Post-Cardiac Arrest Management: Hmm........“Now what!?”

Dr. Ben Wilson MD CCFP (EM)
NOW WHAT??

• WHAT PATHOLOGY IS PRESENT THAT NEEDS TREATMENT?

• WHAT THERAPIES WILL PROVIDE THE GREATEST BENEFIT FOR SURVIVAL AND FUNCTIONAL OUTCOME?
  • AND WHAT OPTIONS ARE PRESENT AT YOUR SITE??

• WHAT CAN I TELL THE FAMILY ABOUT PROGNOSIS AT THIS POINT?
Case: 62 yoM RG: sudden collapse at home

• **HPC**: cleaning out garage with son when fell to the ground. Son trained in first aid – no pulse, started compressions. Mom called 911. 12 minutes to arrival.
Case: 62 yoM RG: sudden collapse at home

• **EHS**: pulseless, shock indicated/delivered x 1 and *ROSC achieved*. Intubated with ETT, epi 1mg x 1 given, no other drugs required en route.

• **ED vitals**: GCS 4, Pupils 3mm unreactive. BP 85/60, P 95, SpO2 100 on 100% O2 bagged. BG 10

• **ECG**: no STE. Nonspecific T-inversion in precordial leads.
Out of Hospital Cardiac Arrest (OHCA): US Epidemiology data from R.O.C. (1)

- **424,000 cases per year** – 5.2% overall survival
- **211,000 cases treated by EMS** – 10.4% survival
- **42,000 with shockable rhythm, treated by EMS** – 28.3% survival
- **24,000 shockable by EMS and bystander witnessed** – 31.7% survival
  - Better survival (ARR= 1.7%, 3587 patients) with continuous compressions
Resuscitation Outcomes Consortium

- 11 regional centres: 8 in US, 1 in Canada
- coordinated by University of Washington
- investigation and quality improvement in pre-hospital care for OHCA and trauma
“Well his heart has already restarted, so we’re done there.

But GCS 4 and no corneal or pupillary light reflex? I’ll have to tell the family there's not much hope.

But first I should see the guy with bad back pain that keeps bugging the nurses...”
STOP! Prognosis before 72h is problematic. Sandroni et al. Systematic Review. Resus. 2013. (2,3)

<table>
<thead>
<tr>
<th>PROGNOSTIC FEATURE</th>
<th>SENSITIVITY TO IDENTIFY POOR OUTCOME (CPC4-5)</th>
<th>FALSE POSITIVE RATE</th>
<th>N OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCS &lt;= 4 on admission</td>
<td>74%</td>
<td>40%</td>
<td>62</td>
</tr>
<tr>
<td>Motor score 1 at 24hrs</td>
<td>63%</td>
<td>6%</td>
<td>67</td>
</tr>
<tr>
<td>PLR absent at 6-12hrs</td>
<td>33%</td>
<td>25%</td>
<td>31</td>
</tr>
<tr>
<td>“       ” at 24 hrs</td>
<td>21%</td>
<td>9%</td>
<td>496</td>
</tr>
<tr>
<td>PLR and CR absent at 24hrs</td>
<td>14%</td>
<td>5%</td>
<td>386</td>
</tr>
</tbody>
</table>

PLR= pupillary light reflex; CR=corneal reflex
<table>
<thead>
<tr>
<th>Good outcome</th>
<th>Bad outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Conscious and alert with normal function or only slight disability.</td>
</tr>
<tr>
<td>2</td>
<td>Conscious and alert with moderate disability.</td>
</tr>
<tr>
<td>3</td>
<td>Conscious with severe disability.</td>
</tr>
<tr>
<td>4</td>
<td>Comatose or persistent vegetative state.</td>
</tr>
<tr>
<td>5</td>
<td>Brain dead or death from other causes.</td>
</tr>
</tbody>
</table>
72hrs is the earliest time that FPR approaches 0 for some indices of prognosis.

