



# Nonconvulsive Status Epilepticus

An Underrecognized  
Neurological Emergency



**A Clinical Proceedings  
White Paper**

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**Clinical  
Neurological  
Society of America**

# About the Clinical Neurological Society of America

Established in 1974, the Clinical Neurological Society of America was created as an organization for neurologists practicing in clinical and academic settings. Since then, the society has grown into a nationwide organization of clinicians with a mission to improve clinical practice and patient care through education.

As a non-profit 501(c)(6) professional membership organization, CNSA is led by a volunteer board of directors who, like the society's professional members, hail from across the country and treat patients with a range of neurologic conditions.



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## Introduction

Status epilepticus is a condition of prolonged seizures—abnormal excessive or synchronous neural activity in the brain—that can result in brain injury and death.<sup>1</sup> The most recognizable form is convulsive status epilepticus, in which the aberrant neural activity is accompanied by excessive and abnormal muscle contractions.

However, not all seizures are accompanied by convulsions. Another major type of status epilepticus, known as nonconvulsive status epilepticus (NCSE), is characterized by seizure activity as detected on electroencephalogram (EEG) without prominent muscle contractions.<sup>1, 2</sup> The lack of overt motor activity often makes NCSE difficult to identify in a clinical exam, leading to failure to initiate treatment, and subsequent morbidity and mortality.<sup>3</sup> Although clinicians may suspect nonconvulsive status or seizures based on subtle signs and symptoms, EEG is needed to confirm the diagnosis.

### The Bottom Line of NCSE



NCSE is an underrecognized neurological emergency.



EEG is a must.



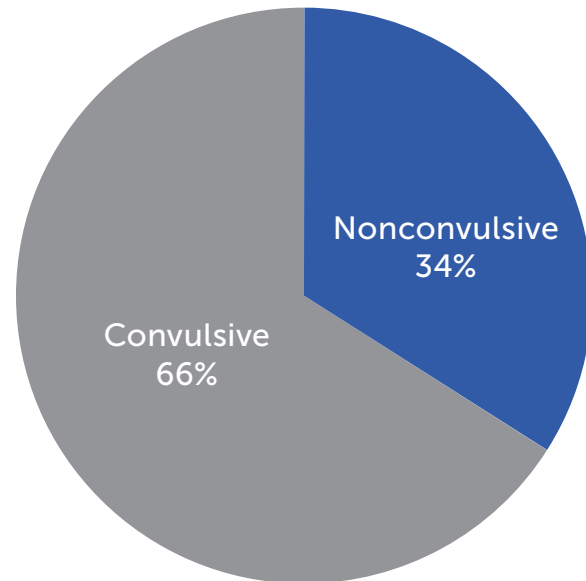
Time is brain!

# Burden of Nonconvulsive Status Epilepticus

Using definitions updated in 2015,<sup>1</sup> an estimated 34% of all patients admitted to the hospital with first-ever status epilepticus due to non-hypoxic causes have NCSE.<sup>4</sup> In clinical practice, NCSE is likely under-diagnosed and under-recognized.

NCSE can occur as a complication of many different primary neurological and non-neurological conditions. Examples include cerebrovascular accident (stroke), hypoxia, sepsis, traumatic brain injury, metabolic causes, tumors, and low antiepileptic drug levels.<sup>4-7</sup> Indeed, NCSE can occur in nearly any condition that affects the homeostasis of the brain's cerebral hemispheres.<sup>8</sup>

