Défibrillateurs dans les Cardiopathies Ischémiques et Dilatées

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Service de Cardiologie
Hôtel-Dieu, Beyrouth
Survival Trends in Heart Failure

Levy D.

5 years survival : < 50%.
Risk of SCD in **Treatment Arms** of CHF-Beta Blocker Trials

- **CIBIS II**
  - Total Deaths: 156
  - Sudden Deaths: 48
  - Sudden Death % of Total Death: 31%

- **MERIT-HF**
  - Total Deaths: 145
  - Sudden Deaths: 79
  - Sudden Death % of Total Death: 54%

- **U.S. CARVEDILOL**
  - Total Deaths: 22
  - Sudden Deaths: 12
  - Sudden Death % of Total Death: 54%
Many studies have shown that in selected cardiomyopathy patients, ICD therapy can reduce mortality by reducing the risk of sudden death.
The main difficulty is to identify the patient at risk who will benefit from ICD implantation.
Survivors of SCD, VF or poorly tolerated VT

Recurrence rate

= 25-30 % at one year
SECONDARY PREVENTION

AVID (Antiarrhythmic Drug Versus Defibrillator)

Resuscitated SCD, Syncopal VT

ICD VS Amiodarone or Sotalol

507 pts VS 509 pts

NEJM 1997; 337:1576
SECONDARY PREVENTION

AVID (Antiarrhythmic Drug Versus Defibrillator)

![Graph showing survival rates over years with comparison between Antiarrhythmic drugs and ICD, indicating a statistically significant difference (P<0.02).]
SECONDARY PREVENTION

AVID  (Antiarrhythmic Drug Versus Defibrillator)

**NEJM**
1997; 337:1576
SECONDARY PREVENTION TRIALS

% Mortality Reduction

ICD vs AA drugs

Mortality Reduction ICD vs AA drugs

AVID
3 years
31%

CASH
2 years
37%

CIDS
3 years
20%
Meta-analysis of secondary prevention trials

Sudden cardiac death

<table>
<thead>
<tr>
<th>Secondary prevention</th>
<th>ICD Group, n/n</th>
<th>Control Group, n/n</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVID</td>
<td>24/507</td>
<td>55/509</td>
<td>0.44 (0.28–0.70)</td>
</tr>
<tr>
<td>CASH</td>
<td>13/99</td>
<td>64/189</td>
<td>0.39 (0.22–0.67)</td>
</tr>
<tr>
<td>CIDS</td>
<td>30/328</td>
<td>43/331</td>
<td>0.70 (0.45–1.09)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>67/934</td>
<td>162/1029</td>
<td>0.50 (0.38–0.66)</td>
</tr>
</tbody>
</table>

### Meta-analysis of secondary prevention trials

<table>
<thead>
<tr>
<th>Secondary prevention</th>
<th>Patients Who Died/All Patients</th>
<th>RR</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICD Group, n/n</td>
<td>Control Group, n/n</td>
<td></td>
</tr>
<tr>
<td>AVID (19)</td>
<td>80/507</td>
<td>122/509</td>
<td>0.66</td>
</tr>
<tr>
<td>CASH (23)</td>
<td>36/99</td>
<td>84/189</td>
<td>0.82</td>
</tr>
<tr>
<td>CIDS (22)</td>
<td>83/328</td>
<td>98/331</td>
<td>0.85</td>
</tr>
<tr>
<td>Subtotal</td>
<td>199/934</td>
<td>304/1029</td>
<td>0.76</td>
</tr>
</tbody>
</table>

All-cause mortality
SECONDARY PREVENTION

ACC/AHA/NASPE 2002 Guidelines

ICD indications in CAD and DCM pts

- Cardiac arrest due to VF or VT not due to a transient or reversible cause.

- Spontaneous sustained VT.
M 68y, DCM since 1996, EF = 20%
1999 : Syncope => Fast VT

210/min
2000 : Syncope and choc

Endocavitary tracing
ICD interrogation

Endocavitary tracing

SINUS & PACED RHYTHM

VENTRICULAR FIBRILLATION

CHARGING

ICD interrogation
PLACE OF ICDs IN PRIMARY PREVENTION
Primary Prevention Trials

**isch CM**
- CABG PATCH
- MADIT
- MUSTT

**dilated CM**
- CAT
- AMIOVERT
- MADIT II
- DEFINITE
- SCD-HeFT
MADIT II

Post-MI patients
EF ≤ 30%

1232 pts

ICD

vs

conventional medical therapy

N Engl J Med
2002; 346:877
MADIT II

Survival

ICD

No ICD

P=0.007

- 31% at 20 M

Years

N Engl J Med
2002; 346:877
MADIT II

Mortality Events

Non Cardiac
- Conv Therapy: 4.1%
- ICD: 3.5%

Cardiac
- Conv Therapy: 13.7%
- ICD: 10.0%

Arrhythmic
- Conv Therapy: 9.4%
- ICD: 3.6%

Non Arrhythmic
- Conv Therapy: 3.7%
- ICD: 5.5%
**Meta-analysis of primary prevention trials in CAD pts**

