New Technologies and Approaches to Cardiac Arrest

MRC Academy
June 24, 2014
You live and practice in the nation’s hotbed of cardiac arrest research
Dr. Keith Lurie
"I admire your persistence doctor. But face it, you've lost this patient."
Scope of the Problem:

- >300,000 Americans experience out-of-hospital cardiac arrest (OOHCA) annually and an additional >300,000 suffer an in-hospital cardiac arrest: this remains the leading cause of death in the USA
- Overall survival rates are dismal, < 5% for OOHCA and ~17% for in-hospital cardiac arrest
- Standard CPR inherently inefficient
Conventional CPR Provides Only...

10 – 20% of normal blood flow to heart

20 – 30% of normal blood flow to brain
The Brain

- 10,000,000,000 neurons, each with axonal and dendritic connections
- Estimated 500,000,000,000,000 synapses
- Although 2% of body weight
- Receives 15% of the cardiac output
- Utilizes 20% of the body’s oxygen
- Has little ability to store
Cerebral Blood Flow

- Normal cerebral blood flow is about 50mL/100g brain/min
- For 70 kg:
  \[2\% \times 70 = 1.4 \text{ kg} = 1400\text{g} = \sim 700\text{mL/min}\]
Physiologic Changes of No Flow

- 15 seconds - loss of consciousness
- 1 minute - cessation of brainstem function (agonal respirations, fixed pupils)
- 4-5 minutes - depletion of glucose and ATP (anaerobic metabolism)
- 4-6 minutes - traditional "irreversible damage"
Standard CPR

How it works
(or doesn’t)
Compression Phase (2 theories)

- **Cardiac Pump Theory**
  - Heart is squeezed between sternum & spine

- **Thoracic Pump Theory**
  - Compression causes a positive pressure that causes:
    - Blood to leave the heart (cardiac output)
    - Air to exit the lungs
    - Intracranial pressure (ICP) to increase
Decompression Phase

- Vacuum (negative pressure) develops in chest drawing:
  - Air back into lungs
  - Blood back into heart (preload)
- ↑ PRELOAD leads to ↑ CARDIAC OUTPUT
- Coronary blood flow occurs
- ICP is lowered
Decompression Phase

- Lungs and chest wall recoil lead to small but very important ↓ IP.
- When IP ↓ to < atmospheric pressure, venous blood and respiratory gases are drawn into chest.
- ↓ IP during decompression improves venous return and “primes the pump” for the subsequent compression.
Inefficiencies of Standard CPR (S-CPR)
Inefficiency #1

- Filling of the heart (preload) is dependent upon the chest wall’s ability to recoil during decompression phase.
- Chest wall recoil may be compromised by:
  - Stiff chest
  - Broken ribs
  - Just doing it wrong
Complete Chest Wall Recoil

Incomplete Chest Wall Recoil
- Results in reduced preload
Inefficiency #2

- Air rushes in through an open airway and wipes out the vacuum we’re relying on to fill the heart.
- Heart stops filling as soon as vacuum is equalized.
Devices to Enhance Circulation
Active Compression Decompression CPR or ACD
ACD CPR device

- Metronome
- Force Gauge
- Suction Cup
- Handle
ACD CPR: Compression

- Actively compressing the chest, increasing IP pressure and thereby forcing blood out of chest. Just like s-CPR.
**ACD CPR: Decompression**

- Actively decompressing the chest, decreasing IP pressure, thereby drawing blood into the chest.
- Markedly increases coronary flow.
- Markedly decreases ICP, thus promoting a markedly increased flow to the brain.
ACD-CPR Optimizes Chest Wall Recoil
Does it Work?
Standard vs. ACD CPR: Survival


**Human Study**

- **Standard CPR** (n=377)
- **ACD CPR** (n=373)

### Odds ratios shown above bars
- 1.5
- 1.5
- 1.4
- 1.9
- 2.0
- 3.2*
- 2.5*

* Statistically significant difference
** Discharge without neurologic impairment
Standard vs. ACD CPR:
Survival


Human Study

Standard or ACD CPR during BLS and ACLS

![Graph showing survival rates for standard CPR and ACD CPR](image-url)

- **Survivors (%)**
  - **ROSC**
  - **1 hr**
  - **ICU admission**
  - **24 hr**
  - **Discharge**
  - **1 yr**