## Classification of First-Ever Status Epilepticus



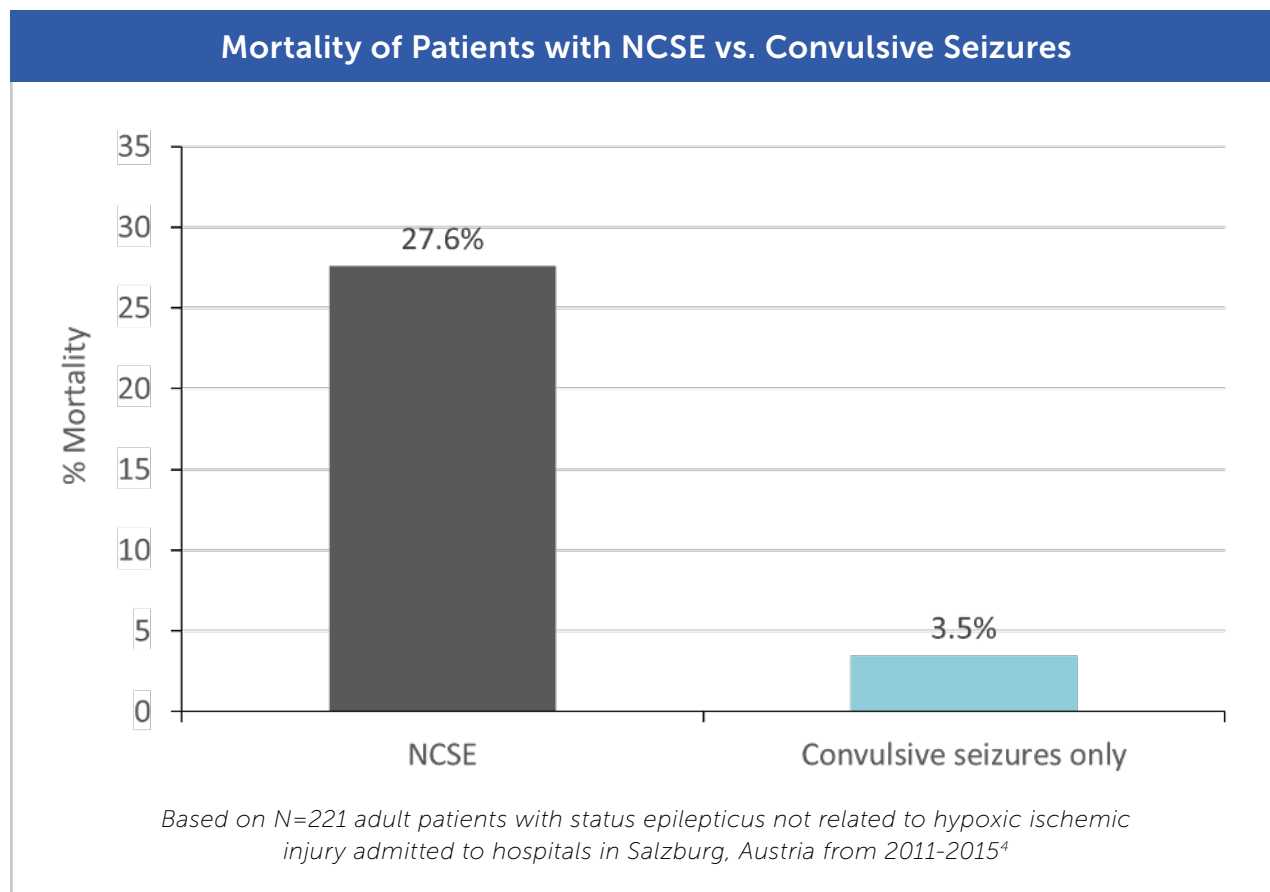
*Based on N=221 adult patients with status epilepticus not related to hypoxic ischemic injury admitted to hospitals in Salzburg, Austria from 2011-2015<sup>4</sup>*



## Some common causes of NCSE<sup>4-7, 9</sup>

- Cerebrovascular accident (stroke)
- Hypoxia
- Hypoxic-ischemic injury following cardiac or respiratory arrest
- Acute subdural hematoma
- Sepsis
- Traumatic brain injury
- Metabolic causes
- Low anti-epileptic levels
- Tumors
- Central nervous system (CNS) infections
- Ethanol-related
- Recent neurosurgery

NCSE is a medical emergency because it can lead to brain damage and death.<sup>10-13</sup> In adults, mortality rates are substantially higher with NCSE than convulsive status epilepticus, reported as 27.6% vs. 3.5% in a 5-year study of patients admitted to hospitals with status epilepticus not related to hypoxic ischemic injury.<sup>4</sup>



“Status epilepticus, including NCSE, is a medical emergency and should be treated as such. Some people don’t think about it that way, but early recognition and time-targeted treatment are crucial.”