2015 AHA GUIDELINES: (4)

• Prognostication at 72 hrs post-ROSC if no TTM

• Prognostication at 72 hrs post-rewarming if TTM
THE RIGHT ATTITUDE...
Vladimir Negovsky (1909-2003)
“The father of reanimatology” (5)

- first to discover external chest compressions (dogs)
- first to demonstrate DC cardioversion (poor dogs)
- not until 10 years later (’50s) that rediscovered in US!
Post-resuscitation disease — a new nosological entity.
Its reality and significance

Vladimir A. Negovsky*, Alexander M. Gurvitch

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Bld. 2, Moscow, Russian Federation

Received 18 February 1995; accepted 24 March 1995
ILCOR Consensus Statement

Post–Cardiac Arrest Syndrome
Epidemiology, Pathophysiology, Treatment, and Prognostication

Circulation 2008. (7)
The Post-Cardiac Arrest Syndrome (PCAS)

4 MAIN COMPONENTS

1. PERSISTING PRECIPITATING PATHOLOGY
2. POST-ARREST MYOCARDIAL STUNNING
3. SYSTEMIC ICHEMIA/REPERFUSION INJURY
4. HYPOXIC BRAIN INJURY
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PERSISTING PRECIPITATING PATHOLOGY

• OHCA
  • ACS found to be etiology in approx 50% in most observational studies (8)
  • Many of these coronary occlusions present without STE (9)
  • VT/VF from dilated CM is 2nd most common cause of shockable arrest (10)
  • Other common causes (obs cohort in european centre) (11)
    • Nontraumatic hemorrhage 16%
    • Intoxication 14%
    • Near-drowning 10%
    • Pulmonary embolism 8%
    • Other: hypo/hyperkalemia, hypothermia, sepsis, tamponade, tension PTX etc.

• IHCA= much different distribution (fewer are primarily cardiac) (12)
Your 2 best tools to assess primary pathology in cardiac arrest = **ECG and U/S**: (13)

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**A Simplified and Structured Teaching Tool for the Evaluation and Management of Pulseless Electrical Activity**

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Departments of \(^a\)Internal Medicine and \(^b\)Emergency Medicine, and \(^c\)Pulmonary and Critical Care Consultants, Carolinas Medical Center, Charlotte, N.C., USA

Medical Principles and Practice, 2014.
PERSISTING PRECIPITATING PATHOLOGY: ACS

• Early ‘90s landmark trials in STEMI mgmt (non-arrest patients):
  • GUSTO NEJM 1993: (14) thrombolytic regimens for STEMI
  • Early PCI vs Thrombolysis: (15) improved outcomes, reduced bleeds

• How should we be using angiography and PCI in OHCA?
PERSISTING PRECIPITATING PATHOLOGY: ACS

• 15 obs studies: improved survival to hospital d/c associated with emergency coronary angio in patients with STEMI after ROSC (4)

• 9 obs studies: improved neurologically favorable outcome associated with emergency coronary angio in patients with STEMI after ROSC (4)

• NO RCTS
• Fewer studies in NSTEMI but positive trends
NEJM 1997: Prospective observational cohort (9) – 84 patients resuscitated after OHCA with *no obvious cause and no STE*. 40/84 had acute coronary occlusion.
2015 AHA GUIDELINES: (4)

- Early PCI recommended for all STEMI (Class I, LOE-B)

- Early PCI reasonable if comatose, electrically/hemodynamically unstable, and there is suspected cardiac etiology (Class IIa, LOE C-LD)
Ronald
ACS: what if I’m not in a cardiac centre?

- Thrombolysis may improve outcomes in OHCA (Lancet 2001): (16)

  **Historically controlled: safety of thrombolysis during/after CPR unclear at the time**

- Regular CPR vs CPR+lysis at 15 and 30 minutes if no ROSC
- Significant improvements in ROSC (ARR 14%) and survival (ARR 7%)
Is thrombolysis safe during/after CPR?

