Identifying Best Practice for Out-of-Hospital Cardiac Arrest (OHCA) in the Hospital Setting

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Post-cardiac arrest syndrome

- Unique pathophysiologic process involving multiple organs
  - Global tissue and organ injury
  - Reperfusion injury
  - On-going inflammation and injury

- Key components
  - Systemic ischemia / reperfusion response
  - Post arrest brain injury
  - Post arrest myocardial dysfunction

Neumar RW et al. Circ. 2008;118:2452-2483
Post-cardiac arrest syndrome

- “Cardiac” arrest becomes a misnomer
  - From the time the heart restarts it becomes a neurological and systemic disease

- This changes the traditional paradigm of clinical treatment
  - Need to shift focus from supporting cardiac function to supporting neurological and systemic systems

- Poses simultaneous multidisciplinary issues
  - Requires different treatment goals than 10-20 yrs ago

- Young field lacking a home
Guideline-supported best practice for post-arrest care

- Comatose adult patients post-ROSC from OHCA with VF as the initial rhythm should be treated with TH at 32 – 34°C for 12 -24 hours
- HACA
- Australian study
- > 40 non randomized clinical studies in adults
- Supporting studies in neonates
- TTM (36°C for 36 hours)

Hypothermia after CA study group. NEJM 2002;346:549-56.
Bernard SA. NEJM 2002; 346:557-63
Nielsen N. NEJM 2013;369:2197-206
Guideline-supported best practice for post-arrest care

- **Avoid fever**
  - Pyrexia is common post arrest
    - Neurologically mediated
    - Infection
    - Inflammation, cell necrosis
  - Fever is associated with poor survival
  - Risk of poor neurological outcome increases for each degree body temperature over 37 ºC in CA patients
  - May negate benefit of hypothermia


Guideline-supported best practice for post-arrest care

- **Maintain oxyhemoglobin saturation between 94-99 %**
  - Ventilation with 100% oxygen in the first hour after experimental CA results in worse neurologic outcomes
  - Multiple species
  - Cells in a high O2 environment have higher ROS production and decreased mitochondrial respiratory function than cells in normoxic conditions

<table>
<thead>
<tr>
<th></th>
<th>% of cases</th>
<th>Mortality</th>
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<tbody>
<tr>
<td><strong>Hyperoxia</strong></td>
<td>18%</td>
<td>63% [60%, 66%]</td>
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<tr>
<td><strong>Normoxia</strong></td>
<td>63%</td>
<td>45% [43%, 48%]</td>
</tr>
<tr>
<td><strong>Hypoxia</strong></td>
<td>19%</td>
<td>57% [56%, 59%]</td>
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Kilgannon et al. JAMA 2010; 03(21):2165-2171
Guideline-supported best practice for post-arrest care

- Avoid hyper- and hypo-capnea
  - Cerebrovascular reactivity to carbon dioxide tension
    - Hyperventilation
      - Cerebral vasoconstriction – ischemia
    - Increase ITP and lowers CO
  - Hypoventilation
    - Cerebral vasodilation
    - Cerebral edema

Guideline-supported best practice for post-arrest care

- 12 lead ECG ASAP and patients with evidence of STEMI should be treated the same as patients w/o CA, including emergent PCI, irrespective of coma.

- Reasonable to consider urgent catheterization for non-STEMI CA.

- Vasoactive drugs and fluid should be titrated to optimize BP, CO, and systemic perfusion.

- Moderate glucose control is important.
Guideline-supported best practice for post-arrest care

- EEGs should be performed either continuously or frequently during cooling and re-warming
  - Seizures are common after CA (15-40%)
  - Commonly subclinical even in the absence of drugs
  - May also be masked by sedation and paralytics
  - If you don’t look you won’t find them
  - If you don’t know they are there you can’t treat them
  - ? prevention
  - ? appropriate treatment

- Observation > 72 hours is needed in pts treated with TH prior to prognostication and withdrawal of care
  - Traditional prognostication w/o TH can occur on day 3
  - Longer times needed for awakening post CA with TH
  - Often happens on day of admission in “real world”
  - Optimal timing unknown
In-hospital factors associated with improved outcome from OHCA

- Protocol
  - Hemodynamic optimization
  - Oxygenation / Ventilation
  - Hypothermia x 24h
  - Blood glucose
  - Electrolytes
  - Seizure control

- 4 regions in Norway

Langhelle A et al. Resuscitation 2003; 56:247-63
Inter-hospital variability in post-cardiac arrest mortality

**Patient Volume**

- High acuity, high complexity, low volume
  - Largest risk for system failure

- Hundreds of people per hospital that need to be trained to do this well
  - Emergency physicians & nurses, ICU specialty physicians & nurses, cardiologists, neurologists, RT, housestaff, moonlighters, rehabilitation
  - Challenge of updating knowledge in a rapidly changing field

