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Relation Between Time to Arousal and Neurologic Outcomes in Cardiac Arrest Patients Treated with Therapeutic Hypothermia

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Speaker Disclosures

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- Presenter: Anne V Grossestreuer, MSc

- Disclosures: None

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Penn Alliance for Therapeutic Hypothermia (PATH) registry

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- National US registry for data sharing and collaboration on therapeutic hypothermia after cardiac arrest
- Tracks data points related to cardiac arrest and post-cardiac arrest care
- Benchmarks between institutions across the country
- Uses this data to implement the best practice of therapeutic hypothermia (TH) nationally

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Objectives

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- To determine the length of time it takes cardiac arrest patients to regain arousal after cardiac arrest and TH
- Examine factors that affect time to arousal

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Background

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- **Neuroprognostication before Targeted Temperature Management:** American Academy of Neurology neuroprognostication guidelines for comatose SCA patients
  - detailed neurologic exam at 72 hours after arrest
    - myoclonic status epilepticus
    - serum neuron-specific enolase (NSE)
    - somatosensory evoked potential (SSEP)
    - pupillary light response
    - corneal reflexes
    - **motor responses**

Wijdicks EF, Hijdra A, Young GB, Bassetti CL, Wiebe S. Practice parameter: prediction of outcome in comatose survivors after cardiopulmonary resuscitation (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2006;67:203–10

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- Literature support both ways?

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Studies Looking at Time to Arousal

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- **Chandra-Strobos "A Paradigm Redefined: Time Course of Neurological Recovery Following Hypothermia Therapy Post Non-Traumatic Out-of-Hospital Cardiac Arrest"**
  - Patient population: 47 patients with out of hospital arrests; 15 treated with TH (57% with VF as initial rhythm)
  - Findings: Meaningful awakening can occur 7+ days post arrest in patients treated with TH
- **Mayo Neurology paper**
  - Patient population: 227 patients with out of hospital arrests; 128 treated with TH (88% with VF as initial rhythm)
  - Findings: Hypothermia does not delay time to arousal past 72 hours post-arrest

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Methods

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- **Inclusion Criteria:**
  - Patients had a cardiac arrest (any initial rhythm) with ROSC and received therapeutic hypothermia between 2005-2011
  - 3 Hospitals Cohort:
    - Hospital of the University of Pennsylvania
    - Penn Presbyterian Medical Center
    - Pennsylvania Hospital
- **Exclusion Criteria:**
  - Traumatic arrests
  - < 18 years of age
- **Definition of Regaining Arousal:**
  - Purposeful movement
  - Measured by a patient's first recorded Glasgow Motor Score of 6 or a chart notation of purposefully following commands
- **Definition of Neuro Outcome:**
  - return to neurologic baseline (pre-arrest) or GCS 14-15

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Hypothermia Protocol

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- Temperature management was provided using a surface cooling device; most patients also received chilled saline and/or ice bags
- Target temperature, 33°C (with an acceptable range of 32-34°C), was maintained for 24 hours
- Rewarming, at 0.33°C/hour, was done actively using a surface cooling device

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Results: MAKE INTO TAB

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- N = 192
- Mean age = 57±16 years
- 108/192 (56%) were male
- Initial rhythm was VF/VT in 73/190 (38%)
- Survival to hospital discharge was achieved in 82/192 (43%)
- 59/82 (72%) had a good neurological outcome
- **Hypothermia was maintained for 24.0±7.0 hours**
- **Rewarming took place over a mean of 17.4±12.4 hours**

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Results

	n (%)	Mean Time (days)	Range (days)	p
Patients who Regained Arousal	81 (42)	3.8±2.6	0.5 - 14.5	
Survival to Discharge				
Yes	70 (86)	3.6 ± 2.4	0.5 - 14.5	0.26
No	11 (14)	4.5±3.4	1.3 - 13.7	
Discharged Neurologically Intact				
Yes	59 (84)	3.2±1.6	0.5 - 7.4	<0.01
No	11 (16)	6.2±4.5	2.5 - 14.5	

