Preventing Sudden Cardiac Death
Role of the Implantable Cardioverter Defibrillator

Helbert Acosta MD
Cardiovascular Medicine, PC October 8, 2005
SCD DEFINITION

UNEXPECTED DEATH DUE TO CARDIAC CAUSES INVOLVING ABRUPT LOSS OF CONSCIOUSNESS DUE TO DISRUPTION IN CEREBRAL BLOOD FLOW OCCURING WITHIN ONE HOUR OF THE ONSET OF ACUTE SYMPTOMS

Myerburg RJ, Castellanos A. In Braunwald E, ed. Heart Disease, 6th edn. WB Saunders, 2001
EPIDEMIOLOGY OF SCD

- 340,000 to 400,000 out-of-hospital or in an ED cardiac arrests per year in U.S.

At least 50% of SCD are due to lethal arrhythmias

- 80% of arrhythmic SCD are associated to CAD

- 95% out-of-hospital mortality

- Given high mortality, goal is prevention
EPIDEMIOLOGY OF SUDDEN DEATH

- General population
- CAD risk factors
- Prior coronary event
- EF < 35% and CHF
- Prior out-of-hospital cardiac arrest
- Prior MI, low EF, VT

- Myerburg RJ, Castellanos A. Cardiac arrest and CSD. In Braunwald E., Heart Disease. 6th edn. WB saunders,20001 (modified)
ARRHYTHMIC SUDDEN DEATH

The underlying arrhythmia in approximately 80% of SCD was VT/VF.

- Bradyarrhythmias and pulseless electrical activity represent 15 – 20 %.

Mechanisms of SCD

ANATOMIC/ FUNCTIONAL SUBSTRATE
- CAD
- Cardiomyopathy (dilated hypertrophic)
- RV dysplasia
- Primary electrophysiological condition
- Inflammatory.. etc.

ARRHYTHMIA MECHANISMS
- Reentry
- Automaticity
- Trigger activity

LETHAL ARRHYTHMIA

TRIGGERS
- Electrolyte abnormalities, PH, pO2
- Ischemia
- Drug
- Neuroendocrine
- Hemodynamic
- Arising, stretch, sleep

Zipes and Wellens. Circ 1998; 98:2334
ANATOMIC/FUNCTIONAL SUBSTRATE

Animation: Link between scarring and SCD

Myocardial infarction

Hypertrophic Cardiomyopathy
ARRHYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA

EPSYLOM WAVE
Primary electrophysiological Abnormality

Long Qt syndrome

Brugada syndrome
OTHER ABNORMALITIES OF UNKNOWN ETIOLOGY

FATY INFILTRATION AND FIBROSIS OF THE SPECIALIZED CONDUCTION SYSTEM OF THE HEART

SINUS NODE
AV NODE
HIS BUNDLE
BUNDLE BRANCHES
Symptoms

- None!!!!
Inventor of the ICD

Michel Mirowski
1924-1990

First clinical model
- Short-lived
- Shock only
- 250 g
- Nonprogrammable
- Required thoracotomy abdominal implant

First human implant
In 1980
1985 FDA approval
Implantation now
ICD components
How do ICDs work?
LESS THAN PERFECT

- Painful shock
- Emotional stress
  - Anxiety
  - Depression
- Driving limitations
- Job limitations
- Pro-Arrhythmic
- Malfunction (recalls)
- Complications related to implant
# ROLE OF ANTIARRHYTHMIC MEDICATIONS

<table>
<thead>
<tr>
<th>Study</th>
<th>Anti arrhythmic</th>
<th>N of pts</th>
<th>Effect in Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAST-1</td>
<td>Encainide,Flecainide/placebo</td>
<td>1498</td>
<td>↑ (treatment arm)</td>
</tr>
<tr>
<td>SWORD</td>
<td>d-Sotalol/placebo</td>
<td>546</td>
<td>↑ (in treatment arm)</td>
</tr>
<tr>
<td>DIAMOND-CHF</td>
<td>Dofetilide/placebo</td>
<td>1518</td>
<td>No difference</td>
</tr>
<tr>
<td>CHF-STAT</td>
<td>Amiodarone/placebo</td>
<td>674</td>
<td>No difference</td>
</tr>
<tr>
<td>GESICA</td>
<td>Amiodarone/placebo</td>
<td>1200</td>
<td><strong>34% mortality reduction</strong></td>
</tr>
<tr>
<td>EMIAT</td>
<td>Amiodarone/placebo</td>
<td>1500</td>
<td>No difference</td>
</tr>
<tr>
<td>CAMIAT</td>
<td>Amiodarone/placebo</td>
<td>1200</td>
<td>No difference</td>
</tr>
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</table>
EFFECT OF MEDICATIONS IN PREVENTING SUDDEN CARDIAC DEATH

