Risk Stratification for Sudden Cardiac Death

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6th Annual ACC/Saudi Heart Association Joint Meeting
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Jeddah
Case Presentation

- 61 year old moderately obese (BMI 28.1 kg/m²) hypertensive diabetic male 6 months after an anterior wall STEMI with LAD stent, collapses at the airport while arguing with an airline representative
Case Presentation

- CPR is initiated by bystanders and 911 call is made (54 seconds)
AED arrives at scene while CPR being done (2 minutes 10 seconds)
Sudden Death Prevention after STEMI

- AED delivers shock (3 minutes 43 seconds)
Prediction and Prevention of SCD

Case Report

- Transported to a local hospital
- Stabilized, comatose
- Transferred to tertiary hospital
- Hypothermia protocol
- Coronary angiography - LAD patent
- Neurologically intact
- BB, Statin, ASA, ACE

- 9 days post SCA - rehab, diet, exercise, weight loss
Sudden Cardiac Death
Definition

**Sudden death**

- Instantaneous death, unwitnessed death, or death occurring within one hour of the onset of symptoms
Estimating the Mortality Burden of Sudden Arrhythmic Deaths

Source, Population & Reference

CDC ~462,000 Death Cert.
MMWR 51; 123; 2002. Data for 1999 US

Myerburg J. Card Electphy 13; 709; 2002; Zipes
Wellens ~300,000 CVD Circ 98; 2234

AHA ~250,000 CHD = SCD 2003 Heart Disease & Stroke Update

Cobb ~184,000 EMS SEA JAMA 288; 3008; 2002

Estimated Number of SCDs

Deaths (in thousands)
## Incidence of SCD in Specific Populations and Annual SCD Numbers

<table>
<thead>
<tr>
<th>Group</th>
<th>Incidence of Sudden Death (% of group)</th>
<th>No. of Sudden Deaths Per Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population</td>
<td>1/1000/yr</td>
<td>300,000</td>
</tr>
<tr>
<td>Patients with high coronary-risk profile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with previous coronary event</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with ejection fraction &lt; 35%, congestive heart failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with previous out-of-hospital cardiac arrest</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with previous myocardial infarction, low ejection fraction, and ventricular tachycardia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ANATOMIC/FUNCTIONAL SUBSTRATE
- Coronary artery disease
- Cardiomyopathy
- Dilated
- Hypertrophic
- Right ventricular dysplasia
- Valvular
- Congenital
- Primary electrophysiological
- Neurohumeral
- Developmental
- Inflammatory, infiltrative, neoplastic, degenerative, toxic

TRANSIENT INITIATING EVENTS
- Neuro/endocrine
- Drugs
- Electrolytes, pH, pO2
- Ischemia/reperfusion
- Hemodynamic
- Stretch
- Arising/Stress/Sleep
- Alcohol

ARRHYTHMIA MECHANISMS
- Reentry
- Automaticity
- Triggered activity
- Block/cell-to-cell uncoupling

"TRIPLE HIT" MODEL
For the Perfect Storm
Triggers of Sudden Cardiac Death

- Ischemia
- Autonomic changes
- Increased sympathetic tone
- Decreased parasympathetic tone
- Physical exertion
- Hypoxia
- Drug effects
- Electrolyte abnormalities
- Myocardial toxins
Mechanisms of SCD

**Substrate**
Myofibrillar disarray, fibrosis
Microvascular disease

**Anatomic**
Dispersion of repolarization
Delayed Conduction
Anisotropic Conduction

**Electrophysiologic**

**Trigger**
Ischemia
Exercise
Hemodynamic
Arrhythmic

**Arrhythmia**
Reentry
Afterdepolarization

**Mechanism**
VT
VF
Brady
EMD
Age- and Sex-Adjusted Incidence of Treated Out-of-Hospital Cardiac Arrest

**All Treated Cardiac Arrests**

- Annual Incidence (Rate per 1,000)
  - 0.2
  - 0.4
  - 0.6
  - 0.8
  - 1.0
  - 1.2
  - 1.4

