

NOT ALL FIRST SEIZURES ARE CREATED EQUALLY

Is a First Acute Symptomatic Seizure Epilepsy? Mortality and Risk for Recurrent Seizure. Hesdorffer DC, Benn EK, Cascino GD, Hauser WA. *Epilepsia* 2009;50(5):1102–1108. **PURPOSE:** To compare mortality and subsequent unprovoked seizure risk in a population-based study of acute symptomatic seizure and first unprovoked seizure due to static brain lesions. **METHODS:** We ascertained all first episodes of acute symptomatic seizure and unprovoked seizure due to central nervous system (CNS) infection, stroke, and traumatic brain injury (TBI). Subjects were residents of Rochester, Minnesota, identified through the Rochester Epidemiology Project's records-linkage system between January 1, 1955 and December 31, 1984. Information was collected on age, gender, seizure type, etiology, status epilepticus (SE), 30-day and 10-year mortality, and subsequent episodes of unprovoked seizure. **RESULTS:** Two hundred sixty-two individuals experienced a first acute symptomatic seizure and 148 individuals experienced a first unprovoked seizure, all due to static brain lesions. Individuals with a first acute symptomatic seizure were 8.9 times more likely to die within 30 days compared to those with a first unprovoked seizure [95% confidence intervals (CI) = 3.5–22.5] after adjustment for age, gender, and SE. Among 30-day survivors, the risk of 10-year mortality did not differ. Over the 10-year period, individuals with a first acute symptomatic seizure were 80% less likely to experience a subsequent unprovoked seizure compared with individuals with a first unprovoked seizure [adjusted rate ratio (RR) = 0.2, 95% CI = 0.2–0.4]. **DISCUSSION:** The prognosis of first acute symptomatic seizures differs from that of first unprovoked seizure when the etiology is stroke, TBI, and CNS infection. Acute symptomatic seizures have a higher early mortality and a lower risk for subsequent unprovoked seizure. These differences argue against the inclusion of acute symptomatic seizures as epilepsy.

COMMENTARY

It is axiomatic that having more than one unprovoked seizure is necessary to make the diagnosis of epilepsy. In the past, the clinical context in which a first seizure occurred was among the factors taken into account when conferring the diagnosis of epilepsy. Thus, seizures that were temporally related to a recent stroke, metabolic deficiency, or other malady may have been discounted and would not necessarily have led to an epilepsy diagnosis. However, in 2005, the International League against Epilepsy revised the definition of epilepsy such that even a single seizure was sufficient to constitute a diagnosis of epilepsy (1). Essentially, the revised criteria could be construed to mean that all first seizures are created equally—the clinical circumstances did not matter. It is with that backdrop that Hesdorffer and colleagues sought to evaluate whether all first seizures indeed carried an equivalent prognosis.

In order to study this issue, the investigators identified patients who either had had a stroke, traumatic brain injury, or CNS infection. They then assessed whether individual first seizures were directly related to the acute phase of those etiologies or whether the seizure occurred subsequent to the acute phase, thereby creating two subgroups for analysis. If the seizure occurred within a 7-day time period of the insult, the patient was placed into a symptomatic category, as part of the acute phase group. The second group was made up of all patients whose seizures occurred outside of the 1-week acute insult time window, and the seizures were deemed unprovoked. Seizure re-

currence and patient mortality were compared between the two groups.

Hesdorffer et al. identified 410 individuals with one of the three neuropathological categories and a first seizure; 262 patients were placed in the “acute symptomatic seizure” and 148 in the “unprovoked seizure” group. The investigators found significant differences with regard to seizure recurrence and mortality. Individuals in the symptomatic group were almost nine times more likely to die in the first month compared with the unprovoked group, yet they were also much less likely to have a subsequent unprovoked seizure. In contrast, the unprovoked seizure groups were much more likely to have a subsequent unprovoked seizure regardless of the etiology, with 65% of the unprovoked seizure group having a subsequent event as compared to 18.7% of the acute symptomatic group. Therefore, the data suggest that even though individuals may present with the same type of neuropathology, there is clearly a difference in outcome between patients who have their seizure within a week of a stroke, traumatic brain injury, or CNS infection and those whose seizures occur in a temporally later timeframe. In essence, all seizures are not created equally.

Another study found a remarkably similar result in a distinctly different patient group and condition—neonates and neonatal seizures. In 2007, Ronan and colleagues applied the Mizrahi and Kellaway clinical seizure classification to population-based cohorts of neonatal seizures (2,3). They found that the severity and timing of the pathologic process that influenced the presentation of seizures actually was the most important prognostic variable among these infants. In sum, they established that the clinical context in which a seizure occurs is the primary determinant in informing and guiding the

diagnosis and management of the neonates. It perhaps follows that the same may hold true for adult patients as well.

Hesdorffer and colleagues' analysis charts new territory in the fundamental concept of first seizures and epilepsy. This report is somewhat analogous to that of Kwan and Brodie, which proved to be seminal in demonstrating that not all epilepsy patients were the same, particularly, the recognition that some individuals presented with refractory epilepsy from the onset (4). Similarly, the Hesdorffer et al. study shows that some first seizures are indeed epilepsy from the onset. Essentially, these authors present epidemiological facts that are in need of explanation, verification, and replication; ultimately, the outcome of such investigations may lead to an adjustment in the basic understanding of the condition. The findings also serve as a reminder of what eludes both basic and clinical science epilepsy research: the detection of more sensitive and specific biomarkers that can identify, from the onset, which individuals will be predisposed to recurrent, unprovoked seizures.

There are important treatment implications from this review that can be applied clinically. When a person presents with a first seizure, in order to provide accurate counsel to the patient, the clinician must take into account the underlying clinical context, both with regard to etiology and to whether that etiology

is temporally related to the seizure. Patients without an overt lesion, perhaps, need to be followed more closely than individuals who present with a seizure in the setting of a stroke or traumatic brain injury, as this patient type would be somewhat akin to the unprovoked seizure group in the Hesdorffer et al. study. The importance of a thorough clinical history for patients with a first seizure cannot be stressed enough. Hopefully, in time, it will be possible to identify which seizures portend epilepsy and which are likely to have a more benign course.

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References

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