- **Standard CPR** (n=99)
- **ACD CPR** (n=120)

* Discharge without neurologic impairment
Automated ACD
Lucas
## Differences between manual and automated ACD CPR

<table>
<thead>
<tr>
<th>Manual ACD</th>
<th>LUCAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decompression pressure neg15-20#</td>
<td>Decompression pressure neg 3#</td>
</tr>
<tr>
<td>High quality CPR</td>
<td>High quality CPR</td>
</tr>
<tr>
<td>Cheap</td>
<td>Expensive</td>
</tr>
<tr>
<td>Broad use</td>
<td>Limited use</td>
</tr>
<tr>
<td>Interrupted</td>
<td>Continuous</td>
</tr>
<tr>
<td>Switch q 2 min</td>
<td>Never gets tired</td>
</tr>
<tr>
<td>Less safe, access</td>
<td>More safe, access</td>
</tr>
<tr>
<td>Should stop to defib</td>
<td>Defib during CPR</td>
</tr>
<tr>
<td>Stay and play</td>
<td>Move to hospital</td>
</tr>
</tbody>
</table>
LUCAS/ITD should be thought of more as ECMO than as standard CPR
The problem is...

- Air rushes in through an open airway and wipes out the vacuum we’re relying on to fill the heart.
- Heart stops filling as soon as vacuum is equalized.
- First noted with ACD CPR in St. Paul in 1992
- A U of M anesthesiologist figured this out
- They went to the lab…
The Solution

The Impedance Threshold Device (ITD)
Airflow Through the ITD

Chest Decompression

Influx of air is prevented, enhancing the vacuum in the chest.
Airflow Through the ITD

Chest Compression

Patient can freely exhale.

Patient Ventilation

Patient can be freely ventilated.
ITD Optimizes Chest Vacuum
Effect of Inspiratory Impedance

Greater vacuum (negative pressure) in the chest during chest wall recoil phase
Airway Pressures in Patient in Cardiac Arrest: ITD + ACD CPR


ACD CPR w/ Sham ITD

ACD CPR w/ Facemask + ITD

ACD CPR w/ ET + ITD Ventilation
Improved Blood Pressure
(putting it all together)

P<0.05 for differences between S-CPR & S-CPR + ITD, and ACD-CPR & ACD-CPR + ITD

ACD/ITD CPR
in humans
ACD CPR +/- Valve:
End-Tidal CO₂

End-Tidal CO₂

Duration of CPR (minutes)

n=11
n=10
n=10
n=10
n=9
n=8
n=8
n=10
n=7

Without Valve
With Valve

End- Tidal CO₂

Time (min)

ACD CPR +/-
Valve:
Plaisance, P, Lurie, KG, Payen, D. Circ. 2000;101:989-994

Human Study
ACD CPR +/- Valve:
Diastolic Arterial Pressure

Plaisance, P, Lurie, KG, Payen, D. Circ. 2000;101:989-994
ACD CPR +/- Valve: Coronary Perfusion Pressure

Time (min)

Coronary Perfusion Pressure (mmHg)

With Valve

Without Valve

Duration of CPR (minutes)

n=11

n=10

n=9

n=8

n=7

n=10

n=10

n=10

n=8

Plaisance, P, Lurie, KG, Payen, D. Circ. 2000;101:989-994

Human Study
Paris Survival Study:
ACD CPR ± ITD

- Prehospital study
- 200 patients/arm (ACD vs. ACD/ITD)
- ROSC:
  - 38.5% - ACD
  - 48% - ACD/ITD
- ICU admission
  - 28.5% - ACD
  - 39.5 – ACD/ITD
- 24 Hour Survival
  - 22% - ACD
  - 32% - ACD/ITD
The ResQ Trial
Comparative Effects of Standard CPR Versus Active Compression Decompression CPR with Augmentation of Negative Intrathoracic Pressure for Treatment of Out-of-Hospital Cardiac Arrest: Results from a Randomized Prospective Study

Tom P. Aufderheide, MD; Ralph J. Frascone, MD; Marvin A. Wayne, MD; Brian D. Mahoney, MD; Robert A. Swor, DO; Robert M. Domeier, MD; Michael L. Olinger, MD; Richard G. Holcomb, PhD; David E. Tupper, PhD; Demetris Yannopoulos, MD; Keith G. Lurie, MD
"Cardiopulmonary resuscitation with augmentation of negative intrathoracic pressure should be considered as an alternative to standard CPR to increase long-term survival after cardiac arrest."

