Seizures are one of the most common complications of stroke.\textsuperscript{1,2} Overall, 5\%–15\% of stroke patients will experience a seizure within 2 years of stroke. The reported risk factors for and incidence of seizures after stroke vary widely, likely secondary to differences in study design, study populations, and use of antiepileptic drugs (AEDs). In previous studies, the main risk factors for poststroke seizures include stroke subtype, location, and severity. Poststroke seizure rates are highest in those with intraparenchymal hemorrhage and large supratentorial ischemic strokes, and lowest after transient ischemic attacks, lacunar infarcts, and brainstem strokes.\textsuperscript{1,2} Although frequently encountered in clinical practice, there are few evidence-based guidelines for therapy of poststroke seizures.

Poststroke seizures are classified as “early” or “late” according to their temporal proximity to the stroke.\textsuperscript{3} Early seizures, also termed acute symptomatic seizures, occur within the first week following stroke. These early seizures are likely provoked by the metabolic and physiologic derangements associated with acute infarction or hemorrhage. Late seizures begin after a latent period of variable duration, usually weeks to years. Late seizures are thought to result from epileptogenesis, changes in neurons and networks that result in permanent hyperexcitability. Prior studies do not elucidate whether early seizures are merely epiphenomena of acute brain injury, and whether they may have a negative effect on long-term neurologic outcome or increase the risk for development of subsequent late seizures and epilepsy. Two studies in this issue of \textit{Neurology}\textsuperscript{4,5} provide important new information about incidence and risk factors for early poststroke seizures, and the consequences of early seizures on outcome.\textsuperscript{4,5}

Beghi et al.\textsuperscript{4} confirmed the major independent risk factors for early poststroke seizures in a large prospective cohort of patients with first stroke. Patients with both primary intracerebral hemorrhage (ICH) and cerebral infarct were included. The study has many strengths, including large sample size, inclusion of only incident strokes, clear definition of time period for early seizures (first 7 days), excellent stroke classification by etiology, stroke subtype (neuroimaging in all patients), and stroke severity (NIH Stroke Scale and modified Rankin scale), and complete follow-up. Acute symptomatic seizures occurred within 1 week of stroke in 45 of 714 patients (6.3\%) with first seizure, a higher incidence of early poststroke seizures than reported in prior studies.\textsuperscript{1,6–8} The majority of early seizures (73\%) occurred within the first 24 hours after stroke onset, when acute physiologic derangements are most severe. Most of the seizures were focal-onset (68.1\%), and 3 patients had prolonged seizures meeting the definition for status epilepticus.

Early seizures were most common in patients with ICH (16.2\%) and cerebral infarct with hemorrhagic transformation (12.5\%), compared to cerebral infarct without hemorrhage (4.2\%). An increased risk for acute symptomatic seizures with brain hemorrhage is also seen after traumatic brain injury,\textsuperscript{9} suggesting that blood extravasation plays an important role in the genesis of early seizures after brain injury. As expected, cortical involvement was associated with a higher risk for early seizures (9.8\%). In multivariate analysis, only stroke type (ICH and hemorrhagic infarction) and cortical lesion were independent predictors of early seizures.

The second study by De Herdt et al.\textsuperscript{5} includes 522 patients with spontaneous ICH. Again, the authors utilized a strong study design with excellent assessment of risk factors and nearly complete follow-up at 6 months. The overall incidence of early seizures (14\%) is slightly higher than that reported in other ICH cohorts, likely because of the prospective design and careful seizure ascertainment. In multivariate analysis, the study confirms the previously described association between cortical involvement and early seizure occurrence. The incidence of early seizures was 22\% with lobar ICH compared to 8\% in deep ICH. Approximately 50\% of the seizures occurred at the time of stroke onset. Cortical involve-
ment, more severe stroke, previous ICH, and younger age were associated with a higher incidence of onset seizures. Nine patients had recurrent seizures, associated with prior ICH, multiple ICH, lobar location, and one or more old vascular lesions.

The 2 studies report different effects of early seizures on outcome, possibly because of variable lengths of follow-up. Beghi et al. found 30-day mortality to be much higher among patients with early seizures (12.5%) than those without early seizures (6.3%, relative risk 2.6). De Herdt et al. found that early seizures were not independent predictors for mortality at 7 days and 6 months, and did not influence functional outcome at 6 months. These differences might be explained by dissimilarities in the included stroke subtypes, particularly inclusion of patients with cerebral infarct in the Beghi et al. study.

A limitation of both studies is that only clinical seizures were analyzed; EEG was performed only when indicated by the treating physician. Since loss of consciousness without motor movements and brief episodes of mental confusion were not included as possible seizures, lack of EEG recording may have resulted in an underestimate of seizure frequency. Studies utilizing continuous EEG monitoring in the intensive care unit have reported rates of electrographic seizures ranging from 2% to 11% after ischemic stroke and 13%–28% after ICH.10,11

In clinical practice, neurologists are commonly faced with the decision of whether to give prophylactic AEDs after acute stroke, and which AED to start after a first early poststroke seizure. Such decisions must balance the risk for early seizures with the known adverse effects of AEDs such as phenytoin on outcome after stroke.12 No conclusions can be drawn about the efficacy of AEDs to prevent or treat early seizures from these observational studies. In the Beghi et al. cohort, only 4 patients received prophylactic AEDs, and none of these had early seizures. Twenty-three patients were treated with AEDs after a first early seizure, but early seizure recurrence rates in this group are not reported. In the De Herdt et al. cohort, no patients received prophylactic AEDs. Sixty-two patients were treated with AEDs after a single seizure, but the recurrence rate in this group compared to those not receiving AEDs is not reported. Only 9 patients had recurrent seizures overall. Data on treatment efficacy of electrographic-only acute symptomatic seizures are similarly elusive.

Together, these studies demonstrate that acute symptomatic seizures are very common after stroke, particularly in high-risk subgroups. Why, then, have no studies addressed prophylaxis or treatment of these early seizures? Unfortunately, these studies also highlight why obtaining good data about the efficacy of AEDs and long-term impact of early seizures on outcome is so difficult. Beghi et al. enrolled 714 patients in 31 Italian centers, but only 45 patients had early seizures, many occurring in the first 24 hours, before patients were enrolled in the study. De Herdt et al. needed to recruit 562 patients with ICH over a 5-year period to find 71 patients with early seizures. A large number of centers and long follow-up will be necessary to adequately power clinical trials of AED treatment, long-term outcome, and development of epilepsy. Enrolling only high-risk subgroups would lower the needed sample size, but will also make overall recruitment more difficult. In the absence of good evidence, clinicians must weigh the pros and cons of AED treatment in each individual patient, starting AEDs only in those in the highest risk subgroups (e.g., lobar ICH) or those who have already experienced seizures.

Finally, neither of these studies examined the importance of early seizures in the development of late seizures and epilepsy. Prior studies have shown that early seizures are an independent risk factor for late unprovoked seizures.2,13,14 Hopefully, these well-designed cohorts will be followed over longer time periods to assess the occurrence of late poststroke seizures as well.

DISCLOSURE
Dr. Herman received editorial fees from Current Treatment Options, Ltd.; serves on the editorial board of Journal of Clinical Neurophysiology; performs EEG and continuous EEG monitoring in her clinical practice (35% effort); and receives research support from Lundbeck Inc., UCB, Fidelity Biosciences Research Initiative, and the American Epilepsy Society.

REFERENCES