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Results

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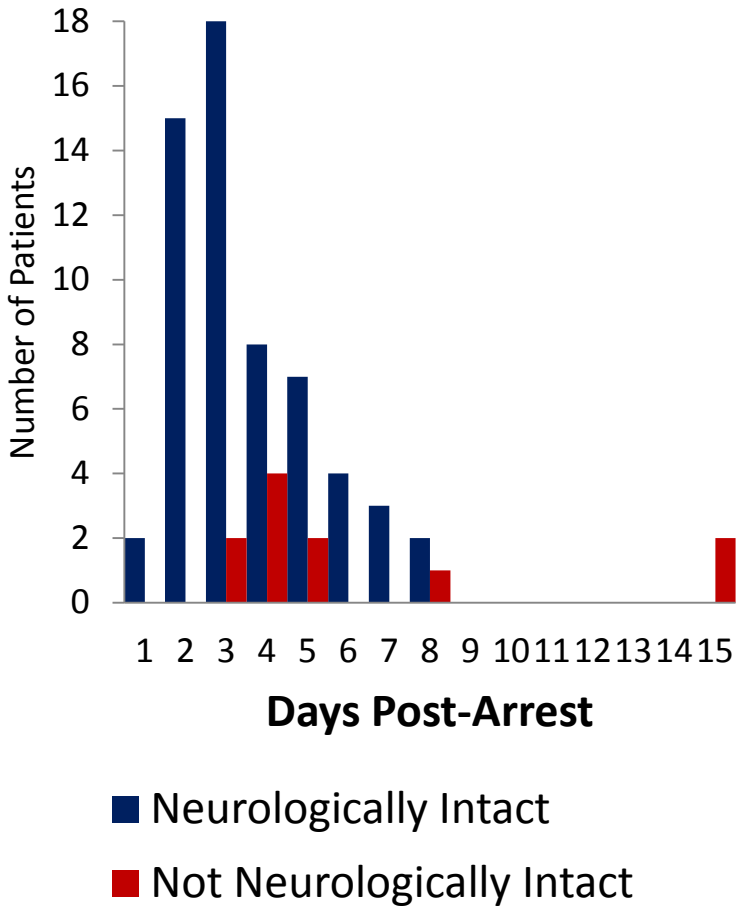
