Conflict of Interest

- None to declare
Cardiac Arrest

- **Pediatric**: Survival rate to hospital discharge from IHCA increased significantly (from 24% to 43%)
  
  Girota, Circ Cardiovasc Qual Outcomes 2013

- **Pediatric**: OHCA survival remains poor (3.3% for infants <1yr; 9.1% for children, 1-11yrs; 8.9% for adolescents, 12-18yrs)
  
  Atkins, Circulation 2009

- **Good neurologic outcome** is reported in approximately 60% of survivors – First cause of neurological consultation in the PICU
  
  Hickey, Neurol Clin 2006
Prognostication After Cardiac Arrest

Early and reliable prognostication of neurologic outcome in pediatric survivors of cardiac arrest is essential to enable effective **planning level of care** and **family support** (whether it be to continue or discontinue life-sustaining therapies) – **end-stage disease**.
Prognostication After Cardiac Arrest

Withdrawal of care in a child with a potentially salvageable quality of life

NEGATIVE

POSITIVE

Survival of a child with devastating neurological deficit and no quality of life
Prognostication After Cardiac Arrest

Prognostication in comatose survivors of cardiac arrest: An advisory statement from the European Resuscitation Council and the European Society of Intensive Care Medicine

Days 1-2

Cardiac arrest

Controlled temperature

Rewarming

(2014) 1779–1789
Prognostication After Cardiac Arrest

Prognostication in comatose survivors of cardiac arrest: An advisory statement from the European Resuscitation Council and the European Society of Intensive Care Medicine

Days 1-2
- Cardiac arrest
  - Controlled temperature
  - Rewarming
  - Exclude confounders, particularly residual sedation
  - Unconscious patient, M=1-2 at ≥72h after ROSC
    - One or both of the following:
      - No pupillary and corneal reflexes
      - Bilaterally absent N20 SSEP wave
    - Wait at least 24h

Days 3-5
- Magnetic Resonance Imaging (MRI)
- EEG, NSE
- SCRT

Two or more of the following:
- Status myoclonus ≤48h after ROSC
- High NSE levels
- Unreactive burst-suppression or status epilepticus on EEG
- Diffuse anoxic injury on brain CT/MRI

Indeterminate outcome
- Observe and re-evaluate

Use multimodal prognostication whenever possible

(1) At ≥24h after ROSC in patients not treated with targeted temperature
(2) See text for details.

(2014) 1779–1789
Prognostication In Children

- **Definition** of good/poor outcomes is variable
- 30-50% of “good outcome” may have below-average scores on the Mental **Developmental Index**

*Robertson PCCM 2002*

- Decision for withdrawal of care (parents; no blinding)
- **Treatment programs**
- Additional recovery – **long-term** evaluation
2015 Recommendation—New
EEGs performed within the first 7 days after pediatric cardiac arrest may be considered in prognosticating neurologic outcome at the time of hospital discharge (Class IIb, LOE C-LD) but should not be used as the sole criterion.
2015 Recommendation—New
The reliability of any 1 variable for prognostication in children after cardiac arrest has not been established. Practitioners should consider multiple factors when predicting outcomes in infants and children who achieve ROSC after cardiac arrest (Class I, LOE C-LD).
Prognostication - Clinics

- 26/42 with poor outcome; PPV for poor outcome was 91% [CPR>10 min; GCS<5; absence breathing and PLR at 24 hours]
  
  Mandel, J Pediatric 2002

- **Motor Response** had a specificity of 53% to predict poor outcome (absent PLR of 100%)
  
  Carter, Intensive Care Med 2005

- **Absent motor and pupillary responses** had a PPV for poor outcome of 100% at 24 hours after arrest
  
  Abend, Ped Crit Care Med 2012
Prognostication - EEG

Electroencephalogram (EEG)

- Electrodes
- Brain

EEG reading
Prognostication - EEG

- 26/42 with poor outcome; PPV for poor outcome was 100% for discontinuous EEG activity (<10μV), epileptiform EEG activity
- Suppressed tracing or flat EEG = poor outcome