See Articles page 301
Methods

- S-CPR
- ITD + ACD-CPR (Intervention)
Hypothesis

Survival to hospital discharge with favorable neurologic function is higher in patients receiving an ITD + ACD-CPR compared to patients receiving Standard CPR (S-CPR).
Methods:

Study Design

- Prospective, randomized, controlled clinical trial with data analyzed on intent to treat basis
- Seven US sites (population base: 2.3 million):
  - 46 EMS agencies
  - 4950 EMS providers
  - 25 IRBs
- Patients assigned, based upon weekly block randomization, to control or intervention group
- Study period: February 2005 – July 2010
- All study personnel blinded to aggregate data
Results
Results:

Primary Endpoint

Survival to Hospital Discharge with Favorable Neurologic Outcome

*53% improvement

P = 0.019

OR 1.58

CI (1.07, 2.36)
Results:

Consistency Across Age Groups

<table>
<thead>
<tr>
<th>Age at Time of Arrest (years)</th>
<th>Survival to Hospital Discharge with Favorable Neurologic Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>29</td>
<td>Control (n = 47)</td>
</tr>
<tr>
<td>30 - 39</td>
<td>Intervention (n = 75)</td>
</tr>
<tr>
<td>40 - 49</td>
<td>6</td>
</tr>
<tr>
<td>50 - 59</td>
<td>13</td>
</tr>
<tr>
<td>60 - 69</td>
<td>11</td>
</tr>
<tr>
<td>70 - 79</td>
<td>8</td>
</tr>
<tr>
<td>&gt;79</td>
<td>2</td>
</tr>
</tbody>
</table>

- **<29**: 1 (Control) / 3 (Intervention)
- **30 - 39**: 6 (Control) / 8 (Intervention)
- **40 - 49**: 11 (Control) / 13 (Intervention)
- **50 - 59**: 10 (Control) / 20 (Intervention)
- **60 - 69**: 9 (Control) / 14 (Intervention)
- **70 - 79**: 8 (Control) / 11 (Intervention)
- **>79**: 2 (Control) / 6 (Intervention)
Results:

Consistency Across Genders

Survival to Hospital Discharge with Favorable Neurologic Outcome

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 813)</th>
<th>Intervention (n = 840)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>6.5%</td>
<td>9.9%</td>
</tr>
<tr>
<td>Female</td>
<td>4.4%</td>
<td>7.1%</td>
</tr>
</tbody>
</table>

P=1.00 for differences based on gender

Odds ratio for effect of intervention based on gender: 1.60
95% CI (1.10, 2.33)
Consistent Benefit Throughout Enrollment

Survival to Hospital Discharge with Favorable Neurologic Outcome

<table>
<thead>
<tr>
<th>Cumulative Enrollment</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>5</td>
<td>172</td>
<td>387</td>
<td>713</td>
</tr>
<tr>
<td>Intervention</td>
<td>6</td>
<td>168</td>
<td>395</td>
<td>703</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>340</td>
<td>782</td>
<td>1416</td>
</tr>
</tbody>
</table>
## Results:

### One-year Survival

<table>
<thead>
<tr>
<th></th>
<th>Control (N = 813)</th>
<th>Intervention (N = 840)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>One-Year Survival</strong></td>
<td>48 (5.9%)</td>
<td>74 (8.8%)</td>
<td>0.030</td>
</tr>
</tbody>
</table>

### Emotional:

**Beck Depression Inventory (BDI)**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Intervention</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Score range: 0 – 63)</td>
<td>5.2 ± 6.3</td>
<td>5.5 ± 5.9</td>
<td>0.862</td>
</tr>
</tbody>
</table>

### Functional:

**Disability Rating Score (DRS)**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Intervention</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Score range: 0 – 29)</td>
<td>1.4 ± 3.1</td>
<td>2.2 ± 5.7</td>
<td>0.358</td>
</tr>
</tbody>
</table>

### Cognitive:

**Cognitive Abilities Screening Instrument (CASI)**

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Intervention</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score range: (0 – 100)</td>
<td>92.9 ± 12.0</td>
<td>94.5 ± 4.5</td>
<td>0.473</td>
</tr>
</tbody>
</table>
Conclusions

- Compared to standard CPR, ITD + ACD-CPR resulted in significantly increased survival to hospital discharge with favorable neurological function (53%).

