



Seizures and Strokes for Certain Folks

Incidence and Predictors of Acute Symptomatic Seizures After Stroke.

Beghi E, D'Alessandro R, Beretta S, Consoli D, Crespi V, Delaj L, Gandolfo C, Greco G, La Neve A, Manfredi M, Mattana F, Musolino R, Provinciali L, Santangelo M, Specchio LM, Zaccara G, Epistroke Group. *Neurology* 2011;77(20):1785–1793.

OBJECTIVE: To assess incidence and predictors of acute symptomatic seizures in a prospective cohort of patients with first stroke. **METHODS:** Patients with first stroke hospitalized in 31 Italian centers were recruited. Relevant demographic data, disease characteristics, and risk factors were collected. Acute symptomatic seizures (≤ 7 days) were recorded and correlated to age, gender, family history of epilepsy, and vascular risk factors. **RESULTS:** A total of 714 patients (315 women, 399 men; age 27–97 years) were enrolled. A total of 609 (85.3%) had cerebral infarction (32 cerebral infarction with hemorrhagic transformation [CIHT]) and 105 (14.7%) primary intracerebral hemorrhage (PIH). A total of 141 (19.7%) had a large lesion (>3 cm) and 296 (41.5%) cortical involvement. Twelve patients reported family history of seizures. Forty-five patients (6.3%) presented acute symptomatic seizures, 24 with cerebral infarction (4.2%), 4 with CIHT (12.5%), and 17 (16.2%) with PIH. In multivariate analysis, compared to cerebral infarction, PIH carried the highest risk (odds ratio [OR] 7.2; 95% confidence interval [CI] 3.5–14.9) followed by CIHT (OR 2.7; 95% CI 0.8–9.6). Cortical involvement was a risk factor for PIH (OR 6.0; 95% CI 1.8–20.8) and for CI (OR 3.1; 95% CI 1.3–7.8). Hyperlipidemia (OR 0.2; 95% CI 0.03–0.8) was a protective factor for IPH.

CONCLUSION: The incidence of acute symptomatic seizures is the highest reported in patients with first stroke with prospective follow-up. Hemorrhagic stroke and cortical lesion were independent predictors of acute symptomatic seizures. Hyperlipidemia was a protective factor for hemorrhagic stroke.

Early Seizures in Intracerebral Hemorrhage: Incidence, Associated Factors, and Outcome

De Herdt V, Dumont F, Hénon H, Derambure P, Vonck K, Leys D, Cordonnier C. *Neurology* 2011;77(20):1794–1800.

OBJECTIVE: In patients with spontaneous intracerebral hemorrhage (ICH), the occurrence of early seizures (ES) may be a prognostic marker. Therefore, we aimed to identify incidence, associated factors, and influence on outcome of ES in patients with ICH. **METHODS:** Between November 2004 and March 2009, we prospectively recruited 562 consecutive adults with a spontaneous ICH (Prognosis of InTra-Cerebral Hemorrhage cohort). Patients with previous seizures ($n = 40$) were excluded. ES were defined as seizures occurring within 7 days of stroke onset, and their associated factors were identified with Cox regression. For a subgroup of onset seizures, we used logistic regression. Data influencing outcome (mortality at day 7 and month 6 and functional outcome at month 6) were studied using survival analyses. **RESULTS:** ES occurred in 71 (14%; 95% confidence interval [CI] 11–17) of 522 patients (274 male; median age 72 years, interquartile range 58–79 years). The only factor associated with ES was cortical involvement of ICH (odds ratio [OR] = 2.06; 95% CI 1.28–3.31). Regarding onset seizures ($n = 38$; 7%; 95% CI 5–10), associated factors were previous ICH (OR = 4.76; 95% CI 1.53–14.84), cortical involvement (OR = 2.21; 95% CI 1.11–4.43), younger age (OR = 0.97 per 1 year increase; 95% CI 0.95–0.99), and severity of the neurologic deficit at admission (OR = 1.03 per 1 point increase in the National Institutes of Health Stroke Scale score; 95% CI 1.01–1.06). ES did not influence vital or functional outcome. **CONCLUSIONS:** ES are a frequent complication in patients with spontaneous ICH; however, their occurrence does not influence outcome at 6 months.

Commentary

Vascular disease is recognized as a major risk factor for the subsequent development of seizures and epilepsy in the

elderly (1, 2). Seizures can occur following either ischemic or hemorrhagic stroke, although the risk of seizures is substantially higher in hemorrhagic stroke (3, 4). When seizures occur in the aftermath of stroke, they are broadly divided into early symptomatic seizures and late symptomatic seizures. Early symptomatic seizures typically occur within the first 7 days after stroke and presumably occur as a consequence of physiological disturbance caused by injury to the brain. Such



early seizures have been reported to portend an increased risk for future recurrent seizures and epilepsy (5, 6). Seizures that emerge as a late consequence of acute stroke are presumably the result of epileptogenic changes resulting from stroke-related brain injury. Factors that increase risk for post-stroke seizures include intracerebral hemorrhage, hemorrhagic conversion after ischemic infarction, cortical involvement, and stroke size (3, 4). However, the incidence and prognostic implications of early seizures have not been fully defined. Two recent studies additionally clarify these issues by taking a prospective look at the relationship between acute stroke and early seizures, focusing on their incidence, their predictors, and their prognostic potential (7, 8). Of note, both studies define early seizures as manifesting within the first 7 days after a stroke. Both studies prospectively follow large stroke populations within which stroke type, severity, and localization are well characterized and for which follow-up was consistently performed.

