE occurring within 1 week after stroke that were considered to be provoked by the stroke. Unprovoked seizures and SE developing beyond 1 week after stroke were called “late.” The diagnosis was based on direct observation of seizures by the medical staff at the time of hospitalization or on the history of the neurologist in charge of the patient or was determined according to reliable descriptions obtained from ambulance personnel when seizures occurred during transportation or from the patients or close family members when seizures occurred at home. EEG was performed 24 to 48 hours after the seizures in all PFS patients. EEGs were considered abnormal when focal, lateralized, or generalized slowing or epileptiform discharges were present. All hospital and outpatient records since the stroke were reviewed. Survivors were contacted by telephone or in person in 1998 and again in 2000. Follow-up data were evaluated for a mean of 3.7 years.
Results

Among 1174 hospitalized first-time stroke patients (mean age, 59.7 years; range, 17 to 103 years; 681 men, 493 women), 180 (15%) experienced a PFS. Of the 180 PFS patients (mean age, 62.2 years; range, 41 to 85 years; 88 men, 92 women), 17 (%9) developed SE. Of the 180 PFS patients, 121 (67%) had ischemic stroke and 59 (33%) had an intracranial hemorrhage. Approximately one half of the patients with SE (53%; 9 of 17) had SE manifested by seizures classified as generalized in onset, and the remainder (47%; 8 of 17) had seizures that were partial in onset. No difference was noted between PFS patients with (group 1, n=17) and without (group 2, n=163) SE for sex, age, stroke risk factors, seizure types, and EEG findings (Table 1). The presence of SE was not associated with stroke type, cause, topography, cortical involvement, or size of lesion (Table 1). However, SE occurred more frequently among the most disabled patients (Rankin scale >3; P=0.002; Table 1).

In 7 of 17 patients with SE, SE occurred within the first 7 days after stroke (early onset; Table 2). Of these 7 patients, SE occurred as the first epileptic symptom in 6 patients (In 2 of these 6 patients, stroke began with SE); in 1 patient, ≥1 seizure occurred before SE. In 10 patients, SE occurred >7 days after stroke (late onset). In 3 of these 10 patients, SE occurred as the first epileptic symptom. Stroke risk factors, stroke type, and functional disability of SE patients were not significantly different in patients with early- or late-onset SE (Table 2).

Recurrent SE occurred in 5 of 17 patients with SE (Table 3). In 5 of 7 patients with early-onset SE, recurrent SE occurred. However, none of the 10 patients with late-onset SE experienced recurrent SE. Stroke type and functional disability did not have a significant role in the recurrence of SE. Statistical analyses demonstrated that early-onset SE was not associated with stroke type, cause, topography, cortical involvement, or size of lesion.
associated with a higher risk for additional SE occurrence ($P=0.003$; Table 3).

Nine of the 17 patients with SE and 81 of the 163 patients without SE died, with an overall 50% mortality in patients with PFS (Table 4). Two patients in group 1 and 24 in group 2 died within the first month after the stroke (Table 4). In group 1, death was a direct consequence of SE in 2 patients (who died during the first month after stroke), was attributed to cardiovascular disease in 5 patients, and was due to unrelated causes in 2 patients. In group 2, death was related to seizures in 10 patients, 38 deaths were caused by cardiovascular disease, and 33 deaths were from unrelated causes. There was no significant difference in mortality rate between those patients with and those without SE (Table 4). However, the mortality rate of patients with early-onset SE was higher than in patients with late-onset SE (Table 4).

After multivariate analysis (Table 5), only poor functional disability (OR=4.36) appeared to be an independent clinical factor for developing SE (goodness-of-fit $\chi^2=11.502; df=6; P=0.0741$), and only age (OR=1.06) appeared to be an independent factor for mortality (goodness-of-fit $\chi^2=20.419; df=6; P=0.0047$).

### Discussion

Changes in cerebral blood flow, hypoxia, involvement of the cerebral cortex by hemorrhage or infarct, and development of epileptogenic changes in cortical neurons, their connections, or their environment have been proposed as potential mechanisms underlying seizures in patients with stroke.14–16 In this retrospective series of 1174 patients with stroke, PFS occurred in 15%. Of the patients with PFS, 9% had SE. Many authors have examined seizure disorders after stroke, but few have noted the interaction between SE and stroke.2,7 The incidence of SE after stroke either is low or is not cited at all in some reports.1–5,17–20 Three studies reported the rate of SE as 19%, 17%, and 14%,7,21,22 We found that SE occurred in 9% of all patients admitted for a PFS to our Neurology Department.

In this study, there was no relationship between the occurrence of SE and sex, age, stroke risk factors, stroke type (ischemic or hemorrhagic), stroke topography and cause, cortical involvement, or size of lesion in patients with PFS. Comparisons across studies are difficult because many authors have examined the possible etiologies of SE in large series, but only a few have noted the interaction between etiologic factors and SE in poststroke SE patients.7 Rumbach et al,7 in a study of 159 patients with PFS, also found no relationship between SE occurrence and risk factors and stroke type. In our series, neither seizure types, such as generalized or partial onset, nor EEG findings of SE patients were significantly different from those of patients without SE.

Consistent with a prior report, we found that SE was associated with poor functional disability score. Patients with SE have poorer functional disability than those without SE.