- Not just what you do but how well you do it

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Hospitals treating more than 50 CA per year had significantly better survival than those treating less than 20 CA per year

OR 0.62, 95% CI 0.45-0.86

Carr et al. Resuscitation 2009;80:31-34
Regionalization of post-resuscitation care

Hospital role

Nichol et al. Circulation 2010; 121:709-29

- EMS medical director works with hospitals to develop a regional plan

- **Level 1 centers** – PCI capable, therapeutic hypothermia + **comprehensive system of care**

- **Level 2 (induction) centers**
  Stabilize and transfer to Level 1 centers as soon as possible

- Quality improvement

- Feedback loop
Spoke and hub model
- Many other similar successful programs
1.5 year planning process
- Garner administrative/clinical support and provide training

ARCTIC Team
- EM physicians and nurses
- ARCTIC attendings – only 5 dedicated physicians
- CCU fellow
- CCU NP
- Medical director
- Full time RN ARCTIC coordinator

ARCTIC Alert from field
- VCU never on diversion for ARCTIC pts

Clinical consistency

Education

Feedback and single contact for EMS and induction centers

Provides long term neurocognitive follow-up
EM team focuses on stabilizing patient
- Initiates early goal directed therapy for hemodynamics, ventilatory support, metabolic support, neuroprotection

Endovascular cooling strategy with 4 dedicated machines
- ARCTIC team places cooling catheter and begins standard post-arrest care
- Controlled re-warming

Expeditious treatment of STEMI
- Concomitant PCI and cooling in lab

Patients admitted to only one ICU (CICU) with specially trained, dedicated ARCTIC nurse staffing
Goal directed therapy
- Hemodynamic
- Ventilation /Oxygenation
- Metabolic
- Continuous EEG monitoring

Standardized electronic orderset for first 3 days
- Teaching points

72 hr moratorium on withdrawal of life support

1 hour battery of neuropsychiatric testing prior to discharge

3 month post discharge detailed neuro-cognitive testing with brain injury specialists

3 and 6 month phone follow-up

EMS feedback on all cases

Continuous quality review of data and ongoing evidence based system changes
- Bi-annual clinical pathway review

NIH and AHA funded research hub
Induction Centers

- ARCTIC program provides on-site and on-line live education and training for nursing & physician staff
- Dedicated phone line to VCU transfer center for consulting with one of five ARCTIC attending physicians
- Initiate external cooling
- Protocol management of bundled care / paralytics / sedatives
- Air or ground transport
  - If STEMI treated on site, transport dispatched and waiting for PCI to be completed
- Survivors return to their prior physicians care
Neurocognitive outcome assessment

- Not just a research issue
- Major clinical issue
- Discharge planning / safety
- Family dynamics
- No mechanisms for routine assessment
- What is the best tool to assess
  - Must include memory, executive functioning, visuospatial function
- No follow-up
- No third party payer coverage for cognitive rehabilitation
Neuro-cognitive testing

- Repeatable Battery for the Assessment of Neuropsychological Status
  - Immediate memory
    - List learning
    - Store memory
  - Visuospatial / constructional orientation
    - Complex figure copy / trail making
    - Line orientation
  - Language
    - Picture naming
    - Semantic fluency
  - Attention
    - Digit spanning
    - Coding
  - Delayed memory
    - Recall of above
- Beck Depression Scale
Cognitive impairment after cardiac arrest in CPC 1 & 2 and MRS ≤3 patients

Peberdy MA et al. Presented ReSS 2013. Dallas, Tx

Cognitive impairments after cardiac arrest: CPC 1 and CPC 2

- Impaired (below cutoff score)
- Mildly Impaired (below expectations)
- Severely Impaired (at or below 10th percentile)

- Verbal Fluency
- Immediate Auditory Attention
- Sustained Auditory Attention
- Immediate Visual Attention
- Sustained Visual Attention
- Information Processing Speed
- Auditory Learning
- Visual Memory
- Fine Motor Speed (Dexterity Dominant Hand)
- Immediate Auditory Memory
- Delayed Auditory Memory
- Visuoconstruction
- Visual Analysis
Why aren’t more hospitals providing comprehensive post-arrest care?