—Khalid Alsherbini, MD

NCSE can also result in prolonged hospitalization, which itself is associated with a host of problems.

“Patients who need prolonged intubation require rehabilitation not only for their underlying condition, but also for issues related to long-term hospitalization. Lengthy hospital stays increase the risk for infection, tracheostomy, feeding tube placement, and other sequelae.”

—Angela M. Crudele, MD

Although age and underlying etiology are the non-modifiable predictors for outcomes in NCSE, seizure burden and duration of NCSE remain important modifiable factors with a strong impact on outcome, highlighting the importance of early diagnosis and management of this condition.<sup>4, 14-16</sup> NCSE is frequently associated with brain injury and poor functional outcomes after open cardiac surgery<sup>17</sup> and an increased risk of disability and death following ischemic stroke.<sup>18</sup> In patients with intracerebral hemorrhage, nonconvulsive seizures are associated with poor outcomes, increased intracranial pressure, metabolic crisis, and expanding hemorrhages.<sup>19-21</sup>

## Criteria for Defining Status Epilepticus & NCSE

The criteria used to define status epilepticus have changed over the years, which affects estimates of prevalence, incidence, morbidity, and mortality. One of the changes has been the duration of seizures that define the condition, which has historically been 30 minutes.

### International League Against Epilepsy Definition and Classification

In 2015, the International League Against Epilepsy revised the definition and classification of status epilepticus, resulting in two time points that serve to guide clinicians.<sup>1</sup>

1. The time when a seizure is likely to be prolonged and should be treated:  
5 minutes for convulsive status epilepticus and 10 minutes for NCSE.
2. The time when a seizure may cause long-term neuronal damage:  
30 minutes for convulsive status epilepticus and 60 minutes for NCSE.

However, these times are based on limited evidence, particularly for NCSE, and the onset of brain damage can vary based on clinical factors.<sup>1</sup>

### Diagnosis of NCSE Using EEG

Many criteria for the diagnosis of NCSE utilizing EEG have been published. One frequently used, known as the Salzburg criteria, focuses on EEG parameters for NCSE, which specifies the presence of more than 25 epileptiform discharges per 10 seconds.<sup>22</sup> Other prominent criteria from the American Clinical Neurophysiology Society (ACNS) specify the presence of EEG seizures for at least 10 continuous minutes or a total duration of at least 20% of any 60-minute period.<sup>23</sup>

In addition to the various criteria that may be used to define NCSE, it is important to highlight that EEG readings, even using the ACNS published consortium, remain variable among epileptologists, especially for patterns that do not meet the above suggested criteria for a diagnosis of NCSE.





## Recognition and Diagnosis of NCSE

A major challenge in recognizing NCSE is the lack of specific, identifiable clinical symptoms and signs. Although altered consciousness is the most frequent clinical finding in NCSE,<sup>24</sup> it occurs in a plethora of different medical conditions. Indeed, patients do not need to have primary neurologic illnesses to experience NCSE. Altered consciousness in NCSE ranges from mild impairment (“wandering confused”) to comatose.<sup>1, 2</sup> Other clinical signs reported in NCSE include oral or ocular muscle twitches and eye deviations, which may occur in 50% of patients.<sup>25</sup> However, these signs are typically subtle and it is generally agreed that NCSE is extremely difficult to identify through a clinical exam alone.

“ Altered mental status is a common finding in NCSE, but it is also present in a wide variety of other conditions. Patients can be aphasic and having a stroke or comatose or unconscious. Altered mental status is a sensitive finding but it’s not specific.”

– **Gregory K. Bergey, MD**

Instead, reliable detection of NCSE requires EEG. Without the use and accurate interpretation of EEG, NCSE can be substantially underdiagnosed.<sup>4, 24</sup>

“ The clinical exam has definite limitations in diagnosing NCSE. We’ve all been through multiple cases where patients don’t look like they are seizing but if you put them on EEG, they are having nonconvulsive seizures or NCSE. Patients can show a wide range of clinical manifestations.”

– **Khalid Alsherbini, MD**



# Importance of early diagnosis with EEG

Early diagnosis of NCSE is critical because delays are associated with treatment refractoriness and increased mortality.<sup>26, 27</sup>

“Outcomes depend on the cause of the initial seizure and how quickly it’s identified and treated. Without prompt detection, patients can get varying grades of brain damage. Early detection can be a tipping point for inpatient versus outpatient therapy.”