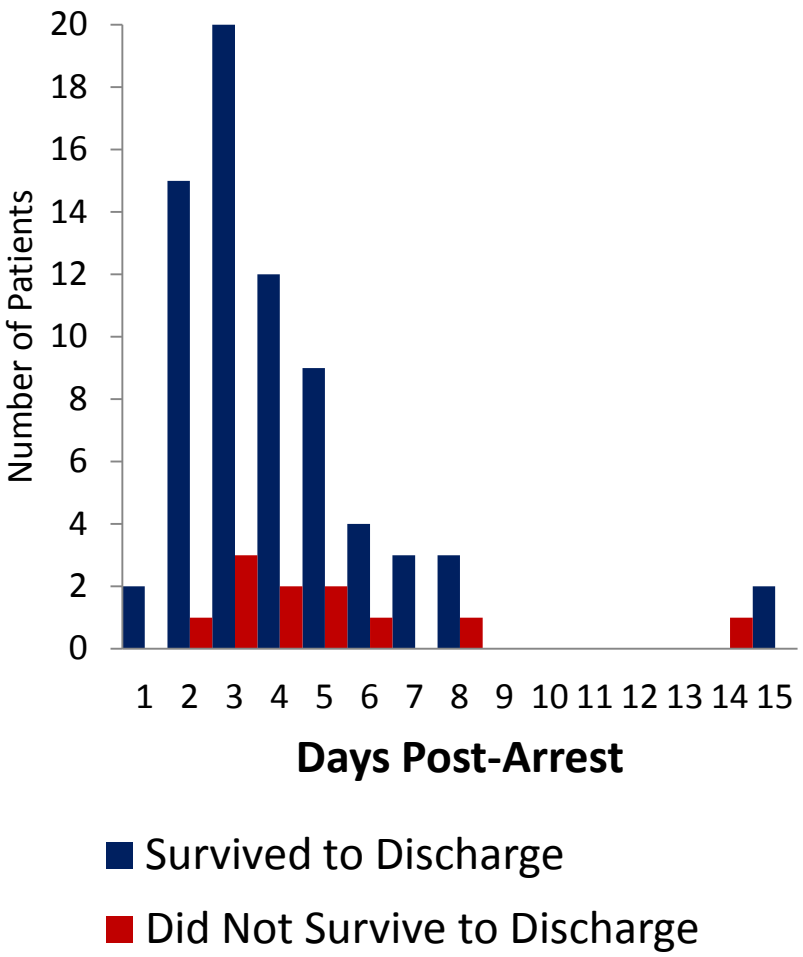
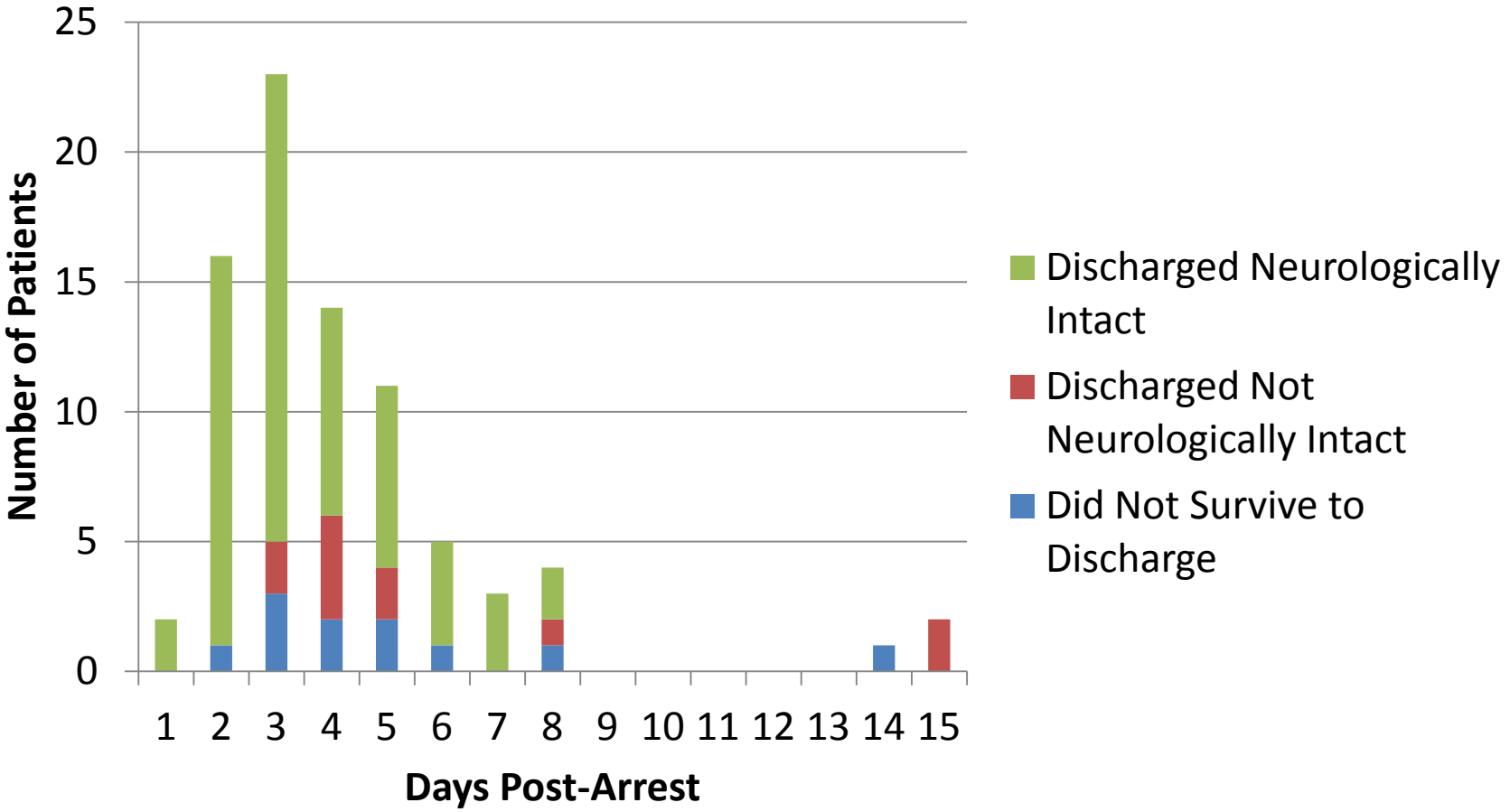
Time to Arousal by Neurologic Outcome at Discharge