- Obs cohort for PE: benefit > cost (17)
- RCT all OHCA: benefit > cost (18)

- Yes, in unstable PE and OHCA, benefits likely outweigh risks.
Thrombolysis for treatment of acute massive pulmonary embolism with hemodynamic instability is safe and likely improves outcomes. (19,20)

- No RCT, only observational studies to date

AHA GUIDELINES 2015: (4)
- Fibrinolytics reasonable in hypotensive patients with suspected PE (Class IIb, LOE C)

Embolectomy after unsuccessful thrombolysis for hemodynamically unstable PE results in greater survival (ARR 31%) and prevention of recurrence compared to repeat thrombolysis. (21)
The Post-Cardiac Arrest Syndrome (PCAS)

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4. HYPOXIC BRAIN INJURY
• 165 consecutive ICU pts post-resuscitation after OHCA
• 44% developed hemodynamic instability requiring vasoactive drugs
  • Cardiac index dropped between 4.3 and 7.3 hrs post-ROSC
  • Cardiac Index recovered dramatically by 24hrs post-ROSC in 2/3
    • Associated vasodilation led to slow ween of pressors
• Lack of recovery at 24 hrs predicted death by MODS in 100%
POST-ARREST MYOCARDIAL STUNNING

• In swine model, changes have been shown to closely reflect those seen in humans. (23)

• REVERSIBILITY:
  • Circulation. 1997. Controlled study in swine:
    Dobutamine infusion begun within 15 minutes of successful resuscitation from prolonged VF arrest completely corrected LV systolic and diastolic dysfunction.
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4 MAIN COMPONENTS

1. PERSISTING PRECIPITATING PATHOLOGY

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3. SYSTEMIC ICHEMIA/REPERFUSION INJURY (SIRI)

4. HYPOXIC BRAIN INJURY
SIRI

• PATHOPHYSIOLOGY
  • O2 debt → endothelial activation and systemic inflammation (24)
  • Activated immunologic and coagulation pathways → MODS, infection risk (25)
    • “sepsis-like syndrome” (26)
  • ‘Endotoxin tolerance’ → leukocyte hyporesponsiveness
  • Steroid hyporesponsiveness → relative adrenal insufficiency (27,28)

• CLINICAL MANIFESTATIONS
  • Intravascular volume depletion – vasodilation and third-spacing
  • ARDS
  • Impaired microvascular circuitry and oxygen delivery
  • Increased susceptibility to infection
AHA GUIDELINES 2015: (4)

- WHAT YOU MIGHT CONSIDER BUT IS NOT SUPPORTED BY ANY CONCLUSIVE EVIDENCE:
  - STEROIDS (SIRI, BP)
  - PROPHYLACTIC ANTIBIOTICS
SIRI: HEMODYNAMICS

- Likely to need 3.5-6.5 L crystalloid within first 24 hrs due to vasodilation and third-spacing (22)
  - Monitor preload to keep RA pressure 8-13 mmHg

- Observational studies only regarding BP goals:
  - Clear trends toward better survival and neuro outcomes when SBP >90 (29,30)
  - Evidence of improved survival in some studies at higher MAPs (31)
  - Most vulnerable time period during recovery is unclear
  - In some cases, low BP may be a marker of bad outcome rather than a cause
AHA GUIDELINES 2015: (4)

• Avoid and immediately correct hypotension post-ROSC. Target SBP >=90mmHg, MAP>=65mmHg (Class IIb, LOE C-LD)

• Note: goals may differ for patients based on pre-existing HTN
• No specific pressor/inotrope recommendations: consider patient characteristics
2 observational studies (32,33) correlate hypocapnea (<30mmHg) with:
- Increased mortality, OR 2.52
- Poor neurologic outcome, OR 2.43

Same studies report trends that hypercapnea (>50mmHg) correlated with worse outcomes as well but less strongly

- Higher PaCO2 may be permissible in patients with acute lung injury or high airway pressures as benefit outweighs potential cost
SIRI: RESPIRATORY CARE, pt2- oxygenation