– Angela N. Crudele, MD

“If nonconvulsive seizure detection is delayed, patients may be already in refractory stage of status epilepticus that you can’t control.”

– Khalid Alsherbini, MD

In recognition of the potential for negative outcomes of status epilepticus, multiple professional societies recommend prompt EEG in various patient groups.<sup>2, 28-30</sup>



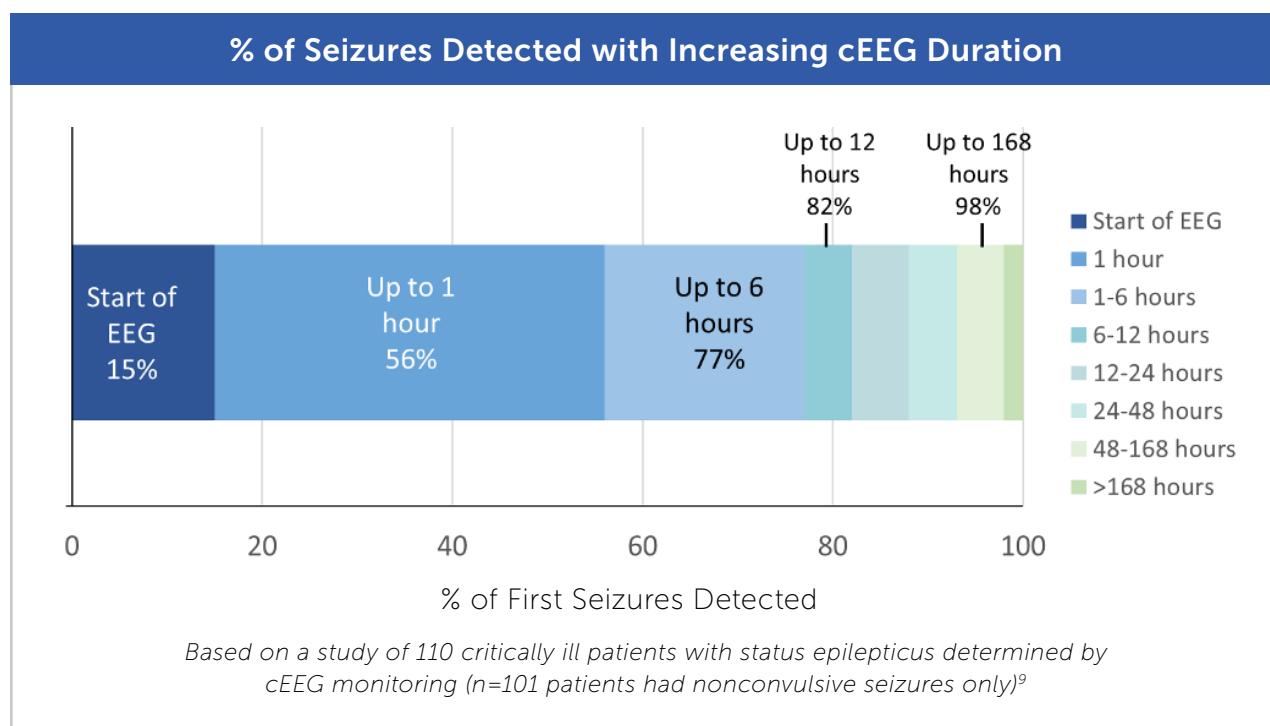
Professional Guidelines Recommending Prompt EEG in Patients with Status Epilepticus	
Professional Society	Prompt EEG recommended for...
Neurocritical Care Society	Patients with suspected status epilepticus (within 15-60 minutes) <sup>2</sup>
International Multidisciplinary Consensus	Patients with convulsive status epilepticus who do not return to functional baseline within 60 minutes <sup>28</sup>
American Heart Association	All comatose patients after return of spontaneous circulation <sup>29</sup>
American Heart Association/ American Stroke Association	Patients with intracerebral hemorrhage and abnormal mental status <sup>30</sup>