Ventricular Fibrillation

- Decrease 56% from .85 to .38/1000; RR .44

**Asystole**

- Annual Incidence (Rate per 1,000)
  - 0.2
  - 0.4
  - 0.6
  - 0.8
  - 1.0
  - 1.2
  - 1.4

**Pulseless Electrical Activity**

- Annual Incidence (Rate per 1,000)
  - 0.2
  - 0.4
  - 0.6
  - 0.8
  - 1.0
  - 1.2
  - 1.4

Modified from Myerburg, R

Distribution of clinical status of individuals suffering sudden cardiac death

Assessment of Sudden Death Risk Following MI

- SCD accounts for approximately 50% of the total mortality in the first year post MI with a considerable drop in the risk of SCD over the next 12 to 24 months.

- The time dependence of the risk of SCD in post MI patients limits the opportunity for effective prevention strategies to the early post MI period.

- Prediction of SCD is dependent on stratification techniques that are practical, sensitive and have a high predictive accuracy for SCD.

- Prevention of SCD is dependent on cost-effective intervention.
Assessment of Sudden Death Risk Following MI

- LVEF is an independent predictor of total mortality
- Risk of SCD increases progressively as LVEF decreases as a continuous variable
- LVEF dichotomized at .40 to distinguish low from high risk patients for total mortality and SCD
- LVEF lacks specificity for predicting SCD
Assessment of Sudden Death Risk

*Risk Stratification*

- **Noninvasive**
  - LVEF
  - ETT
  - Holter Monitor
  - SAECG
  - HRV
  - BRS
  - QT Dispersion
  - TWA

- **Invasive**
  - EPS
Assessment of Sudden Death Risk Following MI

Freedom from SCD

- Low risk subgroups free of CV event
- High risk subgroups post MI

Myerberg, R Sudden Death in Zipes Cardiovascular Electrophysiology, 2000
58 y o male with acute anterior MI with cardiogenic shock requiring IABP, pressors for 5 days

PTCA of LAD with VF at 16 hours post onset of CP, with noncritical disease in circ. and RCA

LVEF 20% anterior hypo. Class II/III CHF, BP 90, on ACE, BB, plavix ready for discharge

Which of the following additional strategies would you take to prevent SCD in the first three months after discharge?

A. ICD implant prior to discharge
B. Family CPR training and AED
C. Lifevest
D. No additional therapy
Assessment of Sudden Death Risk Following MI

- Risk stratification needs to be evaluated based on actual clinical utility

- Clinical utility is defined by modification of current practices or intervention in a way that unequivocally and significantly prolongs life
## Post-MI Trials - Antiarrhythmics

<table>
<thead>
<tr>
<th>Trial</th>
<th>Design</th>
<th>Harm</th>
<th>Neutral</th>
<th>Benefit</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impact</td>
<td>Mexiletine vs P</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cast I</td>
<td>Flecainide, Encainide vs P</td>
<td>✓</td>
<td></td>
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<tr>
<td>Cast II</td>
<td>Moricizine vs P</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta-Blocker</td>
<td>Propranolol</td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
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<tr>
<td></td>
<td>Timolol</td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Metoprolol</td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td></td>
<td>Acebutolol vs P</td>
<td></td>
<td></td>
<td></td>
<td>✓</td>
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<tr>
<td>Julian</td>
<td>d, I Sotalol vs P</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sword</td>
<td>d - Sotalol vs P</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EMIAT</td>
<td>Amio vs P</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>CAMIAT</td>
<td>Amio vs P</td>
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<td></td>
<td></td>
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<tr>
<td>Diamond-MI</td>
<td>Dofetilide vs P</td>
<td>✓</td>
<td></td>
<td></td>
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<tr>
<td>Alive</td>
<td>Azimilide vs P</td>
<td>✓</td>
<td></td>
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</table>
Prophylactic ICD therapy does not reduce overall mortality in high-risk patients who have recently had a myocardial infarction. Although ICD therapy was associated with a reduction in the rate of death due to arrhythmia, that was offset by an increase in the rate of death from nonarrhythmic causes.

