MHIF FEATURED STUDY: 
**Exact Trial**

**DESCRIPTION:** an early phase, non-randomized, study evaluating direct administration of a modified adenovirus vector expressing multiple isoforms of the VEGF (human vascular endothelial growth factor) gene.

The route of administration will be one-time intramyocardial injections directly into the free wall of the left ventricle via TECAP.

**CRITERIA LIST/ QUALIFICATIONS:**

**Inclusion:**
- Diagnosis of Chronic angina due to obstructive coronary artery disease
  - CCS Angina class II-IV
- History of reversible left ventricular ischemia

**Exclusion:**
- Current electrocardiographic abnormalities that would interfere with ST-segment analysis
- Severe Congestive heart failure defined as NYHA III or IV, or LVEF less than 25%
Today’s Outline

• Case 1
• Case 2
• Review of sudden cardiac death after myocardial infarction
  • Epidemiology
  • Pathogenesis
  • Primary prevention therapies
• Case 3
Case 1: Cardiology office consultation

41 year old female with palpitations

Baseline
Assessment
• Paroxysmal SVT, probable AVNRT

Plan
• Start metoprolol 25 bid
• EP consultation for consideration of ablation

48 hours later in Hutchinson ED
Adenosine

Assessment
• Recurrent SVT aborted with adenosine
• Type 2 myocardial infarction due to sustained arrhythmia

Plan
• Transfer to ANW for:
  • Echocardiogram
  • Coronary CTA
  • EP consultation
Discharged on Hospital Day #8

Cardiology Problem List
• NSTEMI due to SCAD or vasculitis
• Mixed ischemic/non-ischemic cardiomyopathy
• Paroxysmal SVT

Plan
• DAPT, statin, BB, ACEI
• HF clinic follow up in 1 week
• SVT ablation once rheumatologic disease stable
5 days after discharge
Case 2: Emergency room consultation

58 year old female with 2 days of CP

BEFORE
3 days later
Discharged on Hospital Day #5

Cardiology Problem List
• Anterior STEMI
• Ischemic cardiomyopathy
• LV thrombus

Plan
• BB, ACE, ARA statin
• Short term triple therapy (DES + LV thrombus)
• Cardiology clinic in 1 week
3 Days After Discharge
Objectives

• Define sudden cardiac death

• Review SCD epidemiology and pathogenesis

• Review pharmacologic and device therapies for prevention of early SCD after acute myocardial infarction
Sudden Cardiac Death
Definition and Epidemiology

CLINICAL PRACTICE GUIDELINE

2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition or Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden cardiac arrest (S2.2.2-2)</td>
<td>SCA is the sudden cessation of cardiac activity such that the victim becomes unresponsive, with either persisting gasping respirations or absence of any respiratory movements, and no signs of circulation as manifest by the absence of a perceptible pulse. An arrest is presumed to be of cardiac etiology unless it is known or likely to have been caused by trauma, drowning, respiratory failure or asphyxia, electrocution, drug overdose, or any other noncardiac cause.</td>
</tr>
<tr>
<td>Sudden cardiac death (S2.2.2-2)</td>
<td>Sudden and unexpected death occurring within an hour of the onset of symptoms, or occurring in patients found dead within 24 h of being asymptomatic and presumably due to a cardiac arrhythmia or hemodynamic catastrophe.</td>
</tr>
</tbody>
</table>

JACC 2018;72(14)
Figure 1A: SCD Incidence and Total Events (52.2.2-1)

图1A：室颤和总事件（52.2.2-1）

Figure 2: Causes of Sudden Cardiac Death

图2：猝死原因
Edema
Scar
- conduction
- repolarization
- autonomic modulation

Sudden Death in Patients with Myocardial Infarction and Left Ventricular Dysfunction, Heart Failure, or Both

**VALIANT 2003**
Valsartan v captopril
AMI
EF < 40% or clinical HF
7% had SCD within 3 years of AM

Highest SCD rate early after AM

First 30 days:
1.4% SCD rate

2 year monthly steady-state:
0.14% SCD rate

NEJM 2005;352(25)