Beghi et al. (7) included both ischemic and hemorrhagic strokes in their analysis of 714 patients. They additionally subdivided patients with ischemic stroke to identify those who had hemorrhagic conversion, those who had cortical involvement, and those who had larger lesions (>3 cm). Early seizures occurred in 6.3% of patients. Approximately three quarters of these early seizures occurred within the first 24 hours. The incidence of early seizures was 16.2% for patients with intracerebral hemorrhage, 12.5% for patients with ischemic stroke and hemorrhagic conversion, and 4.2% in patients with uncomplicated ischemic stroke. Cortical involvement was associated with a higher risk of early seizures (9.8%) than was subcortical involvement (3.8%). Intracerebral hemorrhage and cortical involvement were both predictors of early seizures. The mortality rate at 30 days was twice as high in patient who had experienced a seizure (12.5%) than in those who did not experience a seizure (6.3%).

De Herdt et al.⁸ limited their analysis to 562 patients who presented with spontaneous intracerebral hemorrhage. Early seizures occurred in 14% of patients, and nearly half of these occurred at stroke onset. Cortical involvement was associated with an increased risk of early seizures and with seizures at stroke onset. Past intracerebral hemorrhage history, younger age, and more severe neurologic deficits also were associated with higher risk of onset seizures. The presence of early seizures did not increase morbidity or mortality risk at 7 days or at 6 months of follow up.

These two studies provide concordant observations regarding early seizure risk factors that include intracerebral hemorrhage and cortical involvement, confirming other similar reports (3, 4). They also demonstrate that the early symptomatic seizures are commonly encountered in the setting of acute cerebral hemorrhage, and both reported an incidence of approximately 15%. However, the studies disagree on the extent to which early symptomatic seizures predict morbidity and mortality. Beghi et al. (7) report that early seizures doubled the risk of post-stroke mortality at 30 days, whereas De Herdt et al. (8) report no association between early seizures and subsequent morbidity or mortality at 7 days or at 6 months. This difference may be related to the different stroke

types included in each of the studies; Beghi et al. (7) included ischemic infarctions.

Unfortunately, neither study employed systematic use of EEG in the evaluation of stroke patients. EEG studies were done when indicated by clinically obvious seizures, but electrographic seizures in patients with altered mental status almost certainly were missed in both studies. Thus, the incidence of early seizures in the setting of acute stroke may, in fact, be higher than these studies report. Indeed, previous work in a smaller study population has demonstrated that early electrographic seizures without overt clinical seizure activity can occur in up to 18% of patients with intracerebral hemorrhage, and an additional 13% of patients have clinically apparent early seizures (9). Confirmation of these observations would be a useful addition to the literature on early seizures after stroke.

Information regarding the use of antiepileptic medications within these two studies is also quite limited. As a practical matter, one is often faced with the question of whether or not to initiate antiepileptic medication in patients who have suffered a stroke, either empirically or after a seizure has occurred. Beghi et al. (7) treated a total of 27 patients with antiepileptic medications, 23 of whom were treated after having had a seizure. No information is provided regarding subsequent seizure recurrence or control nor is choice of medication specified. Similarly, De Herdt et al. (8) report that a total of 34 patients were treated with antiepileptic medication after having had a seizure. Of these, 28 remained on antiepileptic medication at discharge, but subsequent seizure recurrence at 6 months of follow-up is not reported. A distinction is made between benzodiazepines and other antiepileptic medications, but no additional information on medication choice is provided.

These two studies are valuable in that they have identified and prospectively followed two large populations of patients with acute stroke, confirming risk factors for early seizures and demonstrating similar incidence of early seizures in acute cerebral hemorrhage within both populations. Beghi et al. (7) also provide useful observational information regarding early seizures in ischemic stroke. One would hope that these populations will continue to be followed and that additional information will eventually become available. It would be useful to know, for example, the incidence of late seizures at subsequent time points and the extent to which early seizures or early treatment with antiepileptic medications are predictive of seizure recurrence at a later time or the development of epilepsy in patients with acute stroke.

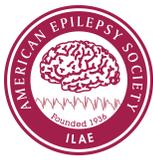
by Robert T. Wechsler, MD, PhD

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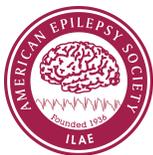
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