Days to Arousal



Alternate Chart



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Results

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- No Association with Time to Arousal
  - Age, Gender (female: 3.6 ± 2.4 days; male: 3.9 ± 2.7 days), Race
- DNR
  - 94 patients were made DNR by family during their hospital course
  - 39/94 (41%) patients had care withdrawn during the 72 hours post-arrest
  - Of the patients who regained arousal but expired before discharge, 9/11 (82%) were made DNR (comfort care only) by family

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Important Findings

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	Mean Time to Wake Up (days)	p
Neurologically Intact	3.2 ± 1.6	<0.01
Not Neurologically Intact	6.2 ± 4.5	
No Renal Insufficiency	3.4 ± 2.1	0.02
Renal Insufficiency	5.2 ± 3.9	
Paralytic Used	3.5 ± 2.1	0.07
No Paralytic Used	5.4 ± 6.0	
VF/VT Arrest	3.1 ± 1.6	0.02
PEA/Asystole Arrest	4.4 ± 3.3	
Out of Hospital	3.5 ± 2.2	0.17
In Hospital	4.4 ± 3.5	

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Limitations

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Conclusions

- Time to arousal after resuscitation and TH use is highly variable, and often longer than 3 days
- Earlier arousal is associated with better neurologic status on hospital discharge
- Time to arousal is prolonged in patients with renal insufficiency
- Further research is required to determine optimal timing of neuroprognostication in the post-arrest setting

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Out of Hospital Shockable Arrests

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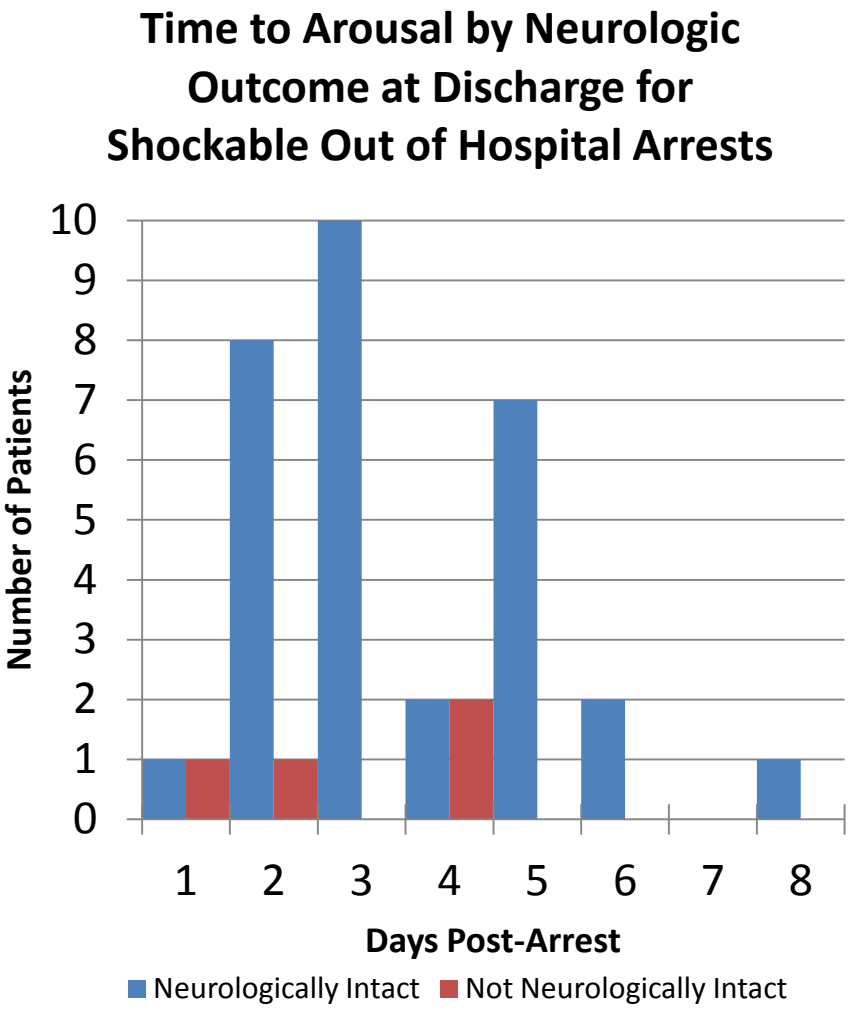
- 62/192 (32%) of patients who received TH arrested outside of the hospital and had a shockable initial rhythm
- 38/62 (61%) survived to discharge
- Mean time to wake up was 3.0 ± 1.5 days (range: 0.5 – 7.4 days)
- Of those who regained arousal
  - 33/35 (94%) survived to discharge
  - 31/35 (89%) had a good neurologic outcome at discharge
  - 12/35 (34%) regained arousal later than 72 hours post-arrest and were discharged with a good neurologic outcome



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Causes of in-hospital death after arousal

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- re-arrest (27%)
- hemodynamic instability (27%)
- sepsis (9%)