• In dog model RCT, post-ROSC hyperoxygenation (100%) vs normoxygenation (21%) during 1st hour \(\rightarrow\) significantly more neuronal death and oxidative damage on brain histochemistry. (34)
  • Similar study on rats but functional outcome measured – impaired cognition (35)

• Observational human data show improved survival with less hyperoxic exposure. (36)
AHA GUIDELINES 2015:

• Maintain PaCO2 in normal physiologic range (35-45mmHg) (Class IIb, LOE B-NR)

• Avoid hypoxia after ROSC. Use highest available O2 concentration until SaO2 or PaO2 can be measured. (Class IIa, LOE C-EO)

• Titrate FiO2 to SaO2 of 94% when possible. (Class IIa, LOE C-LD)
SIRI: GLUCOSE MANAGEMENT

• No evidence of difference in 30d mortality benefit between strict (goal 4-6mM) vs moderate (6-8mM) goals for blood glucose.

Journal of Intensive Care Medicine, 2007.(37)

• AHA GUIDELINES 2015: (4)
  • The benefit of any specific target range of glucose management is uncertain in adults with ROSC after cardiac arrest. (Class IIb, LOE B-R)
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3. SYSTEMIC ICHEMIA/REPERFUSION INJURY (SIRI)
4. HYPOXIC BRAIN INJURY
I'm speaking with myself, number one, because I have a very good brain and I've said a lot of things.

My primary consultant is myself, and I have a good instinct for this stuff.
HYPOXIC BRAIN INJURY

• EPIDEMIOLOGY

• 5 yr cohort of post-ROSC deaths in UK ICU (38). 126 deaths/205 admissions
  • Cause of death defined as cardiac, multi-organ failure, or neurologic

  • OHCA: 68% of deaths neurologic cause
  • IHCA: 23% of deaths neurologic cause
HYPOXIC BRAIN INJURY

• PATHOPHYSIOLOGY
  • Poor tolerance to ischemia + unique response to reperfusion
  • Hrs-days: excitotoxicity, free radical formation, faulty protease cascades (39,40) ➔ NECROSIS, APOPTOSIS

• CLINICAL RESULT
  • Impaired autoregulation ➔ must rely on CPP (and therefore BP)
  • Cerebral edema
  • Sx: neurocognitive deficits, seizures ➔ coma ➔ persistant veg state ➔ death
BRAIN INJURY: TARGETED TEMPERATURE MANAGEMENT (TTM)

• HISTORY
  • 1958- *first case reports* of rare survival after cardiac arrest w/TH x 24-72h (43)
  • 1960- *first small controlled studies in dogs*: trends toward benefit (44,45)
  • 1960’s- abandoned after several negative studies using temps mostly in 20s!
  
  • 1990’s- series of positive animal studies re-ignited interest and clarified best temperature targets and lengths for benefit and safety in human studies (46)

• 2002- NEJM publishes 2 landmark RCTs that lead to standard of care for over a decade (47,48)
  • Inclusion: Adults, VF OHCA, <60mins before ROSC, coma after ROSC
  • Treatment: 12h - 24h at 32-34C
  • Benefit: ARR of poor outcome (CPC) 16-23%
Nielsen et al. NEJM 2013 (49)

- Adult OHCA *all rhythms*, comatose after ROSC
- Comparison of TTM at 33 vs 36 degrees for 24hrs
- N=950
- Results: No differences in survival or neurologic outcome
AHA GUIDELINES 2015 (4):

- Comatose adult pts after cardiac arrest should be considered for TTM

- VF/pVT OHCA (class I, LOE B-R)
- IHCA or non-shockable rhythms (class I, LOE C-EO)

- Temp 32-36 (class I, LOE B-R)
- Duration at least 24h (class IIa, LOE C-EO)
BRAIN INJURY: SEIZURE MANAGEMENT

• Seizure activity post-ROSC common: 12-22% \(^{(50,51)}\)