<table>
<thead>
<tr>
<th>Patients Who Died/All Patients</th>
<th>RR</th>
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<td><strong>ICD Group, n/n</strong></td>
<td><strong>Control Group, n/n</strong></td>
<td></td>
</tr>
<tr>
<td>CABG Patch</td>
<td>15/446</td>
<td>28/454</td>
</tr>
<tr>
<td>MADIT</td>
<td>3/95</td>
<td>13/101</td>
</tr>
<tr>
<td>MADIT II</td>
<td>27/742</td>
<td>46/490</td>
</tr>
<tr>
<td>MUSTT</td>
<td>12/161</td>
<td>90/353</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>57/1494</td>
<td>177/1452</td>
</tr>
</tbody>
</table>

Meta-analysis of primary prevention trials in CAD pts

<table>
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<tr>
<th>Patients Who Died/All Patients</th>
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<tr>
<td><strong>ICD Group, n/n</strong></td>
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</tr>
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<td>CABG Patch (20)</td>
<td>101/446</td>
<td>95/454</td>
</tr>
<tr>
<td>MADIT (24)</td>
<td>15/95</td>
<td>39/101</td>
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<td>MADIT II (13)</td>
<td>105/742</td>
<td>97/490</td>
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<tr>
<td>MUSTT (21)</td>
<td>35/161</td>
<td>158/353</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>260/1494</td>
<td>391/1452</td>
</tr>
</tbody>
</table>

Favors Treatment Favors Control

Ezekowitz.
Ann Intern Med.
2003;138:445

All-cause mortality
Will Amiodarone and/or an ICD improve survival compared to placebo in patients with:

- **CHF** (NYHA Class II and III) due to ischemic or nonischemic dilated cardiomyopathy

  - and

  - **EF ≤ 35%**
SCD-HeFT protocol

Inclusion criteria

Placebo (847)  Amiodarone (845)  ICD implant (829)

40 months average follow-up

- Optimize: βB, ACE-I, Diuretics
SCD-HeFT Endpoints

• Primary
  – To compare all cause mortality after 2.5 years of follow-up (Power: 90% to detect 25% benefit)

• Secondary
  – Mortality – Ischemic, Non-Ischemic
  – …
SCD-HeFT

Patients characteristics

- NYHA II 70%, NYHA III 30%
- Ischemic 52%, non-ischemic 48%
- ACE Inhibitor or ARB 87%
- Beta-blocker 78%

NEJM
Janv 2005
SCD-HeFT Results

Mortality by Intention-to-treat

<table>
<thead>
<tr>
<th>Group</th>
<th>HR</th>
<th>97.5% CI</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone vs. Placebo</td>
<td>1.06</td>
<td>0.86, 1.30</td>
<td>0.529</td>
</tr>
<tr>
<td>ICD Therapy vs. Placebo</td>
<td>0.77</td>
<td>0.62, 0.96</td>
<td>0.007</td>
</tr>
</tbody>
</table>

-23 %

NEJM Janv 2005
SCD-HeFT – Results

CAD patients

**Hazard Ratio (97.5% CI)**

- Amiodarone vs. placebo: 1.05 (0.81–1.36)
- ICD therapy vs. placebo: 0.79 (0.60–1.04)

**P Value**

- 0.66
- 0.05

**Mortality Rate**

- Amiodarone (5-yr event rate, 0.417)
- ICD therapy (5-yr event rate, 0.359)
- Placebo (5-yr event rate, 0.432)

**Months of Follow-up**

NEJM
Janv 2005
SCD-HeFT – Results

DCM patients

Amiodarone vs. placebo
1.07 (0.76–1.51)
0.65

ICD therapy vs. placebo
0.73 (0.50–1.07)
0.06

Hazard Ratio (97.5% CI)
P Value

Mortality Rate

Amiodarone
0.258
(5-yr event rate, 0.258)

Placebo
0.279
(5-yr event rate, 0.279)

ICD therapy
0.214
(5-yr event rate, 0.214)

Months of Follow-up

NEJM
Janv 2005
Meta-analysis of Randomized Controlled Trials:
ICD for the Prevention of Mortality in Nonischemic Cardiomyopathy