- BETA BLOCKERS
  Goldstein et al, JACC, 2001

- ACE INHIBITORS
  - Sudden Death: RR 20%
  - Cardiovascular Death RR 18%
  Domanski et al, JACC 1999

- STATINS

- BIDIL (HYDRALAZINE + ISOSORBIDE)

- SPIRINOLACTONE

**MERIT-HF TRIAL**

RR = 39%
TO WHOM THE ICD SHOULD BE OFFERED?
LANDMARK TRIALS

Secondary Prevention Trials
(post VT/VF arrest)

AVID: Antiarrhythmics Vs ICD

CASH: Cardiac arrest study
    Hamburg

CIDS: Canadian Implantable defibrillator Study

Primary Prevention trials
Pts at high risk for SCD

MADIT I (Multicenter Automatic Defibrillator implantation)

MUSTT (Multicenter Unsustained Tachycardia Trial)

MADIT II

SCD-HeFT (Sudden cardiac Death Heart failure Trial)
## Secondary Prevention trials

<table>
<thead>
<tr>
<th>TYPE OF PT</th>
<th>AVID (N=1016)</th>
<th>CASH (N=288)</th>
<th>CIDS (N=659)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VF/VT</td>
<td>32%</td>
<td>46%</td>
<td>34%</td>
</tr>
<tr>
<td>Mean LVEF</td>
<td>61%</td>
<td>61%</td>
<td>33%</td>
</tr>
<tr>
<td>Decrease in arrhythmic death</td>
<td>47%</td>
<td>61%</td>
<td>33%</td>
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<tr>
<td>Survival benefit</td>
<td>31% at 3 yrs</td>
<td>23% over 5 yrs</td>
<td>20% over 3 yrs</td>
</tr>
<tr>
<td>Sign.</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
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</table>

- Survival benefit: 33% over 3 yrs
- Decrease in arrhythmic death: 33% over 3 yrs
- Mean LVEF: 61% over 3 yrs
- Type of PT: VF/VT

**CIDSCIDS**

- **N=659**
- **N=288**
- **N=1016**
# Primary Prevention ICD Trials

( Post MI at high risk)

<table>
<thead>
<tr>
<th>Type of pt</th>
<th>MADIT I N=196</th>
<th>MUSTT n=704</th>
<th>MADIT II (2002) N=1232</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF</td>
<td>CAD/MI/NSVT +EPS</td>
<td>CAD/NSVT/+EPS</td>
<td>CAD/MI&gt;1 MONTH</td>
</tr>
<tr>
<td>Design</td>
<td>ICD Vs Drug Rx</td>
<td>EP GUIDED Vs placebo</td>
<td>ICD vs Conv. Rx</td>
</tr>
<tr>
<td>Mortality Reduction</td>
<td>54%</td>
<td>72% SCD 60% MORTALITY</td>
<td>31%</td>
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ISCHEMIC VS NONISCHEMIC CARDIOMYOPATHY
Primary Prevention ICD Trails in CHF

<table>
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<tr>
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<th>DEFINITIVE</th>
<th>SCD-HeFT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=458</td>
<td>N=2500</td>
</tr>
<tr>
<td>Type of pt</td>
<td>LVEF&lt;35%</td>
<td>LVEF&lt;35%</td>
</tr>
<tr>
<td></td>
<td>NSVT</td>
<td></td>
</tr>
<tr>
<td>Therapy</td>
<td>Standard vs ICD</td>
<td>Standard vs Amiodarone vs ICD</td>
</tr>
<tr>
<td>Results</td>
<td>80 % reduction in arrh death</td>
<td>Reduction of 23% of all cause mortality</td>
</tr>
</tbody>
</table>
Sudden cardiac Death in Heart Failure Trial (SCD-HeFT)

- 2521 pts
- Isch CPM: 52%
- Non-Isch CMP: 48%

847 → stand Rx + pb
845 → stand + Amio
829 → stand + ICD

SCD-HeFT Primary Endpoint: All Cause Mortality

Mortality by Intention-to-treat

- Amiodarone vs. placebo: Hazard Ratio (97.5% CI) 1.06 (0.86 - 1.30), P = 0.53
- ICD therapy vs. placebo: Hazard Ratio (97.5% CI) 0.77 (0.62 - 0.96), P = 0.007

