Missed diagnosis of prehospital status epilepticus
Is it serious, doctor?

Status epilepticus (SE) represents one of the most frequent neurologic emergencies, with potentially severe morbidity and mortality. Considerable attention has been directed towards implementation of treatment protocols, and recently of anesthetic treatment, but prognostic studies focused on early recognition of SE by emergency medical services (EMS) are lacking.

In this issue, Semmlack et al. studied out-of-hospital SE occurring in adults (excluding events following cardiac arrest), retrospectively identified over a 10-year interval through medical and EEG databases of an urban Swiss university hospital. The authors stratified convulsive and nonconvulsive episodes, and carefully assessed demographic and clinical variables, including the need for mechanical ventilation and medical complications. They defined missed diagnoses as referrals with suspected conditions unrelated to seizures or SE, with an altered neurologic status that could not be explained by other acute illnesses, followed by an emergency department evaluation resulting in the diagnosis of SE. The primary outcome was return to functional baseline at the time of discharge, while 30-day mortality and in-hospital death were secondary endpoints.

The majority (55%) of 150 patients fulfilling the inclusion criteria had an SE episode that was not recognized by the EMS. Missed diagnoses were particularly prevalent in nonconvulsive episodes (64%), vs convulsive SE (15%, all with evolution toward subtle SE). Among 124 nonconvulsive SE episodes, missed diagnosis during prehospital assessment was independently related to increasing age and lack of seizure history. Combining these 2 variables yielded an area under the curve of 84% for prediction of missed diagnosis. Patients not recognized as having SE were less likely to receive benzodiazepines before hospital admission (20% vs 51%), and had a lower chance of recovery to baseline, although infectious complications, need for mechanical ventilation and anesthetic treatment, and, most importantly, mortality were not affected.

The principal limitations of this study include its retrospective design and the use of a nonspecific primary outcome, functional status at discharge: this may be influenced by hospitalization duration, or by medical comorbidities. In fact, mortality (a robust endpoint) was similar among the groups. Furthermore, as recognized by the authors, their SE definition involved an immediate diagnostic workup, which may have led to underascertainment of missed SE, since a longer time interval and prolonged EEG may be needed to reach diagnostic certainty, especially in nonconvulsive SE.

In addition, the potential consequences of missed SE diagnoses may have been reduced by the rapid EMS transport time afforded by the limited geographic catchment area of the hospital. Although the multivariate analysis found that SE etiology had no independent effect on whether the initial diagnosis of SE was made or missed, potentially confounding factors may have been undetectable due to the relatively small number of patients presenting with each etiology. For the analysis, etiologies as diverse as acute ischemic stroke and alcohol withdrawal were grouped into a single “potentially fatal” category, and compared with a “non-potentially fatal” category. Ideally, a larger patient population would yield more granular data about etiologies, illuminating any that are more likely to obscure the clinical recognition of nonconvulsive SE or affect functional outcome. Acute stroke, in particular, is a common emergency causing neurologic deficits that could mask both the recognition of nonconvulsive SE and its sequelae, contributing to a persistently worsened functional baseline.

This study is important. In the context of sparse evidence supporting specific treatment choices beyond the first step, represented by benzodiazepines, it appears of utmost importance to provide appropriate therapy as early as possible: patients with missed SE diagnoses had lower rates of early benzodiazepine administration. That SE diagnosis was missed in the majority of patients, especially in nonconvulsive episodes, appears logical and concerning, and raises important practical questions.

How can EMS personnel identify nonconvulsive SE more accurately? Should portable EEG devices
with a reduced montage be used by EMS? Who would interpret these recordings, and how often? Beyond such diagnostic issues, would routine administration of benzodiazepines in the presence of possible nonconvulsive SE (i.e., altered mental state without an obvious cause) be advisable? We know that overtreatment with benzodiazepines increases the need for intubation for airway protection and prolongs hospitalization, and reassuring data regarding benzodiazepine safety from the San Francisco prehospital SE study apply only to convulsive SE, while nonconvulsive SE predominated in the current study. An empiric SE treatment approach might also lead to overtreatment of patients with psychogenic nonepileptic events, triggering potentially severe complications. The current study did not include children; in view of their marked differences in SE etiologies and outcomes, no generalizations can be inferred for the pediatric population.

The lack of effect on mortality, whether SE is initially diagnosed or is missed, has potentially major implications. As opposed to animal studies, human observations indicate that case-fatality rates are not influenced by adherence to treatment guidelines, but depend primarily on underlying etiology. Moreover, in this study, the need for mechanical ventilation and anesthetic treatment, a surrogate of SE refractoriness, did not differ among missed and nonmissed SE diagnoses. It appears, to some extent, that cellular mechanisms rather than treatment details govern the cessation of SE. Thus, an inherently treatable SE episode is likely to be ultimately controlled successfully, regardless of initial deviations from protocols or missed diagnoses.

Until prospective data further refine this study’s innovative findings, primum non nocere applies. It is reasonable to avoid the risks of overtreatment in diagnostically uncertain prehospital situations, and to focus efforts on providing useful diagnostic information to EMS responders. For example: obtunded elderly patients with no history of seizure should routinely be suspected of nonconvulsive SE and always merit an emergency EEG.

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**REFERENCES**