All-Cause Mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Years of Enrollment</th>
<th>No. of Patients</th>
<th>Risk Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAT</td>
<td>1991-1997</td>
<td>104</td>
<td>0.83 (0.45-1.82)</td>
</tr>
<tr>
<td>AMIOVIRT</td>
<td>1996-2000</td>
<td>103</td>
<td>0.87 (0.31-2.42)</td>
</tr>
<tr>
<td>DEFINITE</td>
<td>1998-2002</td>
<td>458</td>
<td>0.65 (0.40-1.06)</td>
</tr>
<tr>
<td>SCD-HeFT</td>
<td>1997-2001</td>
<td>792</td>
<td>0.73 (0.50-1.04)</td>
</tr>
<tr>
<td>COMPANION</td>
<td>2000-2002</td>
<td>397</td>
<td>0.50 (0.29-0.98)</td>
</tr>
<tr>
<td>Combined</td>
<td></td>
<td>1854</td>
<td>0.69 (0.55-0.87)</td>
</tr>
</tbody>
</table>

Without COMPANION: RR 0.74; 95% CI, 0.58-0.96; P=0.02
ICD implantation is reasonable for primary prevention in patients

- with LVEF < 30–35%
- on optimal background therapy including ACEi, beta-blocker, and an aldosterone antagonist.

(Class of recommendation I, level of evidence A)
ICD therapy is recommended for primary prevention in patients with:

- ischemic and non-ischemic heart disease
- who have an LVEF less than or equal to 30%,
- with NYHA functional class II or III symptoms
- while undergoing chronic optimal medical therapy,
- and have reasonable expectation of survival with a good functional status for more than 1 year.

(Class I recommendation)
Limitations of ICD Therapy
Complications of ICD Therapy

Device-related
- Infection or erosion
- Hematoma
- Pneumothorax
- Lead dislodgment
- Inadequate defibrillation threshold
- Connection problems
- Lead malfunctions or fractures
- Electromagnetic interference

Therapy-related
- Frequent shocks, appropriate or inappropriate
- Acceleration of ventricular tachycardia
- Psychological reactions
- Longer or additional hospitalization (possibly for right ventricular pacing)
Limitations of ICD Therapy

ICD therapy is associated with an increased risk of HF hospitalization

(new or worsened heart failure)

= Deleterious effect of ventricular pacing (ventricular desynchronization)
EF < 30% is the single most powerful independent predictor for SCD

Present indications of prophylactic ICD therapy in CAD and DCM patients is based mainly on ejection fraction

Witch is not the ideal risk-stratification method
ICD indications based only on EF will prevent a limited number of all sudden deaths in CAD pts and DCM pts
> 50% of the deaths in CAD patients occurred in patients whose EF was > 30%

and 20% occurred in patients with an EF >50%.
Many ICD pts will never use their devices:

in primary prevention:

- Appropriate ICD therapy at 1 year: 21%
- Appropriate ICD therapy at 3 year: 32%
- Annual rate: 10%

*Theuns Eur J Heart Failure 2005; 7: 1027*
Multiple studies completed within the past decade have demonstrated that ICDs can improve survival in selected patients with CAD and DCM.

Ejection fraction < 30 – 35% is the main selection filter for implanting ICDs in CAD pts and DCM pts...

but is far from an ideal risk-stratification test on which to base prophylactic ICD therapy.
CONCLUSIONS

Future Challenge

Develop a better screening method based on multiple parameters to identify the true indications of prophylactic ICD therapy
### Results

