NHLBI-related Activities on the Treatment of Cardiac Arrest: Current Status and Future Directions

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Age- and Sex-Adjusted Incidence Rates of Acute Myocardial Infarction, 1999 to 2008.

Decrease in incidence of MI attributed to better risk factor control: decreased smoking, better BP control, lower LDL targets

Think Sudden Cardiac Arrest is a Heart Attack?

That’s like comparing apples and oranges.
Incidence of Sudden Cardiac Arrest in Different At-Risk Patient Groups

What causes Sudden Cardiac Arrest?

**Table 1  Cardiac causes of cardiac arrest**

- Ischaemic cardiac disease (coronary artery disease)
- Ischaemic cardiomyopathy
- Dilated cardiomyopathy
- Hypertrophic cardiomyopathy
- Non-atherosclerotic disease of coronary arteries
- Valvular heart disease
- Arrhythmogenic right ventricular cardiomyopathy
- Infiltrative and inflammatory myocardial disease
- Congenital heart disease
- Primary cardiac electrical abnormalities

**Table 2  Noncardiac causes of cardiac arrest**

- Pulmonary embolism
- Lung disease (hypoxic cause of cardiac arrest)
- Electrolyte abnormalities
- Bleeding, nontraumatic (hypovolaemic cause of cardiac arrest)
- Subarachnoid haemorrhage
- Drug overdose
- Suffocation
- Drowning
- Sudden infant death syndrome

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Fig. 4. Previously silent coronary artery disease is likely to be the predominant disease condition contributing to sudden cardiac death in the general population.

*Tables 1 & 2: Hollenberg J et al, J of Internal Medicine, 2013.*

*Fig. 4: Chugh SS, et al, Progress in CV Diseases, 2008.*
Witnessed Out-of-Hospital Cardiac Arrest

- Two cardiologists go to the Regal Cinema, Bethesda, MD to view the movie Random Hearts

- October 1999 (pre-community AED)

- Witnessed arrest by bystanders and victim’s wife

- As cardiologists arrive, the patients has agonal breathing. Bystander says they were CPR trained, but the person does not need CPR as he is ‘breathing’

- Cardiologists evaluate person on ground. No pulse. “Call 911” CPR initiated. Pulse with compressions, but not without. After some time pulse returns and patient regains consciousness

- EMTs arrive. Normal blood sugar. Taken to hospital for eval

Random:
- Who sees
- Who treats
- Who responds

Critical:
Response time
Treatment - Resuscitation

Chance of Survival from Cardiac Arrest*

Minutes to Defibrillation

- 96% chance of survival in the first minute
- 80% chance of survival in the second minute
- 70% chance of survival in the third minute
- 60% chance of survival in the fourth minute
- 50% chance of survival in the fifth minute
- 40% chance of survival in the sixth minute
- 30% chance of survival in the seventh minute
- 20% chance of survival in the eighth minute
- 10% chance of survival in the ninth minute

http://stayalive.com.au
Survival Rates over Time after AED Implementation in Stockholm, Sweden

In 2005, Stockholm provided AEDs to Fire Brigade to improve response times.
# Time to Intervene at Different Stages Preceding Cardiac Arrest

<table>
<thead>
<tr>
<th>Clinical Status</th>
<th>A. Prodromes</th>
<th>B. Onset of Terminal Event</th>
<th>C. Cardiac Arrest</th>
<th>D. Biological Death</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Signs &amp; Symptoms</strong></td>
<td>New or worsening cardiovascular symptoms</td>
<td>Abrupt change in clinical status</td>
<td>Sudden collapse</td>
<td>Failure of resuscitation</td>
</tr>
</tbody>
</table>
| | • Chest pain  
  • Palpitations  
  • Dyspnea  
  • Weakness | • Arrhythmias  
  • Hypotension  
  • Chest pain  
  • Dyspnea  
  • Lightheadness | • Loss of effective circulation  
  • Loss of conciousness | Failure of electrical, mechanical, or CNS function after initial resuscitation |
| **Time for Intervention** | Days to Months | Instantaneous to 1 hour | Minutes to weeks |

Myerburg R, Cardiac Arrest and Sudden Death in Heart Disease, 5th edition, 1997.
Annual rates of fatal Sudden Cardiac Arrest: Approx. 300,000 to 370,000 people.