23% Relative Reduction in All Cause Mortality For ICD Therapy (p-value 0.007)

Reference:
ROLE OF BIVENTRICULAR PACING ON SCD

Two trials addressing effect in mortality

COMPANION
CARE-HF
COMPANION TRIAL

Ischemic and non-ischemic
LVEF ≤ 35%
QRS > 120 ms
P End point: All cause mortality
first hospitalization

S End point: all cause mortality
CRT 24% (p .059)
CRT+ICD 36% (p .003)

CARE-HEF TRIAL

- 813 PTS
- CLASS III-IV
- CRT vs STANDARD RX
- EF<35%, QRS>120ms
- P. end point:
  All cause mort
  hospitalization

Reduction In All-cause Mortality with ICDs: Trials Summary

- **MADIT**
  - 27 Months*
  - 54%

- **MUSTT**
  - 39 Months*
  - 55%

- **MADIT-II**
  - 20 Months*
  - 31%

- **COMPANION**
  - 16 Months*
  - 36% (CRT-D)

- **SCD-HeFT**
  - 45.5 Months*
  - 23%

*Denotes average follow-up times.

EP STUDY

- STRIP INDUCING VT
NON INVASIVE RISK STRATIFICATION

- HRV
- T WAVE ALTERNANT
- HR TURBULENCE
- SIGNAL AVERAGE ECG
ACC/AHA GUIDELINES 2002

CLASS I

Cardiac arrest due to VF or VT

Spontaneous VT + structural heart disease

spontaneous VT with normal heart no amenable for other treatment

syncope + induction of VT or VF on EPS

Nonsustained VT, post MI, LV dysf., inducible VT or VF
  (no suppressible by class I antiarrhythmic)
ACC/AHA GUIDELINES 2002

- **CLASS IIa**
  
  LVEF ≤ 30, 1 mo post MI and 3 mo post CABG

- **CLASS II b**
  
  Cardiac arrest presumed due to VF and EPS can not be done
  VT + syncope awaiting heart transplant
  Familial or inherited cond.: Long QT, HCM
  Nonsust. VT, CAD, LV dysf., EPS + VT/VF
  Recurrent syncope of unknwn etiology, EPS+,LV dysf.
  syncope + FH of unexplained sudden death + Brugada ecg
CLASS III

Syncope of undetermined cause, normal heart, EPS –
Incessant VT or VF
VT curable with ablation or surgery (WPW, RVOT VT)
VT or VF due transient or reversible cause
  (AMI, electrolyte imbalance...)
Psychiatric or terminal illnesses
ACC/AHA GUIDELINES 2002

- **CLASS IIa**
  - LVEF \( \leq 30 \), 1 mo post MI and 3 mo post CABG

- **CLASS IIb**
  - Cardiac arrest presumed due to VF and EPS can not be done
  - VT + syncope awaiting heart transplant
  - Familial or inherited cond. : Long QT, HCM
  - Nonsust. VT, CAD, LV dysf., EPS + VT/VF
  - Recurrent syncope of unknown etiology, EPS+, LV dysf.
  - Syncope + FH of unexplained sudden death + Brugada ecg
## ICD Class I Recommendations

### Level of Evidence

<table>
<thead>
<tr>
<th>Evidence</th>
<th>Indications</th>
</tr>
</thead>
</table>
| A        | Secondary Prevention:  
- In patients with current or prior symptoms of HF and reduced LVEF who have a history of cardiac arrest, VF, or hemodynamically destabilizing VT²  
| A        | Primary Prevention:  
- SCD-HeFT Ischemic Patients, 40 days post MI, with LVEF ≤ 30% and NYHA Class II or III  
- SCD-HeFT Non-Ischemic Patients with LVEF ≤ 30% and NYHA Class II or III³ |

## ICD Class II Recommendations

### Level of Evidence

<table>
<thead>
<tr>
<th>Evidence</th>
<th>Indications</th>
</tr>
</thead>
</table>
| IIa      | Recommendation  
- SCD-HeFT Patients with LVEF 30 - 35% and NYHA Class II or III  
| IIb      | Recommendation  
- Ischemic Patients, 40 days post MI, LVEF ≤ 30% and NYHA Class I  
| C        | Non-Ischemic Patients with LVEF ≤ 30% and NYHA Class I³ |
WHAT DO WE DO NOW?
SELECTION OF PATIENT INDICATIONS

- In pts with permanently decreased LVEF < 30% regardless the etiology or functional class, ICD is indicated.