- 20% risk reduction in mortality with ICD (non-significant) \( p=0.14 \)
- Mortality reduction Year 1: 39% Year 2: 27% Year 3: 31% \( p<0.02 \)
- 23% risk reduction in mortality with ICD (non-significant) compared to amiodarone/metoprolol \( p=0.08 \)
<table>
<thead>
<tr>
<th>Study Treatment Period</th>
<th>CIDS</th>
<th>AVID</th>
<th>CASH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomization</td>
<td>ICD vs. amiodarone</td>
<td>ICD vs. empirical therapy with amiodarone or sotalol</td>
<td>ICD vs. amiodarone, metoprolol, propafenone</td>
</tr>
<tr>
<td>Primary Endpoint</td>
<td>All-cause mortality</td>
<td>All-cause mortality</td>
<td>All-cause mortality</td>
</tr>
<tr>
<td>Size and Scope</td>
<td>659 patients; 1:1 randomization</td>
<td>1,016 patients; 1:1 randomization</td>
<td>518 patients; 1:1:1:1 randomization</td>
</tr>
</tbody>
</table>
| Inclusion Criteria     | - Documented VF  
- Cardiac arrest  
- VT with hemodynamic compromise  
- VT with syncope  
- VT with symptoms and LVEF ≤40%  
- VT with syncope with symptoms and LVEF ≤40%  
- VT with BP <80 and LVEF ≤40%  
- Cardiac arrest survivor with documented VT | - Primary VF  
- VT with syncope  
- VT with symptoms and LVEF ≤40%  
- VT with BP <80 and LVEF ≤40% | |
| Mean Follow-Up         | 36 months    | 31 months                 | 57 months                 |
| Study End              | January 1997 | April 1997                | March 1998                |
| Results                | - 20% risk reduction in mortality with ICD (non-significant)  
- p=0.14 | Mortality reduction  
- Year 1: 39%  
- Year 2: 27%  
- Year 3: 31%  
- p<0.02 | - 23% risk reduction in mortality with ICD (non-significant) compared to amiodarone/metoprolol  
- p=0.08 |
<table>
<thead>
<tr>
<th>Study Treatment Period</th>
<th>CABG PATCH</th>
<th>MADIT</th>
<th>MUSTT</th>
<th>MADIT II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Principle Investigator</td>
<td>J. Thomas Bigger, Jr., MD</td>
<td>Arthur J. Moss, M.D.</td>
<td>Alfred E. Buxton, M.D.</td>
<td>Arthur J. Moss, M.D.</td>
</tr>
<tr>
<td>Randomization</td>
<td>ICD + CABG vs. CABG</td>
<td>ICD vs. OPT</td>
<td>EP guided therapy for prevention of SCD and spontaneous VT vs. no antiarrhythmic therapy</td>
<td>ICD + OPT vs. OPT</td>
</tr>
<tr>
<td>Primary Endpoint</td>
<td>All-cause mortality</td>
<td>All-cause mortality</td>
<td>Arrhythmic death or cardiac arrest</td>
<td>All cause mortality</td>
</tr>
<tr>
<td>Size and Scope</td>
<td>900 patients; 37 centers; 1:1 randomization</td>
<td>196 patients; 32 centers (30 in the U.S.; 2 in Europe); 1:1 randomization</td>
<td>767 patients; 85 centers in US and Canada</td>
<td>1232 patients; 76 centers in US and Europe; 3:2 randomization</td>
</tr>
<tr>
<td>Risk Identifier</td>
<td>• Abnormal SAECG</td>
<td>• Inducible/non suppressible VT</td>
<td>• Asymptomatic VT (3-30 beats) less than 6 months before</td>
<td>• N/A</td>
</tr>
<tr>
<td></td>
<td>CABG PATCH</td>
<td>MADIT</td>
<td>MUSTT</td>
<td>MADIT II</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------------------</td>
<td>--------------------------</td>
<td>----------------------------------------</td>
<td>-------------------------------------</td>
</tr>
<tr>
<td>Coronary Disease</td>
<td>• Recent CABG</td>
<td>• Prior MI</td>
<td>• MI, CABG or PTCA ≥ 96 hours</td>
<td>• Prior MI</td>
</tr>
<tr>
<td>EP Study</td>
<td>N/A</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Ejection Fraction</td>
<td>LVEF&lt;36%</td>
<td>LVEF ≤ 35%</td>
<td>LVEF ≤ 40%</td>
<td>LVEF ≤ 30%</td>
</tr>
<tr>
<td>Mean follow-up</td>
<td>32 months</td>
<td>27 months</td>
<td>39 months (median)</td>
<td>20 months</td>
</tr>
<tr>
<td>Termination Date</td>
<td>1995</td>
<td>March 1996</td>
<td>1999</td>
<td>November 2001</td>
</tr>
<tr>
<td>Results</td>
<td>• No reduction in all-cause mortality with ICD, p=0.63</td>
<td>• 54% reduction in all-cause mortality at 4 years, p=0.009</td>
<td>• Substudy: at 5 yrs, 55% mortality risk reduction (ICD subarm vs. non antiarrhythmic treatment arm), p=0.04</td>
<td>• 31% risk reduction in mortality at 20 months, p=0.016</td>
</tr>
</tbody>
</table>
MADIT II substudy: mortality by time from last MI in both arms.

The bar chart shows the mortality rates in different quartiles for both the CONV and ICD arms. The quartiles are defined by time from the last MI: Quartile 1 (1.17 mo), Quartile 2 (18.59 mo), Quartile 3 (60-121 mo), and Quartile 4 (>121 mo). The mortality rates are as follows:

- Quartile 1: CONV 15.6%, ICD 13.8%
- Quartile 2: CONV 15.8%, ICD 9.8%
- Quartile 3: CONV 22.1%, ICD 15.3%
- Quartile 4: CONV 26.7%, ICD 16.9%

The chart illustrates the time-dependence of mortality risk and the benefit of ICD in the MADIT II patient population.
T Wave Alternans Identifies Low-Risk Patients Who May Not Benefit From ICD Therapy

TWA exercise testing

An automatic (ie, computer-generated) system that computes beat-to-beat fluctuations was used to interpret TWA tests. A positive TWA was defined as the presence of sustained TWA $\geq 1.9$ microvolts for at least 1 minute with an onset heart rate $\leq 110$ bpm. TWA was negative if it did not meet criteria for positive and if the maximum negative heart rate was $\geq 105$/min.