Poststroke Epilepsy
Kanokwan Boonyapisit, M.D.
Division of Neurology
Department of Medicine
Siriraj Hospital

DEFINITION

• Acute symptomatic seizures
• Late poststroke seizure
• Poststroke epilepsy

DEFINITION

• Acute symptomatic seizures: seizures occur within one week after acute stroke
• Late poststroke seizure: unprovoked seizure that occurs > 1 week after acute stroke
• Poststroke epilepsy

DEFINITION

Acute symptomatic seizures is defined as a clinical seizure occurring at the time of a systemic insult or in close temporal association with a documented brain insult. Suggestions are made to define acute symptomatic seizures as those events occurring within 1 week of stroke, traumatic brain injury, anoxic encephalopathy, or intracranial surgery.  


Acute symptomatic seizures: seizures occur within one week after acute stroke
Late poststroke seizure: unprovoked seizure that occurs > 1 week after acute stroke
Poststroke epilepsy

Summary: Acute symptomatic seizures should be considered part of a differential diagnosis that includes acute stroke, traumatic brain injury, anoxic encephalopathy, or intracranial surgery.  

Its intent is to encompass circumstances for which some practitioners and expert epileptologists manage patients as if epilepsy is present after a single unprovoked seizure, because of a very high risk of recurrence. Such examples may include patients with a single seizure occurring at least a month after a stroke or a child with a single seizure conjoined with a structural or remote symptomatic etiology and an epileptiform electroencephalography (EEG) study.

- 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
- Subjects were residents of Rochester, Minnesota, identified through the Rochester Epidemiology Project’s records-linkage system between 1/1/55 and 12/31/84.
- Information was collected on age, gender, seizure type, etiology, status epilepticus (SE), 30-day and 10-year mortality, and subsequent episodes of unprovoked seizure.

- 262 individuals experienced a first acute symptomatic seizure and 148 individuals experienced a first unprovoked seizure, all due to static brain lesions.

### Risk of subsequent unprovoked seizure

<table>
<thead>
<tr>
<th></th>
<th>Acute symptomatic seizure</th>
<th>First unprovoked seizure</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>71.5% (95% CI = 59.7–81.9%)</td>
<td></td>
<td></td>
<td>p = 0.001</td>
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<tr>
<td>Traumatic brain injury</td>
<td>46.6% (95% CI = 30.4–66.3%)</td>
<td></td>
<td>p &lt; 0.001</td>
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<tr>
<td>CNS infection</td>
<td>63.5% (95% CI = 21.2–88.6%)</td>
<td></td>
<td>p = 0.010</td>
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</tbody>
</table>
• Acute symptomatic seizures
• Late poststroke seizure
  =?
• Poststroke epilepsy

"The new definition is not uncontroversial, mostly due to conflicting data on the actual recurrence risk of seizures after a first late-poststroke seizure and whether a diagnosis benefits patients."

**Epidemiology of Poststroke Epilepsy**

- Long-term cumulative risk of PSE after a cerebrovascular event varies between 2% and 13%

- Both early and late seizures are more common after hemorrhage than after infarctions, with the exception of total anterior circulation infarctions

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Type</th>
<th>Follow-up (years)</th>
<th>Patients</th>
<th>Cases</th>
<th>Cumulative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al. (2011)</td>
<td>2011</td>
<td>Retrospective</td>
<td>3</td>
<td>1000</td>
<td>12</td>
<td>1.2% (10 yrs)</td>
</tr>
<tr>
<td>Kuschke et al. (2014)</td>
<td>2014</td>
<td>Prospective</td>
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<td>1000</td>
<td>50</td>
<td>5.0% (3 yrs)</td>
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<tr>
<td>Leite et al. (2015)</td>
<td>2015</td>
<td>Retrospective</td>
<td>10</td>
<td>1000</td>
<td>100</td>
<td>10.0% (3 yrs)</td>
</tr>
<tr>
<td>Maclntyre et al. (2016)</td>
<td>2016</td>
<td>Retrospective</td>
<td>5</td>
<td>1000</td>
<td>50</td>
<td>5.0% (5 yrs)</td>
</tr>
<tr>
<td>Martinez et al. (2017)</td>
<td>2017</td>
<td>Prospective</td>
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<td>1000</td>
<td>50</td>
<td>5.0% (2 yrs)</td>
</tr>
<tr>
<td>Perez et al. (2018)</td>
<td>2018</td>
<td>Retrospective</td>
<td>3</td>
<td>1000</td>
<td>30</td>
<td>3.0% (3 yrs)</td>
</tr>
</tbody>
</table>

**Cumulative risk at the end of the study (3-10 yrs)**

- Overall risk: 3.2% (7 yrs), 12.4% (10 yrs)
- Ischemic stroke: 2.3% (3 yrs), 4.4% (10 yrs)
- ICH: 18.2% (10 yrs)
- SAH: 12.5% (5 yrs), 21.7% (10 yrs)

Remarks:
- Include series with follow-up > 3 yrs
- Include prospective series with follow-up > 3 yrs
- Include only series with adequate no. of ICH with follow-up > 3 yrs
- Include only series with adequate no. of SAH with follow-up > 3 yrs
Predictors include:
- Stroke severity
- Cortical symptoms
- Hemorrhage
- Total anterior circulation infarcts
- Young age at stroke
- Early seizures

Causes of SE from different series

Frequency and Mortality of SE

POSTSTROKE EPILEPTOGENESIS
TREATMENT

- There is no evidence to date that treatment with AEDs prevents the development of PSE and the risk of seizure after stroke is relatively low, so primary prevention is usually not appropriate.
- Short-term treatment is often initiated if multiple early seizures occur or after a single seizure in cases of ICH or hemorrhagic transformation.

AEDS SELECTION

- In the case of a late seizure, the patient should be informed of a high recurrence risk and offered seizure prophylaxis.
- Individual factors such as constant supervision, lack of ambulation and low risk of seizure-related injury, or very mild seizures, etc. may be reasons to defer treatment.

- Antiepileptic drug selection should be made in the same manner as for other forms of epilepsy.
- Potential drug interactions especially between enzyme inducing AEDs and drugs used in secondary prophylaxis should be considered.
Drug interaction with warfarin

- Metabolites through CYP3A4, 2C9
- Phenytoin, phenobarbital and carbamazepine reduce the concentration of warfarin by up to 50-65%
- Phenobarbital and carbamazepine also reduce the anticoagulation effects of warfarin metabolites
- Newer AEDs do not have significant interaction with anticoagulant

Intestinal absorption and renal elimination of NOACs are dependent on the intestinal and renal permeability glycoprotein (P-gp) efflux transporter protein system

- Some NOACs are substrates of the hepatic CYP3A4 enzymes
- Induction of P-gp or CYP3A4 might decrease serum NOAC levels, reduce anticoagulant effects and lead to an increase in embolic risk.

PROGNOSIS

- PSE is often described as an easily manageable form of epilepsy, where monotherapy suffices to control seizures
- However, only reports from small case series exist with varying results
• Compared with the information on the risk of developing PSE, there is less information on morbidity or mortality associated with the condition.
• In patients aged 18–50, poststroke epilepsy was associated with increased mortality also after adjustment for confounders

Arntz et al. 2015

CONCLUSION

• Major cause of epilepsy after middle age
• Over the last decade, there have been remarkable improvements in the management of stroke, revascularisation, secondary prophylaxis, and rehabilitation.

• Post stroke epilepsy (PSE) thereby occurs in an optimistic medical context, but advances in management of poststroke seizures have not quite matched those seen in other stroke treatment domain.