- If LVEF > 30 < 35%, functional class has to be II or III to be a candidate for a defibrillator.

- CAD, LVEF > 35 AND < 45%
  
  No syncope. No nonsustained VT = observation, Holter Q 6 months

  Nonsustained VT and or syncope = EPS, if positive ICD

  If negative medical Rx vs ICD

- Non ischemic, LVEF > 35%, no VT, no syncope = observation

  If syncope or VT ICD could be considered
Examples

- 47 YO FEMALE WITH NONISCHEMIC CMP, LVEF 28 %. NO SYNCOPE NO VT

- 68 YO MALE S/P MI LVEF 43%. HOLTER: NONSUSTAINED VT

- 57 YO FEMALE, HTN, CHF DEVELOPED SUDDEN VF ARREST, k+ 2.1 ON DIURETICS LVEF 47%
**Cost Effectiveness**

Total cost ICD - total cost conventional therapy

\[ \text{average total survival benefit} \]

\[ \text{additional cost of ICD therapy} \]

\[ \text{year of life saved} \]

ICD THERAPY FOR PRIMARY PREVENTION OF SUDDEN DEATH IS CONSIDERED COST EFFECTIVE

ICD COST $ 20,000 TO $ 30,000 PER YEAR OF LIFE SAVED

*Larsen et al, Circulation 2002*
COST EFFECTIVENESS OF ICD

Effect on total National Healthcare Expenditures (NHE)

1999 Total NHE

$1.2 trillion\(^3\)

ICDs=0.2% of NHE
($2.3 billion\(^2\))

2005 Total Estimated NHE

ICDs=0.4% of NHE
($6.9 billion\(^2\))

Even if ICD therapy were to triple, it would still account for less than one half of 1% of total NHE\(^8,7\)

Cost-effectiveness of ICD therapy compares favorably with other life-saving interventions\(^8,9\)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Cost per Life Year Saved (US $1,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTCA(^6) (Chronic CAD, severe angina, 2 VQI)</td>
<td>$10.2</td>
</tr>
<tr>
<td>CABG(^6) (Chronic CAD, mild angina, 3 VQI)</td>
<td>$18.2</td>
</tr>
<tr>
<td>Hypertension(^9) (NHLBI, mm, age 40)</td>
<td>$23.2</td>
</tr>
<tr>
<td>ICD(^9) both Ejection Fraction</td>
<td>$25.7</td>
</tr>
<tr>
<td>Captopril (\text{100mg}, 24h, 30%)</td>
<td>$28.4</td>
</tr>
<tr>
<td>Cardiac transplant (\text{100mg}, 24h, 30%)</td>
<td>$44.3</td>
</tr>
<tr>
<td>Peritoneal dialysis(^1)</td>
<td>$57.3</td>
</tr>
</tbody>
</table>

Expensive
Borderline cost-effective
Cost-effective
Highly cost-effective
QUESTIONS?
HOW OLD IS TOO OLD?

- PICTURE OF MY 104 YEAR OLD PATIENT
History of Fibrillation and Defibrillation

Carl Ludwig (1816-1895) and his discovery of electrical stimulus-induced ventricular fibrillation, 1850.

American thoracic surgeon saved the first human life by this method, 1947. University hospital of Cleveland.
Cardiac Death Prevention Trials: Relative vs Absolute Risk Reduction¹-⁴

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Reduction in Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-Blocker*</td>
<td>-35%</td>
</tr>
<tr>
<td>ACE Inhibitor†</td>
<td>-19%</td>
</tr>
<tr>
<td>Statin‡</td>
<td>-30%</td>
</tr>
<tr>
<td>ICD§</td>
<td>-31%</td>
</tr>
</tbody>
</table>

- Relative reduction in risk
- Absolute reduction in risk

This is a noncomparative representation of trial outcomes that resulted in dramatic shifts in treatment practices.
AVID: Cost Effectiveness

- Total average cost over 3-year follow-up
  - $85,522 ICD
  - $71,421 medical therapy
- Average survival benefit 0.21 years
- C/E ratio: $66,677 per year of life saved

Larsen et al, Circulation 2002