## Use of continuous EEG

Increasing evidence indicates that routine EEG performed for 20 minutes is inadequate to detect nonconvulsive seizures and NCSE. Instead, continuous EEG (cEEG) monitoring over hours to days is needed.<sup>9</sup> Continuous EEG in critically ill patients more than doubles the number of NCSE cases detected.<sup>31, 32</sup> Use of cEEG is also associated with lower patient mortality than routine EEG.<sup>33, 34</sup> In its 2015 guidelines, the American Clinical Neurophysiology Society recommends critical care continuous EEG for diagnosis of nonconvulsive seizures, NCSE, and other paroxysmal events in critically ill patients.<sup>35</sup>

“Recognition of NCSE has increased dramatically. It’s probably not because NCSE is becoming more common, but because we are recognizing it more frequently due to the use of continuous EEG.”

– Gregory K. Bergey, MD



## Practical shortcomings with widespread use of cEEG

Although the use of cEEG is desirable to help identify nonconvulsive seizures, its widespread use faces practical considerations such as hardware costs and the need for experts to administer and interpret the results.<sup>36</sup>

“Even in institutions that have cEEG, not all will have a technician in-house overnight. For a long time in my institution, we didn’t have staff overnight to administer EEG, and this is a large university hospital with a wide catchment area.”

– Shelly Rishty, MD

In 2017, a 7-point scoring system known as 2HELPS2B was developed to estimate seizure risk in critically ill patients undergoing cEEG.<sup>37</sup> In this model, 1 hour of cEEG is sufficient to stratify patients according to seizure risk and to recommend cEEG monitoring duration.<sup>36</sup>

“We now have tools such as the 2HELPS2B that can help us determine how long to monitor patients with cEEG.”

– **Veeresh Kumar N. Shivamurthy, MD**

## Use of rapid EEG

Although professional guidelines recommend prompt use of EEG for the assessment of status epilepticus, in reality, access to EEG monitoring and interpretation is often delayed.<sup>38</sup> A survey of Society of Critical Care Medicine members found that rapid, 24-hour access to cEEG interpretation was available in only 32% of intensive care units.<sup>39</sup>

In response to the need for emergency EEG monitoring, several rapid EEG technologies have been developed.<sup>40</sup> Rapid EEG can reduce time to diagnosis versus conventional EEG and help inform clinical decisions.<sup>41</sup>

“With a shortage of EEG technicians and limited resources, rapid EEGs coupled with 2HELPS2B can aid in stratifying seizure risk, help determine whether patients should be transitioned to continuous or long-term EEG and consequently, improve the cost-effectiveness of continuous EEG.”

– **Veeresh Kumar N. Shivamurthy, MD**

“Rapid EEG is useful as an alternative for the initial EEG, while you are getting the patient transferred to an institution where they can have long-term continuous EEG. It’s not meant to be the definitive screen that you keep on for 24 hours.”

– **Shelly Rishty, MD**

Even in centers with access to cEEG, rapid EEG applied for at least 2 hours can be used as a screening tool.<sup>42</sup>

“We use rapid EEG as a screening tool because we have limited EEG machines. We monitor with rapid EEG for a minimum of 2 hours and use the 2HELPS2B score to determine who should be placed on cEEG.”

– **Khalid Alsherbini, MD**

Rapid EEG technologies may also help reduce unnecessary treatments.<sup>43, 44</sup>

“Rapid EEG can be useful to screen patients in rural or underserved areas or smaller medical centers to determine whether they need to be sent to larger medical centers with cEEG capabilities. It can help prevent the needless transfer of patients, allowing them to stay with their families and safety nets, but also identify patients who should be transferred for escalation of care.”

– **Angela N. Crudele, MD**





## Treatment of NCSE

The principal goal of treatment in status epilepticus is to stop clinical and electrographic seizures.<sup>2</sup> Emergency treatment is recommended for patients who exhibit continuous seizure activity for 10 minutes or more.<sup>1</sup> Per guidelines from the Neurocritical Care Society, all patients with status epilepticus should receive treatment with first- and second-line antiseizure drugs therapies, as well as maintenance therapy, even if seizures are immediately controlled.<sup>2</sup> Guidelines from the American Heart Association and American Stroke Association recommend antiseizure medications for patients with spontaneous intracerebral hemorrhage, impaired consciousness, and confirmed EEG seizures to reduce morbidity.<sup>30</sup> Importantly, most guidelines were developed primarily for convulsive status epilepticus rather than NCSE.