- Unreactive pattern

- Sleep waves / Continuous

Mandel, J Pediatric 2002
Pampiglione, Lancet 1968
Tasker, Arch Dis Child 1988

Ducharme-Crevier, Ped Crit Care Med 2017
Prognostication - EEG

- High PPV for a poor outcome for unreactive EEG or discontinuous background both during TH and NT

<table>
<thead>
<tr>
<th>EEG category</th>
<th>PPV for unfavorable outcome (95% CI)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Hypothermic</td>
</tr>
<tr>
<td>Continuous and reactive</td>
<td>27% (12–42%)</td>
</tr>
<tr>
<td>Continuous and unreactive</td>
<td>80% (67–93%)</td>
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<tr>
<td>Discontinuous and/or suppressed</td>
<td>93% (84–100%)</td>
</tr>
<tr>
<td>Continuous and unreactive or discontinuous and/or suppressed</td>
<td>88% (77–98%)</td>
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</tbody>
</table>

n=35

*Kessler, NCC 2011*
Prognostication - EEG

Early electroencephalographic findings correlate with neurological outcome in children following cardiac arrest

*Pediatr Crit Care Med. 2016*

Adam P. Ostendorf, M.D.¹, Mary E. Hartman, M.D., M.P.H.², and Stuart Friess, M.D.²

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**0 to ≤12 hours post-ROSC (n=43)**

- Seizures present: 5
- Seizures absent: 15
- Score 1-3: 10
- Score 4-5: 13

**12 to <24 hours post-ROSC (n=19)**

- Seizures present: 1
- Seizures absent: 10
- Score 1-3: 6
- Score 4-5: 5
Electroencephalographic monitoring during hypothermia after pediatric cardiac arrest

N.S. Abend, MD
A. Topjian, MD
R. Ichord, MD
S.T. Herman, MD
M. Helfer, MD
M. Donnelly, REEGT, RPSGT
V. Nadkarni, MD
D.J. Dhugos, MD, MSCE
R.R. Clancy, MD

47% seizures (mostly NCSz)

47% seizures (mostly NCSz)

Neurology® 2009;72:1931-1940
**AWAKENING**

**DAY 1-2**
- Continuous Pattern Reactive EEG

**DAY 3-4**
- Continuous Pattern Reactive EEG

**DAY 5-7**
- Malignant Patterns Unreactive EEG

**PROBABLE AWAKENING**

**NEUROLOGICAL EXAMINATION**
- EEG
- MR PLR

**PROBABLE POOR RECOVERY**
- Malignant Patterns Unreactive EEG

**NO RECOVERY**
- Malignant Patterns Unreactive EEG

**LONG-TERM SUPPORT**
Prognostication - SSEPs

- 26/42 with poor outcome; PPV for poor outcome was 100% for absent N20 on SSEPs
- Prediction of poor outcome: sensitivity of 75% and specificity of 92%
- Prediction of poor outcome: sensitivity of 61% and specificity of 95% *
- PPV of poor outcome of 92% *

Mandel, J Pediatric 2002
Carter, ICM 1999
Carter, ICM 2005
Beca, J Pediatric 2002
De Meirleir, Pediatric Neurol 1987
PROBABLE AWAKENING

DAY 1-2
Continuous Pattern
Reactive EEG

DAY 3-4
Continuous Pattern
Reactive EEG

DAY 5-7
Continuous Pattern
Reactive EEG

PROBABLE POOR RECOVERY

Malignant Patterns
Unreactive EEG

Malignant Patterns
Unreactive EEG

Bilateral absent N20

NO RECOVERY
Prognostication - Biomarkers

Neuron-specific enolase and S-100B are associated with neurologic outcome after pediatric cardiac arrest*  

*Pediatr Crit Care Med 2009:

Alexis A. Topjian, MD; Richard Lin, MD; Marilyn C. Morris, MD; Rebecca Ichord, MD; Henry Drott, PhD; Carey R. Bayer, EdD, RN; Mark A. Helfaer, MD, FCCM; Vinay Nadkarni, MD, FCCM

<table>
<thead>
<tr>
<th>Marker</th>
<th>Cutoff (μg/L)</th>
<th>Time (Hrs)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Posttest Probability (%)</th>
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<tr>
<td>NSE</td>
<td>51</td>
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<tr>
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<tr>
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</tbody>
</table>

critical care canada FORUM
Leading Science. Leading Practice.
Prognostication - Biomarkers