### Table 2. Risk Factors, Stroke Type, and Functional Disability in SE Patients With Early- and Late-Onset SE

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Early-Onset SE (n=7)</th>
<th>Late-Onset SE (n=10)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean), y</td>
<td>62.6±12</td>
<td>55.3±8.1</td>
<td>0.1427</td>
</tr>
<tr>
<td>Sex, M/F (n=12)</td>
<td>3/4</td>
<td>7/3</td>
<td>0.3499</td>
</tr>
<tr>
<td>Hypertension, n (n=5)</td>
<td>3</td>
<td>3</td>
<td>0.6436</td>
</tr>
<tr>
<td>Diabetes, n (n=5)</td>
<td>1</td>
<td>3</td>
<td>0.6029</td>
</tr>
<tr>
<td>Smoking, n (n=5)</td>
<td>4</td>
<td>3</td>
<td>0.3499</td>
</tr>
<tr>
<td>Hypercholesterolemia, n</td>
<td>...</td>
<td>2</td>
<td>0.4852</td>
</tr>
<tr>
<td>Coronary heart disease, n</td>
<td>2</td>
<td>2</td>
<td>1.000</td>
</tr>
<tr>
<td>Atrial fibrillation, n</td>
<td>3</td>
<td>1</td>
<td>0.250</td>
</tr>
<tr>
<td>Stroke type, n</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic stroke (n=12)</td>
<td>5</td>
<td>7</td>
<td>1.000</td>
</tr>
<tr>
<td>Hematoma (n=5)</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Functional disability (Rankin scale)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\leq3$ (n=5)</td>
<td>2</td>
<td>3</td>
<td>0.34</td>
</tr>
<tr>
<td>$&gt;3$ (n=12)</td>
<td>5</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

### Table 3. Stroke Type, Functional Disability, and Time of Onset of SE With Regard to SE Recurrence

<table>
<thead>
<tr>
<th>Stroke type</th>
<th>Noncurrent (n=12)</th>
<th>Recurrent (n=50)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic stroke (n=12)</td>
<td>7</td>
<td>5</td>
<td>0.2445</td>
</tr>
<tr>
<td>Hematoma (n=5)</td>
<td>5</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Functional disability (Rankin scale)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\leq3$ (n=5)</td>
<td>5</td>
<td>0</td>
<td>0.2445</td>
</tr>
<tr>
<td>$&gt;3$ (n=12)</td>
<td>7</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Time of onset of SE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early (n=7)</td>
<td>2</td>
<td>5</td>
<td>0.00339</td>
</tr>
<tr>
<td>Late (n=10)</td>
<td>10</td>
<td>0</td>
<td></td>
</tr>
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</table>
We found that in 59% of patients with SE (10 of 17), SE occurred 7 days after stroke onset; 5 of the 17 SE patients had recurrent SE. In all patients with recurrent SE, the first episode of SE occurred within the first 7 days after stroke (early-onset SE). In the univariate analysis, we showed that recurrent SE is significantly more likely in patients with early-onset SE.

Our study revealed no significant difference in mortality rate and cause of death among PFS patients with and without SE; a similar finding was reported by Rumbach et al. In this study, death was directly related to SE in 2 of 17 patients with SE (12%; the remaining 7 deaths were related to other causes), which was similar to findings by Rumbach et al (16%). A mortality rate of 23.3% among patients with SE secondary to all causes was reported in 1 study; this rate was even higher among patients with cerebrovascular disease.23 Our findings also have shown that early onset of SE after stroke (within 7 days after stroke) is associated with a higher mortality rate than late-onset SE in univariate analysis. Arboix et al showed that seizures at the onset of a first-ever stroke were an independent prognostic factor for in-hospital mortality and that cortical involvement and agitated acute confusional state at the onset of stroke were independent predictive factors of early seizures in first-ever stroke patients. This study reviews the incidence of SE in the stroke population and focuses on patients without a history of epilepsy or seizures who present with SE or seizures for the first time after an acute stroke. The retrospective design of this study is an important limitation.

Data from this group of patients permit the following statements. First, the incidence of SE in patients with PFS was 9%. Second, on the basis of results of the multivariate analysis, there was no relationship between the SE occurrence and stroke risk factors, stroke type (infarction or hemorrhage), stroke topography and cause, cortical involvement, size of lesion, seizure type, or EEG findings, and the mortality rate for PFS patients with SE was not significantly different from that of patients without SE. Third, on the basis of results of the multivariate analysis, the only identified predictor of SE was poor functional disability, and we also concluded that age at a first-ever stroke is an independent prognostic factor for mortality. Finally, early-onset SE was associated with a higher risk for SE recurrence and with a higher mortality rate than late-onset SE in the univariate analysis.

Acknowledgment

We thank Gamze Çan, MD, Department of Public Health, Karadeniz Technical University, Medical Faculty, Trabzon, Turkey, for her assistance with the analysis of the data.

References

14. Arboix A, Garcia-Eroles L, Juan B, Massons JB, Oliveres M, Comes E. Relevance of early-onset SE in the univariate analysis. Arboix et al showed that seizures at the onset of a first-ever stroke were an independent prognostic factor for in-hospital mortality and that cortical involvement and agitated acute confusional state at the onset of stroke were independent predictive factors of early seizures in first-ever stroke patients. This study reviews the incidence of SE in the stroke population and focuses on patients without a history of epilepsy or seizures who present with SE or seizures for the first time after an acute stroke. The retrospective design of this study is an important limitation.

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