- One year after OOHCA, survival rates with similar neurologic function were also significantly higher in the intervention group (49%).
Many papers have resulted from the ResQ Trial
The ResQ Trial

What happened to all comers, not just CA of cardiac etiology?
Conclusions

In this largest series to-date evaluating long term neurologic recovery after OOHCA, compared to S-CPR, ACD+ITD resulted in a:

- 38.6% increase in survival to hospital discharge with favorable neurologic function (p=0.027)
- 38.9% increase in overall survival to one year (p=0.026)
- 36.2% increase in survival to one year with favorable neurologic function (p=0.062)
Conclusion

These findings support the use of ACD+ITD for treatment of patients with OOHCA from a variety of non-traumatic etiologies.
ResQ Trial

What about the effect of hypothermia?
What about the effect of hypothermia?

- ACD+ITD is neuro-protective independent of TH. Without TH, survival with favorable neurologic function was nearly doubled with ACD+ITD versus S-CPR:
  - At hospital discharge, 5.6% versus 3.0% (p=0.017)
  - At 90 days, 5.0% versus 2.9% (p=0.052)

- In patients with poor neurologic function at hospital discharge, ACD+ITD with TH resulted in a 6-fold improvement in neurologic function by 90 days
The ResQ Trial

What did we learn about the community notification and consultation process?
Conclusion

It wasn’t too difficult or expensive and it was kind of fun.
The ResQ Trial

How does a patient’s outcome influence whether or not they or their will give consent?
Conclusion

If the patient does not have a good outcome, informed consent is much less likely to be given. These findings suggest that some resuscitation trials may unknowingly under-represent those subjects with the worst prognoses due to the unwillingness or inability of the subjects or their families to give consent.
The ResQ Trial

Is the Modified Rankin Score at Hospital Discharge Predictive of One Year Neurologic Function in Survivors after Cardiac Arrest?
Conclusion

MRS at the time of discharge is highly predictive of long-term neurological function at one year.
The ResQ Trial

What are the determinants of VF incidence as first recorded rhythm during out-of-hospital cardiac arrest?
Conclusion

- In the absence of bystander CPR, ACD+ITD significantly increased the incidence of first recorded VF compared to S-CPR leading to an overall doubling of survival with a favorable neurologic outcome.
- Pts were more likely to survive without bystander CPR, but less likely to survive with a favorable neurologic outcome.
ACD/ITD requires a change in our way of thinking:

- It is closer to ECMO than it is to S-CPR
- Cardiac arrest patients can be safely moved (safe for both the provider and the patient)
- Patients can be moved over much longer distances
- Prehospital cooling probably more important
- May change the cath lab paradigm
  - V fib
  - ? ECMO
  - Cath lab as uber ICU
A bazillion trials have demonstrated the effectiveness of the ITD alone, or in combination with ACD.

(well, maybe not a bazillion, but at least 60)
And yet... ACD/ITD is still controversial.

Why?
I don’t know why, but I do know this:

- If I just had a cardiac arrest and there are two lines forming:
  - S-CPR line
  - ACD/ITD line
- You’ve got to keep an open mind about research, but not so open that your brains fall out
Use of Supraglottic Airways (SGAs) in Cardiac Arrest

Benefit:
SGAs may be inserted blindly and without interruption of chest compressions
Ventura County (CA) EMS

- Attempted to increase survival rates by adding SGA (King) and ITD to arrest protocols
- Studied three 9-month periods:
  1. Control: BLS: 30:2 comp to vent ratio; ET intubation (ETI) primary advanced airway
  2. BLS: 30:2 with early ITD on facemask; then SGA became primary airway with ITD
  3. BLS: 30:2 with early ITD on facemask; ETI with ITD primary airway; SGA only if ETI failed
- Measured ETCO$_2$ and survival to hospital discharge

Results: ETCO$_2$

- **10-min EMS CPR (X)**
  - 1: ET Primary: 21.6 mmHg
  - 2: ITD & SGA: 30.8 mmHg
  - 3: ITD & ETI: 25.1 mmHg