Serum Biomarkers of Brain Injury after Pediatric Cardiac Arrest

Crit Care Med. 2014

Ericka L Fink, MD, MS1, Rachel P Berger, MD, MPH6, Robert SB Clark, MD1, Robert S Watson, MD, MPH1, Derek C Angus, MD, MPH2, Rudolph Richichi, PhD5, Ashok Panigrah, MD4, Clifton W Callaway, MD, PhD3, Michael J Bell, MD1, and Patrick M Kochanek, MD1

n=43

AUC = 0.96

AUC = 0.86
Prognostication - Biomarkers

Trajectory Analysis of Serum Biomarker Concentrations Facilitates Outcome Prediction after Pediatric Traumatic and Hypoxemic Brain Injury

Dev Neurosci 2010;32:396–405

b

NSE concentration (ng/ml)

Time epoch (No.)

Low decliners

Transient risers

Sustained risers

0
50
100
150
200
250

0.2
0.4
0.6
0.8
1.0
1.2

$c$

S100B concentration (ng/ml)

Time epoch (No.)

Low decliners

Transient late risers

Delayed late risers

Sustained late risers

Biomarkers of CNS Injury

Biomarkers

NSE

S-100B

Biomarkers of S-100B

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PROBABLE AWAKENING

DAY 1-2
Continuous Pattern
Reactive EEG

DAYS 3-4
Continuous Pattern
Reactive EEG

DAYS 5-7
Continuous Pattern
Reactive EEG

PROBABLE POOR RECOVERY

EEG
NSE
CT-scan

Continuous Pattern
Reactive EEG

Malignant Patterns
Unreactive EEG

MR
PLR

M_1.2
PLR -/-

EEG
SSEPs
NSE

High NSE Levels

Malignant Patterns
Unreactive EEG

NO RECOVERY

Bilateral absent N20

NEUROLOGICAL EXAMINATION

LONG-TERM SUPPORT
Prognostication - Imaging

- Brain volume (global, hippocampus, temporal)
- Loss of N-acetyl aspartate and delayed lactate peak in the gray matter
- Diffusion-weighted imaging (DWI) = ischemia
- Diffusion tensor imaging (DTI) = development and orientation of axonal fibers and astrocytes
Prognostication - Imaging

- Early injury (ischemia) had a PPV of 82% and a NPV of 86% in children with HIE
  
  *Christophe, AJNR Am J Neuroradiol 2002*

- Absence of ischemia on DWI = all survived (n=5); when DWI showed lesions, ROI associated with poor outcome were cerebral cortical, basal ganglia and cerebellum (n=15)

  *Ouahla, Intensive Care Med 2013*
PROBABLE AWAKENING

DAY 1

- Continuous Pattern Reactive EEG

DAY 2

- Continuous Pattern Reactive EEG

DAY 3-7

- Probable Poor Recovery
  - High NSE Levels
  - Malignant Patterns Unreactive EEG

NO RECOVERY

- Bilateral absent N20

LONG-TERM SUPPORT

- Normal

EEG

NSE

CT-scan

MR

PLR

EEG

SSEPs

NSE

MRI

Malignant Patterns Unreactive EEG

M_1-2 PLR -/-

Ischemia
Multi-Modal Approach
Prognostication After Cardiac Arrest

Neuroprognostication After Pediatric Cardiac Arrest

Matthew P. Kirschen, MD, PhD\textsuperscript{a,b,\textdagger}, Alexis A. Topjian, MD, MSCE\textsuperscript{b}, Rachel Hammond, MS\textsuperscript{c}, Judy Illes, PhD\textsuperscript{d}, and Nicholas S. Abend, MD\textsuperscript{a}

n=18 (0.9-3.4 yrs) surviving ≥ 7 days

n=10
- Neurologists
- Intensivists

n=9

Kappa Statistic

Substantial

Moderate

Fair
Conclusions

- ERC/ESICM guidelines help to prognosticate adult survivors with anoxic brain injury

- Not applicable in children

- Neuro-prognostication remains a complex challenge for clinicians
  - Multi-modal approach
  - Knowledge gaps
  - Multicentric cooperation
  - New “tools”