- Too few pts, too many hospitals
  - Very resource intensive for 5-10 pts a year
- No single specialist
  - General intensivist, cards, pulmonary, anesthesiology, never neurology as primary doc
  - Lack of adequate reimbursement for daily multispecialty care
- Hard to garner institutional and multidisciplinary support
  - Fatalistic attitude – sadly still exists
- Lack of EEG availability and real time reading
- Fear of loosing STEMI patients – want STEMIs but not really CA –halo effect for EMS
- Public reporting of PCI
Public reporting of PCI data and its impact on CA centers

- CA mortality high compared to non-CA STEMI
- Very inhomogeneous group
  - Survival ranging from <10-90% (50%)  
  - Difficult to adequately risk adjust
- CA Centers have proportionately higher “poor outcome” STEMIs than non CA treating hospitals
- Purpose of public reporting
  - Identify centers with “good” or “poor” PCI quality
  - CA deaths are rarely related to the PCI
  - An additional 20 CA STEMI cases results in ~ 8 more deaths annually – triples PCI mortality for that hospital
- Boston experience 2011
- Ethical considerations
- AHA Statement: Track but not publically report PCI in CA
Why aren’t more hospitals providing comprehensive post-arrest care?

- ICU beds are costly
  - Early withdrawal
  - Hard to tie up a bed for 5-7 days when you don’t know if pt will ever wake up
    - Research impact for funding trials long enough to be able to tell outcome

- No post arrest care disease specific DRG
  - No more reimbursement for a lot of extra effort
  - CA – paid same if you withdraw on day 1 or 7
  - Hypothermia DRG = ice on sprain and not neuroprotection for a critically ill patient
Ideal best practice post-arrest program

- Dedicated, engaged leadership with limited numbers of multidisciplinary practitioners to help standardize care
- Ongoing post arrest training to hospital based and EMS providers
- Ability to rapidly translate new data into clinical practice
- High volume so clinicians can get good at what they do
- Ability and willingness to take appropriate post arrest comatose patients to the catheterization lab – free from repercussion
- True implementation of bundled care – TH, PCI, hemodynamic management (continuous $S_cVO_2$ – systemic and cerebral) there are levels of how “much” to do this
Ideal best practice post-arrest program

- EEG monitoring and real time interpretation ability
- Early DNAR “moratorium”
- Family support
- Detailed neuro-cognitive testing with follow-up at discharge
- Ability to send patients to cognitive rehabilitation when needed and have it covered by insurance
- Survivor and family support group
Major gaps to clinical progress

- Limited understanding of human cellular derangements seen in post arrest syndrome
- Depth, duration and mechanisms of TH
- Better tools to assess systemic and cerebral perfusion
- Cerebral monitoring
  - EEG – seizure prevention, identification and treatment
  - Invasive
- Investigation into non-shockable rhythms
- Prognostication
- Early withdrawal
- Neuro-cognitive outcomes assessment
Major issues for research progress

- Lack of research consortium of high volume, early adopter, high performance centers able to control standardization of care to provide a stable platform for bidirectional translational and clinical research

- Final common pathway for any CA interventional trial
  - Trials won’t work if you withdraw care on day 1
  - Must standardize care to a significant degree
  - Require infrastructure development in many hospitals for a small number of enrolled pts per hospital –too costly to be available to screen and enroll 24/7 for handful of pts per year
  - CA “research center” – has to be at forefront
  - If we do not make some attempt to standardize best practice / policy for post arrest care then the outcomes (survival, neuro outcome etc) for all CA interventional trials is doomed to the whim of the individual doc in the ED and ICU.

- Funding
Rapid Induction of Therapeutic Hypothermia & Possible Transport to Dedicated Center

Maintenance of TH & Multidisciplinary Goal-Directed Therapies

Controlled Re-warming, Recovery, Assessment, Rehabilitation, Quality Improvement Feedback loop
Objectives

- Discuss post arrest syndrome pathology
- Describe guideline driven best practice
- Identify best practice “beyond the guidelines”
- Provide an example of a successful comprehensive post arrest program
- Identify challenges to widespread clinical implementation
- Identify challenges to advancements in research
Guiding Principles for Regionalization of Post-Arrest Care

- Patient centered care
- Full circle integration with EMS, community, and induction centers
- High volume
- High quality, truly multidisciplinary care, that is safe, effective, timely, and available 24/7
- Stakeholder consensus on system infrastructure
- Measurable patient outcomes
- Evaluation mechanism to ensure that quality of care measures rapidly reflect changes in evidence-based research
- A role for all local community hospitals so as to avoid a negative impact that could eliminate critical access to local healthcare
- Reduction in disparities of healthcare delivery
- Pockets of hospital excellence
  - can it be disseminated?
  - should all be trying?
Do we have all the answers – No

- But we cannot wait for RCTs to tell us where to make the next move
- None underway in this area currently in US
- If an RCT was funded tomorrow it would likely be 10-15 years for the results to be widely translated into clinical practice
- Another 6 million people will be dead by then
- We need to borrow what is known from similar disease states (TBI and sepsis may be the closest) and begin making smaller, more frequent steps of progress
  - Should all 6000 US hospitals be trying?
- Very young field but the clinical demand has rapidly outstripped our knowledge