- **X + 5 Min**
  - 1: ET Primary: 19.5 mmHg
  - 2: ITD & SGA: 27.2 mmHg
  - 3: ITD & ETI: 22.8 mmHg
Results: Survival

- Overall survival in all periods was not statistically different (9.2 – 12.1%)
- Spike in neurologically impaired survivors during Period 2
- CPC Scores
  - 1: Normal
  - 2: Minor deficits
  - 3: Moderate deficits
  - 4: Major deficits
  - 5: Coma or death
Study Conclusions

- Early use of the ITD and SGA resulted in increased circulation as indicated by higher ETCO$_2$ levels.
- When SGAs were added to the ITD as the primary airway, there was a trend towards poorer cerebral performance in survivors.
- Trend reversed when early use of SGA was discontinued.
- Can we explore this further in an animal model?
Methods

V-fib
No CPR for 4 min

CPR @ 100/min

Post mortem carotid arteriogram

3 min: ET Tube
3 min: King

3 min: ET Tube
3 min: LMA

3 min: ET Tube
3 min: Combitube

Randomization
Results

- Compared to ETI, cerebral blood flow dropped 20 – 53% when a SGA was inserted
- p<0.05 for all comparisons
- Arteriogram showed that with each SGA there was compression of the internal and external carotid vessels
Sample Cerebral Blood Flow (ml/min) Tracing

- Pre-Arrest
- V-fib No CPR
- ET Tube
- Combitube
- ET Tube
- King
- ET Tube
- LMA
Results: Cardiac Arrest Survival

- Largest study to date
- Patients with ET Tube
  - n=8457
- Patients with SGA
  - King; n=909
  - Combitube; n=296
  - LMA; n=239
- Survival 30% better in patients with ET Tube
- No increase in pulmonary complications

Wang et al.
Cardiac Arrest Survival Based Upon Airway

Survival with Good Neurological Function

* * p<0.001 for comparison to SGA

ROC PRIMED data
Aufderheide et al.
NEJM 2011;365(9).

- SGA
- ET Tube
- Facemask

<table>
<thead>
<tr>
<th>Airway</th>
<th>n</th>
<th>Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGA</td>
<td>935</td>
<td>2.8</td>
</tr>
<tr>
<td>ET Tube</td>
<td>6644</td>
<td>6.1</td>
</tr>
<tr>
<td>Facemask</td>
<td>1131</td>
<td>7.2</td>
</tr>
</tbody>
</table>

n=1131
What about epinephrine?
Epi in pigs (Burnett et al, Resusc 2012)
Epi in pigs (Burnett et al)

- ACD-CPR + ITD increased all hemodynamic markers compared to STD-CPR or STD-CPR+ITD
- Epinephrine given during ACD-CPR + ITD:
  - increased mean aortic, cerebral and coronary perfusion pressures
  - decreased carotid blood flow and ETCO₂
- Calculated perfusion pressures do not accurately reflect blood flow and oxygen delivery to end organs.
Epi in humans (Hayashi et al, J Circ 2012)

- 3,161 patients
- 3 groups: ≤ 10, 11-20, ≥ 21 minutes
- Epi group has a significant lower rate of 1 month neurologically intact survival (4.1% vs 6.1%)
- V fib if used w/i 10 min had a significantly higher rate of neurologically intact survival (66.7% vs 24.9%)
- In non V-F arrests rate of survival was low irrespective of the use of epinephrine
What does this mean?

- Epi may make us feel better and the patient feel worse
- Probably much less epinephrine in the future
- Tx should probably be tailored to rhythm and, perhaps, tailored to timing and/or coarseness of the V-F
Conclusion
Nationally less than 5% of patients survive out of hospital cardiac arrest.
This number will move because:

- ACD, hopefully both manual and automated, will be used and become the CPR standard
- Increased use of the ITD
- Continuous compressions
- Medications?
- A more discerning use of epinephrine
- SGA
- Widespread use of therapeutic hypothermia
- More aggressive approach to CA pts including:
  - Post arrest PCI
  - ECMO, LVAD’s
Conclusion

- Many novel approaches will be tested in humans within the next 1 - 2 years.
- Stay tuned!
- This is an exciting time to be involved in cardiac arrest research and hopefully, because you live and work in the right place, many of you will be participating!!
Thank you

Any questions?