• 2 RCT comparing sz prophylaxis after ROSC to none → no benefit
  • Diazepam or magnesium \(^{(52)}\)
  • Thiopental \(^{(53)}\)

• 3 case series involving total of 47 people treated for non-convulsive status epilepticus after ROSC → just 1 survivor with good neuro outcome \(^{(54-56)}\)
AHA GUIDELINES 2015: (4)

• Frequent EEG for identification of seizure activity in comatose patients after ROSC (Class I, LOE C-LD)

• Treat seizure activity with same regimens as seizure of other etiologies (Class Iib, LOE C-LD)
BRAIN DEATH AND ORGAN DONATION

• Viability of organs transplanted from patients who have undergone CPR resuscitation after OHCA have comparable acceptance/rejection rates (57)

• Post-arrest donors provide on avg between 2.9 and 3.9 organs each (58)
Ronald Gump

• **ED vitals:** GCS 4, Pupils 3mm unreactive. BP 85/60, P 95, SpO2 100 on 100% O2 bagged. BG 10
  - HD: SALINE 2L INITIALY, DOPAMINE INFUSION
  - VENT: ETT FIO2 30%, RR14 AT 6ML/KG TV. ETCO2 40
  - BG: OBSERVATION INITIALY, INSULIN IF PERSISTS – GOAL 6-8
  - TTM: REGULAR PR TYLENOL TO PREVENT FEVER, COOLED SALINE INFUSION
  - SEDATION: MIDAZOLAM INFUSION. AVOID PARALYTICS

• **ECG:** no STE. Nonspecific T-inversion in precordial leads.
  - POSSIBLE ACS – PREP TRANSFER FOR EARLY ANGIO AND ICU ADMISSION
A TRULY HAIR-RAISING EXPERIENCE
<table>
<thead>
<tr>
<th>AHA GUIDELINE</th>
<th>RECOMMENDATION</th>
<th>EVIDENCE CLASS AND LEVEL</th>
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</thead>
</table>
| PROGNOSTICATION | - AT 72 HRS AFTER ROSC (OR)  
- AT 72 HRS AFTER REWARMING | CLASS I, LEVEL B-NR  
CLASS IIB, LEVEL C-EO |
| PCI | - EARLY FOR STEMI  
- EARLY IF UNSTABLE, SUSPECTED CARDIAC, OR COMA POST-ROSC | CLASS I, LEVEL B  
CLASS IIA, LEVEL C-LD |
| FIBRINOLYSIS FOR PE | - IF HEMODYNAMICALLY UNSTABLE | CLASS IIB, LEVEL C |
| BLOOD PRESSURE | - AVOID/CORRECT HYPOTENSION, TARGET SBP>90 AND MAP> 65* | CLASS IIB, LOE C-LD |
| VENTILATION | - PACO2 GOAL 35-45 MMHG** | CLASS IIB, LOE B-NR |
| OXYGENATION | - HIGHEST FIO2 POST ROSC UNTIL CAN MEASURE SP02 AND TITRATE  
- TITRATE TO SA02 GOAL 94%+ | CLASS IIA, LOE C-E0  
CLASS IIA, LOE C-LD |
| GLUCOSE MANAGEMENT | - UNCLEAR TARGETS (NOT STRICT) | CLASS IIB, LOE B-R |
| TARGETED TEMPERATURE MGMT | - VF/VT, AT TEMP 32-36C  
- IHCA OR NON-SHOCKABLE RHYTHMS  
- DURATION AT LEAST 24H | CLASS I, LOE B-R  
CLASS I, LOE C-E0  
CLASS IIA, LOE C-E0 |
| SEIZURE MANAGEMENT | - TREAT SEIZURE ACTIVITY AS USUAL | CLASS IIB, LOE C-LD |

*May depend on patient baseline. Observational data show trends at higher levels  
**May be safe to mildly hypoventilate if needed for pulmonary reasons
REFERENCES