Defibrillator Implantation Early after Myocardial Infarction
Cumulative Risk of Death from Any Cause According to Study Group

$P = 0.76$
$P_{adj} = 0.78$

ICD group 116 Deaths
Control group 117 Deaths

<table>
<thead>
<tr>
<th>Months since Randomization</th>
<th>0.0</th>
<th>0.1</th>
<th>0.2</th>
<th>0.3</th>
<th>0.4</th>
<th>0.5</th>
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<tbody>
<tr>
<td></td>
<td>0</td>
<td>6</td>
<td>12</td>
<td>18</td>
<td>24</td>
<td>30</td>
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</table>

Cumulative Risk of Death from Any Cause

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>ICD group</th>
<th>Control group</th>
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<tbody>
<tr>
<td></td>
<td>445 390 366 338 303 253 207 163 137 106 78 48 40</td>
<td></td>
</tr>
<tr>
<td></td>
<td>453 410 380 336 307 267 230 187 151 118 79 49 36</td>
<td></td>
</tr>
</tbody>
</table>

Home Use of Automated External Defibrillators for Sudden Cardiac Arrest

Kaplan-Meier Curves for Death from Any Cause

For survivors of anterior-wall myocardial infarction who were not candidates for implantation of ICD, access to a home AED did not significantly improve overall survival, as compared with reliance on conventional resuscitation methods.

6 days post discharge

ICD placed, progressive CHF, OHT
<table>
<thead>
<tr>
<th>Trial</th>
<th>Year</th>
<th>Patients (n)</th>
<th>LVEF</th>
<th>Additional Study Features</th>
<th>Hazard Ratio*</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>MADIT I</td>
<td>1996</td>
<td>196</td>
<td>&lt; 35%</td>
<td>NSVT and EP+</td>
<td>0.46</td>
<td>(0.26-0.82)</td>
<td>p=0.009</td>
</tr>
<tr>
<td>MADIT II</td>
<td>2002</td>
<td>1232</td>
<td>&lt; 30%</td>
<td>Prior MI</td>
<td>0.69</td>
<td>(0.51-0.93)</td>
<td>p=0.016</td>
</tr>
<tr>
<td>CABG-Patch</td>
<td>1997</td>
<td>900</td>
<td>&lt; 36%</td>
<td>+SAECG and CABG</td>
<td>1.07</td>
<td>(0.81-1.42)</td>
<td>p=0.63</td>
</tr>
<tr>
<td>DEFINITE</td>
<td>2004</td>
<td>485</td>
<td>&lt; 35%</td>
<td>NICM, PVCs or NSVT</td>
<td>0.65</td>
<td>(0.40-1.06)</td>
<td>p=0.08</td>
</tr>
<tr>
<td>DINAMIT</td>
<td>2004</td>
<td>674</td>
<td>&lt; 35%</td>
<td>6-40 days post-MI and Impaired HRV &lt;30 days post-MI HR &gt;90 or NSVT</td>
<td>1.08</td>
<td>(0.76-1.55)</td>
<td>p=0.66</td>
</tr>
<tr>
<td>IRIS</td>
<td>2009</td>
<td>898</td>
<td>&lt; 40%</td>
<td></td>
<td>1.04</td>
<td>(0.81-1.35)</td>
<td></td>
</tr>
<tr>
<td>SCD-HeFT</td>
<td>2006</td>
<td>1676</td>
<td>&lt; 35%</td>
<td>Prior MI of NICM</td>
<td>0.77</td>
<td>(0.62-0.96)</td>
<td>p=0.007</td>
</tr>
<tr>
<td>AVID</td>
<td>1997</td>
<td>1016</td>
<td>NA</td>
<td>Prior cardiac arrest</td>
<td>NA</td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>CASH†</td>
<td>2000</td>
<td>191</td>
<td>NA</td>
<td>Prior cardiac arrest</td>
<td>0.766</td>
<td>‡</td>
<td>1-sided p=0.081</td>
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<tr>
<td>CIDS</td>
<td>2000</td>
<td>659</td>
<td>NA</td>
<td>Prior cardiac arrest, syncope</td>
<td>0.82</td>
<td>(0.60-1.1)</td>
<td>NS</td>
</tr>
</tbody>
</table>
ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices)

