The Need for Basic & Translational Research in Cardiac Arrest Customized Treatment

Robert A. Berg

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Present State of Translational Large Animal CPR Research in the USA

Dismal

Few labs (~10)
Scarce resources
Challenging models
Extreme paucity of young investigators

So what? Who cares?
Big Discoveries Start in Preclinical Labs

• Pipeline for future
  – Closed Chest Massage: Kouwenhoven 1960
  – Defibrillation: Prevost, Hooker, Zipes, Ewy, Kerber, etc.
  – Post-cardiac arrest myocardial dysfunction
    • Kern, 1996; Gazmuri 1996

• Opportunity to try novel interventions prior to exposing humans to potential harm
  – High Dose Epinephrine
  – CC only CPR
How about a recent example?

**Potential Paradigm Shift**

Titrate CPR to patient’s hemodynamics rather than depth/rate/time based CPR

**Patient-centric** CPR with customized hemodynamic titration rather than rescuer-centric one-size-fits-all for ease of training
“Performing CPR without measuring the effects is like flying an airplane without an altimeter”

Max Harry Weil
Coronary Perfusion Pressure
Critically Important for Successful CPR

“Coronary Perfusion Pressure” During CPR

AoD >30 mmHg; CPP >20 mmHg

Sanders, CCM 1984
Michael, Circ 1984
Kern, Resus 1988
Coronary Perfusion Pressure during CPR
Adult OHCA

Paradis, JAMA 1990
Why don’t we titrate CPR to arterial blood pressures?

- Focus of BLS training on OHCA
  - Practicality of BP monitoring is limited
- But IHCA is a major public health problem
  - EMS CPR 175,000/year Nichol, JAMA 2008
  - CPR for IHCA: 200,000/yr Merchant CCM 2011
    - >90% pediatric IHCA in ICU
    - ~50% adult IHCA in ICU
    - CPR in ICU: arterial BP monitoring is common
- Monitor perfusion for OHCA in future?
Evidence for the approach?

• Is there any evidence that physiologically guided CPR is any better than standard CPR?
<table>
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<tr>
<th>No.</th>
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| 1.  | **Hemodynamic directed CPR improves cerebral perfusion pressure and brain tissue oxygenation.**  
PMID: 24945902 [PubMed - as supplied by publisher]  
Related citations                                                                 |
| 2.  | **Hemodynamic-directed cardiopulmonary resuscitation during in-hospital cardiac arrest.**  
PMID: 24783998 [PubMed - in process]  
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Related citations                                                                 |
| 3.  | **Hemodynamic directed cardiopulmonary resuscitation improves short-term survival from ventricular fibrillation cardiac arrest.**  
PMID: 23887237 [PubMed - indexed for MEDLINE]  
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| 4.  | **Hemodynamic directed CPR improves short-term survival from asphyxia-associated cardiac arrest.**  
PMID: 23142199 [PubMed - indexed for MEDLINE]  
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Hemodynamic directed CPR improves short-term survival from asphyxia-associated cardiac arrest.

Hemodynamic Directed Cardiopulmonary Resuscitation Improves Short-Term Survival From Ventricular Fibrillation Cardiac Arrest.

Resuscitation. 2013 May;84(5):696-701 Sutton, Friess, Bhalala, Maltese, Naim, Bratinov, Niles, Nadkarni, Becker, Berg


Physiologically guided:
Target and maintain coronary perfusion pressure > 20 mm Hg

Depth Guided:
Target and maintain compression depth > 33 mm (good cpr)

Depth Guided:
Target and maintain compression depth > 51 mm (great cpr)
Methods & Results:

Baseline: Ventricular Fibrillation (7 min)

- Group 1: Coronary Perfusion > 20 mmHg
- Group 2: Standard 33 mm depth guided
- Group 3: Standard 51 mm depth guided

CPR for 10 min

45 min:
- 8 of 8
- 1 of 8
- 3 of 8

Total number of vasopressor doses administered and defibrillation attempts were not different.
Conclusions:

• Patient-centric physiologically guided resuscitation shows great promise for saving lives

• Resuscitation is complex, more complex than flying an airplane...
What should we do?
Encourage studies specifically suited for the clinical pipeline

- **Significance**
  - Potential for translation in a clinical trial
  - Clinically important outcomes
  - Clinically relevant model

- **Mechanism issue:** how rather than novel
  - How it works to improve outcome
    - E.g., perfusion pressures, blood flows, etc
  - Downplay importance of novel mechanism
Attract Young Investigators

Translational CPR Research

• Incentivize CPR research
  – Especially for young investigators
• Incentivize CPR research training
Summary

• Translational CPR research can lead to paradigm shifts and save lives
  – CPR, defibrillation, cc-only CPR
  – Patient-centric hemodynamic titration vs rescuer-centric CPR?

• CPR research needs active resuscitation
  – Encourage studies for clinical pipeline
  – Attract young investigators
    • As PI’s and as trainees

• Many more lives can be saved!!