“Treatment of NCSE is the same as for convulsive status epilepticus. This can help improve the comfort level of those familiar with treating convulsive status epilepticus.”

– Gregory K. Bergey, MD

### Importance of rapid treatment

Treatment guidelines from the Neurocritical Care Society state that definitive control of status epilepticus should be established within 60 minutes of onset.<sup>2</sup> Prompt treatment of status epilepticus within 60 minutes results in significantly better outcomes than delayed treatment.<sup>45, 46</sup>

“The longer a seizure goes on, the chances of responding to the first medication plummet. If you wait a couple of hours to treat, patients may not respond to the medication and face prolonged intubation from which they may not recover. Outcomes are highly variable.”

– **Angela N. Crudele, MD**

Pharmacologic resistance to benzodiazepines develops rapidly after the onset of status epilepticus.<sup>47</sup> This has been attributed to cell trafficking of GABA-A receptors in the brain that mediate the action of benzodiazepines.<sup>47</sup>

“Rapid diagnosis and treatment of status epilepticus is critical because if not promptly treated, status epilepticus can swiftly evolve into a self-sustaining condition, and become resistant to benzodiazepines and other antiepileptic medications. The decreased responsiveness to benzodiazepines in the early stages of status epilepticus can be elucidated by the time-dependent internalization of synaptic GABA receptors.”

– **Veeresh Kumar N. Shivamurthy, MD**

## **Response to treatment**

Response to treatment with antiseizure medications has been documented in 50-63% of patients with nonconvulsive seizures evaluated in a well-controlled trial.<sup>48</sup> However, treatment success reported in the literature varies widely and may be influenced by duration of seizures, study design and methods, and other factors.<sup>8</sup>

Importantly, adequate dosing is critical to achieving seizure control.

“NCSE is notoriously under-dosed with antiseizure medications. Patients are often referred to us having received medication at doses that are dramatically lower than needed to control seizures. It’s important that the medications be dosed properly for seizure control.”

– **Shelly Rishty, MD**

Treatment of status epilepticus frequently requires use of multiple antiseizure medications; patients who do not respond may require treatment with intravenous anesthetic drugs.<sup>8</sup> Other medications are being actively investigated for refractory seizures in carefully selected patients, including ketamine, which does not suppress respiratory drive.<sup>49</sup>

Ultimately, though early detection using EEG and early treatment of NCSE with adequate doses of antiseizure medications is important, the underlying diagnosis has a major effect on outcomes. Thus, physicians can only control so much with treatment.

“Early diagnosis of NCSE is desirable and it leads to earlier treatment, but patient outcomes are multifactorial.”

– **Gregory K. Bergey, MD**

## Conclusion

NCSE is a frequent complication of acute brain injury that can lead to major morbidity and mortality if not promptly identified and treated. Although many patients with NCSE exhibit altered consciousness and subtle muscle twitches around the eyes and mouth, other patients lack identifiable clinical symptoms and signs, making it extremely difficult to detect without EEG.

Clinicians must have a high index of suspicion for NCSE in at-risk populations and obtain prompt EEG of adequate duration. Rapid EEG can be useful in screening patients for suspected NCSE, who can then be escalated to cEEG if needed. Treatment of NCSE with antiseizure medications can be successful, particularly if initiated early and at adequate doses. Ultimately, outcomes of NCSE also depend on the patient's age and underlying injury or condition.

**“Most coma patients just look like they are sleeping peacefully in bed. If you don't think about NCSE, you will miss every case.”**

**– Angela N. Crudele, MD**

## CNSA's Clinical Proceedings

The Clinical Neurological Society of America has 50 years of experience bringing together leading experts and clinical neurologists for educational programming. CNSA's Clinical Proceedings — a white paper series — are informational resources intended to raise awareness and address unmet needs in neurology.

CNSA recognizes the expert panel members who contributed to the development of this white paper.



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