Long-term outcomes after stroke in infants and children

Kevin A. Shapiro, MD, PhD

Assistant Professor of Neurology, University of California, San Francisco
Pediatric Stroke and Cerebrovascular Disease Center
Stroke in childhood: long-term sequelae

Impact of stroke in childhood is realized over the lifespan

- Vast majority (>95%) of infants with perinatal ischemic stroke survive into adulthood, but about 64% have one or more neurologic disabilities

- Outcomes of stroke later in childhood depend on underlying etiology, but morbidities often include epilepsy and motor and cognitive disabilities
Stroke in childhood: long-term sequelae

Impact of stroke in childhood is realized over the lifespan

- Stroke recurrence
- Seizures and epilepsy
- Motor outcomes
- Cognitive outcomes
Stroke recurrence

Recurrence after neonatal stroke is rare

- Overall incidence <2%
- Risk factors include prothrombotic states and complex congenital heart disease (Kurnik et al., 2003)
Stroke recurrence

Recurrence after stroke in childhood depends on etiology
Seizures after pediatric stroke

Seizures are a major cause of long-term morbidity

- SIPS study investigated characteristics of early and late seizures in infant and children with ischemic stroke across 21 centers in 9 countries

- PIs: Christine Fox (UCSF), Gabrielle de Veber (SickKids)
Seizures after pediatric stroke

Remote seizures and epilepsy are common in children with stroke
- Follow up n = 109, median 12.3 months
- Monthly incidence rate: 1% (95% CI 0.6-1.8%)
- Epilepsy at 1 year: 10%
  - Remote seizures defined as unprovoked seizures >7 days after stroke
  - Epilepsy defined as 1 or more remote seizures and use of maintenance anticonvulsant
Seizures after pediatric stroke

Remote seizures are predicted by acute seizures and younger age

![Graph showing the probability of remote seizure over time after stroke, differentiated by acute seizure status and age group.]
Seizures after pediatric stroke

Predictors of epilepsy

▪ Age at time of stroke
▪ Presence and number of acute seizures

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>1.4 (0.4-5.2)</td>
<td>0.6</td>
</tr>
<tr>
<td>North American</td>
<td>1.1 (0.3-4.5)</td>
<td>0.9</td>
</tr>
<tr>
<td>Hispanic parent</td>
<td>1.0 (0.2-5.0)</td>
<td>1</td>
</tr>
<tr>
<td>Neonatal stroke</td>
<td>1.2 (0.3-4.7)</td>
<td>0.8</td>
</tr>
<tr>
<td>Median years of age (IQR)†</td>
<td>0.7 (0.5-1.0)</td>
<td>0.03*</td>
</tr>
<tr>
<td>History of years of age before stroke</td>
<td>n/a</td>
<td>0.4</td>
</tr>
<tr>
<td>Stroke Risk Factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>0.6 (0.1-3.2)</td>
<td>0.6</td>
</tr>
<tr>
<td>Arteriopathy</td>
<td>0.9 (0.2-3.6)</td>
<td>0.9</td>
</tr>
<tr>
<td>Acute illness</td>
<td>2.8 (0.8-10)</td>
<td>0.1</td>
</tr>
<tr>
<td>Underlying chronic disease</td>
<td>0.7 (0.1-3.5)</td>
<td>0.7</td>
</tr>
<tr>
<td>Head trauma</td>
<td>n/a</td>
<td>1</td>
</tr>
<tr>
<td>Infarct Description</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCA territory</td>
<td>1.4 (0.3-5.4)</td>
<td>0.7</td>
</tr>
<tr>
<td>ACA territory</td>
<td>1.6 (0.3-8.3)</td>
<td>0.6</td>
</tr>
<tr>
<td>PCA territory</td>
<td>0.9 (0.2-4.6)</td>
<td>0.9</td>
</tr>
<tr>
<td>Cortical location</td>
<td>2.3 (0.6-9.0)</td>
<td>0.2</td>
</tr>
<tr>
<td>Multifocal</td>
<td>2.1 (0.6-7.4)</td>
<td>0.3</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>1.9 (0.2-18)</td>
<td>0.6</td>
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<tr>
<td>Acute seizure (any) ‡</td>
<td>11 (1.4-92)</td>
<td>0.02*</td>
</tr>
<tr>
<td>No acute seizure</td>
<td>Ref</td>
<td></td>
</tr>
<tr>
<td>Single acute seizure</td>
<td>5.8 (0.3-101)</td>
<td>0.2</td>
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<tr>
<td>2-10 acute seizures</td>
<td>7.7 (0.8-72)</td>
<td>0.07</td>
</tr>
<tr>
<td>&gt;10 acute seizures</td>
<td>30 (2.9-305)</td>
<td>0.004*</td>
</tr>
</tbody>
</table>
Seizures after pediatric stroke

Neonates with stroke at greatest risk of epilepsy
- Risk is increased with history of postnatal seizures
Seizures after pediatric stroke

Risk in older children depends on presence and frequency of acute seizures

Number at risk
Acute seizure 73 39 28 16 7 3
No acute seizure 209 140 90 47 20 11
Seizures after pediatric stroke

Multiple or prolonged acute seizures increase epilepsy risk

- Patients with >10 acute seizures had a thirty-fold increased epilepsy risk (OR 30, 95% CI 2.9-305)

- Each additional 10 minutes of the longest acute seizure increased active epilepsy risk nearly five-fold (OR 4.7, 95% CI 1.7-13)
Motor outcomes

Motor outcomes best studied after perinatal arterial ischemic stroke

- Hemiplegic cerebral palsy is a common outcome (37%) (Golomb, 2009)

- Concomitant involvement of cerebral hemisphere, internal capsule and basal ganglia almost always associated with abnormal outcome

- Neonatal seizures associated with poorer outcomes (Sreenan et al., 2000; Mercuri et al., 2000)

- Neonatal encephalopathy associated with poorer outcomes (Ramaswamy et al., 2004)
Cognitive outcomes

Cognitive measures significantly lower in children with stroke

- Children with perinatal stroke perform more poorly than older children (Westmacott et al., 2010)
- Combined injury to cortical and subcortical regions predicts poorer outcome than isolated damage to cortical or subcortical areas
- Different periods of peak vulnerability based on lesion location
  - Subcortical injury: Perinatal period (<1 month)
  - Cortical lesions: 1 month to 5 years