Seattle: progressive reductions in number of responses to SCA over to 20 to 30 years. Change due to reduction in ventricular tachycardia events identified by emergency medical services responders. The incidences of PEA and asystole has not changed in 3 decades of observation.
FY2013 NHLBI Funded Research: Sudden Cardiac Death

Search Terms:
• Sudden Cardiac Death

Time Period:
• FY 2013

Total # of Grants:
• 75

Total Funding:
• $31,217,026

http://projectreporter.nih.gov/
**Public-Access Defibrillation and Survival after Out-of-Hospital Cardiac Arrest**

The rate of survival after out-of-hospital cardiac arrest is low. It is not known whether this rate will increase if laypersons are trained to attempt defibrillation with the use of automated external defibrillators (AEDs).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>CPR Only (N=107)</th>
<th>CPR plus AED (N=128)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volunteer response activated — no. (%)‡</td>
<td>57 (53.8)</td>
<td>89 (69.5)</td>
<td>0.06</td>
</tr>
<tr>
<td>Bystander CPR — no. (%)§</td>
<td>62 (62.0)</td>
<td>81 (64.8)</td>
<td>0.55</td>
</tr>
<tr>
<td>Shock delivered with non-EMS AED — no. (%)</td>
<td>2 (1.9)</td>
<td>44 (34.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Interval between call to EMS and first rhythm assessment — min †</td>
<td>8.7±5.5</td>
<td>6.0±4.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ventricular fibrillation or ventricular tachycardia as first rhythm — no. (%)¶</td>
<td>43 (47.3)</td>
<td>71 (57.7)</td>
<td>0.66</td>
</tr>
<tr>
<td>Interval between call to EMS and arrival of EMS — min</td>
<td>5.6±3.4</td>
<td>5.7 (3.3)</td>
<td>0.63</td>
</tr>
<tr>
<td>Patient admitted to hospital — no. (%)</td>
<td>29 (27.1)</td>
<td>50 (39.1)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

- Laypersons can effectively be trained and perform CPR with and without use of AEDs
Clinical Trial: Prehospital Treatment Using Hypothermia

Effect of Prehospital Induction of Mild Hypothermia on Survival and Neurological Status Among Adults With Cardiac Arrest: A Randomized Clinical Trial

Francis Kim, MD; Graham Nichol, MD, MPH; Charles Maynard, PhD; Al Hallstrom, PhD; Peter J. Kudenchuk, MD; Thomas Rea, MD, MPH; Michael K. Copass, MD; David Carlbom, MD; Steven Deem, MD; W. T. Longstreth Jr, MD; Michele Olufka, RN; Leonard A. Cobb, MD

DESIGN, SETTING, AND PARTICIPANTS A randomized clinical trial that assigned adults with prehospital cardiac arrest to standard care with or without prehospital cooling, accomplished by infusing up to 2 L of 4°C normal saline as soon as possible following return of spontaneous circulation. Adults in King County, Washington, with prehospital cardiac arrest and resuscitated by paramedics were eligible and 1359 patients (583 with VF and 776 without VF) were randomized between December 15, 2007, and December 7, 2012. Patient follow-up was completed by May 1, 2013. Nearly all of the patients resuscitated from VF and admitted to the hospital received hospital cooling regardless of their randomization.

CONCLUSION AND RELEVANCE Although use of prehospital cooling reduced core temperature by hospital arrival and reduced the time to reach a temperature of 34°C, it did not improve survival or neurological status among patients resuscitated from prehospital VF or those without VF.

N= 1359 patients
583 with VF
776 without VF

Outcome: Survival to hospital discharge

Survival:
VF: 62.7% intervention and 64.3% in control

W/o VF: 19.2% intervention and 16.3% in control

Conclusion: Prehospital mild hypothermia did not improve survival or neurological status.
Researchers are applying imaging and biomarker strategies to identify or stratify risk:

Top panel: Transmembrane potential maps of patient’s atria with a pulmonary vein ectopic beat as it traverses the myocardium using MRI imaging

Bottom panel: Use of gray scale measures on MRI plus hsCRP to identify low risk cohort in ICD population
NHLBI Funded Research: High Tech
“Instrumented” Synthetic Pericardium

NIH Grants: HL115415, HL114395, HL112278
Federal vs. Other R & D Funding: **Federal Percentage** Decreases Over Time

NIH Appropriation in Current & Constant Dollars

Doubling of NIH Funding

With Supplemental Appropriation (ARRA)
Current $ (Millions)
1995 Constant $ (Millions)
With 10 to 15% paylines at some institutes (or even less), the current situation makes grant evaluation nearly impossible and is putting truly excellent laboratories out of business. In the spirit of “never waste a good crisis,” a serious evaluation of many NIH extramural policies and programs is warranted. They include centers and other large collective funding efforts as well as expensive clinical and epidemiological research.
Transforming Clinical Trials in Cardiovascular Disease
Mission Critical for Health and Economic Well-being

Elliott M. Antman, MD
Robert A. Harrington, MD

Perhaps the most exciting opportunity for CVD researchers is to capitalize on the advances in systems and computational biology that can inform first-in-human, proof-of-

“As large trials became popular…the original simplicity was lost…leading to increasingly complex trials. The unintended consequence has been to threaten the very existence of RCTs, given the operational complexities and ensuring costs. An ideal opportunity would be to embed randomization in the EMR…introducing randomization into registries sponsored by societies.”
Cost (incremental) = $300,000 or $50/patient
Low Cost Research in Canada

24,000 patients

< $ 2 million