Developed in Collaboration With the American Association for Thoracic Surgery and Society of Thoracic Surgeons

Epstein et al JACC, 2008
# Evidence Based Medicine AEDs

<table>
<thead>
<tr>
<th>Report</th>
<th>Design</th>
<th>% survival</th>
<th>AED</th>
<th>P Value</th>
<th>Results Benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>OBS</td>
<td>42</td>
<td>46</td>
<td>&lt;.02</td>
<td>✓</td>
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<tr>
<td>Weaver</td>
<td>OBS</td>
<td>18</td>
<td>38</td>
<td>&lt;.001</td>
<td>✓</td>
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<tr>
<td>Smith</td>
<td>OBS</td>
<td>22</td>
<td>36</td>
<td>&lt;.001</td>
<td>✓</td>
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<td>Mossenco</td>
<td>OBS</td>
<td>8</td>
<td>26</td>
<td>&lt;.01</td>
<td>✓</td>
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<tr>
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<td>OBS</td>
<td>28</td>
<td>30</td>
<td>NS</td>
<td>X</td>
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<tr>
<td>Page</td>
<td>OBS</td>
<td>44</td>
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<tr>
<td>Myerburg</td>
<td>RCT</td>
<td>11</td>
<td>28</td>
<td>&lt;0.05</td>
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<td>Valenzuela</td>
<td>OBS</td>
<td>44</td>
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<td>Caffrey</td>
<td>OBS</td>
<td>48</td>
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<td>Capucci</td>
<td>RCT</td>
<td>21</td>
<td>44</td>
<td>&lt;.01</td>
<td>✓</td>
</tr>
<tr>
<td>PAD</td>
<td>RCT</td>
<td>15</td>
<td>29</td>
<td>&lt;0.04</td>
<td>✓</td>
</tr>
<tr>
<td>HAT</td>
<td>RCT</td>
<td>6.5**</td>
<td>6.4**</td>
<td>0.77</td>
<td>X</td>
</tr>
</tbody>
</table>

*# of survivors **total mortality
Role of the AED in Preventing SCD

- Evidence based medicine demonstrates decreased time to definitive therapy with defibrillation with AED use
- This results in improved survival in victims of SCA
- The benefit of AEDs is mainly in non-residential settings
- Organizational, institutional, state and federal policies, legislation, and laws serve to promote the widespread use of AED
- For survivors of anterior-wall myocardial infarction who were not candidates for implantation of a cardioverter-defibrillator, access to a home AED did not significantly improve overall survival, as compared with reliance on conventional resuscitation methods.
As evidence-based medicine has defined the clinical benefits of AED use, public policy, laws, funding programs, and court decisions have served the societal interest of promoting use of AEDs by minimizing legal liability.
SCD Incidence and Total SCD Post MI

SCD Incidence Per Cent/Year

Total SCD/Year x1000
Clinical Strategies to Improve Outcomes From Sudden Cardiac Death After STEMI

- Prevention of risk factor development for coronary artery disease
- Primary prevention and secondary prevention of sudden cardiac death
- Appropriate use of beta-blocker, ACE inhibitor, and statin therapy
- Implantable cardioverter-defibrillator use in selected patients
- Community-based public access to defibrillation programs
- Regionalized systems of post-resuscitation hospital care

Estes N, Predicting and Preventing Sudden Cardiac Death *Circulation* 2011, 124:651-656
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