Predictors of SCD
- Old age
- Higher HR
- Lower EF
- BB intolerance
- Prolonged QRS
- Abnormal HR variability
- NSVT
- Sustained VT on EPS
- Late potentials

NEJM 2005;352(25)
Original Contribution

November 5, 2008

Sudden Death After Myocardial Infarction

A. Selcuk Adabag, MD, MS; Terry M. Therneau, PhD; Bernard J. Gersh, MB, ChB, DPhil; et al.

Figure 1. Cumulative Incidence of Sudden Cardiac Death and All-Cause Mortality After Myocardial Infarction Among Residents of Olmsted County, Minnesota

First 30 days: 1.2% SCD rate
Monthly steady-state: 0.12% SCD rate

The blue area on the plot represents the cumulative incidence of sudden death during the first 120 days after the index myocardial infarction.
VALIANT: clinical adjudication versus autopsy

15% of deaths underwent autopsy

42% of arrhythmic deaths reclassified
- 26% recurrent MI
- 12% cardiac rupture
- 4% pump failure

Circulation. 2010;122:597-602
OPTIMAAL: clinical adjudication versus autopsy

19% of deaths underwent autopsy

62% of arrhythmic deaths reclassified

Figure 1  Causes of death in all autopsied patients (n = 180) before and after the result of autopsy was used to determine cause of death.

AJM 2005;118:752-758

Early Post-AM Sudden Cardiac Arrest
Pharmacologic Primary Prevention
**Figure 2.** Survival free of any ventricular arrhythmia. Dotted line = placebo; solid line = carvedilol.

**CAPRICORN 2005**

AMI within 21d  
EF < 40%

JACC 2005;45(4)

**TRACE 1995**

AMI within 7d  
EF < 35%

NEJM 1995;333:1670-1677
ARB

**OPTIMAAL 2003**

AM within 10d
EF < 35%

Lancet 2002;360
NEJM 2003;349

ARA

**EPHESUS 2005**

AM within 3-14d
EF < 40%

JACC 2005;46
Amiodarone

**EMAT 1997**

<table>
<thead>
<tr>
<th>AM during hospitalization</th>
<th>EF &lt; 40%</th>
</tr>
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<tbody>
<tr>
<td>Lancet 1997;350</td>
<td></td>
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Sotalol

**SWORD 1996**

<table>
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<th>AM within 42d</th>
<th>EF &lt; 40%</th>
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<tr>
<td>Lancet 1996;348(924)</td>
<td></td>
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</table>
CAST 1991
AMI with 6d - 2yrs
EF < 40%
PVCs

Pharmacologic Therapy Summary

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<tr>
<th>Medication</th>
<th>Decreases Early SCD</th>
<th>Decreases Early All-Cause Mortality</th>
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<tr>
<td>BB</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
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<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>ARB</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>ARA</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Yes</td>
<td>Nb</td>
</tr>
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<td>Sotalol</td>
<td>Nb</td>
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Remote Post-AMI Sudden Cardiac Arrest
Device Primary Prevention
Improved Survival with an Implanted Defibrillator in Patients with Coronary Disease at High Risk for Ventricular Arrhythmia

**MADIT I 1996**

ICM with EF < 35%
NSVT
EPS

**NEJM 1996;335:1933-40**

Electrophysiologic Testing to Identify Patients with Coronary Artery Disease Who Are at Risk for Sudden Death

**MUSTT 1999**

ICM with EF < 40%
NSVT
EPS

**NEJM 1999;341:1882-90**
Prophylactic Implantation of a Defibrillator in Patients with Myocardial Infarction and Reduced Ejection Fraction

Remote Post-MI ICD Evidence

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<th>Trial</th>
<th>Inclusion</th>
<th>Why not applicable</th>
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<td>MADIT 1996</td>
<td>ICM with EF &lt; 35%</td>
<td>Required &gt; 3 weeks from AMI</td>
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<td></td>
<td>NSVT EPS</td>
<td>Required &gt; 2 months from CABG</td>
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<td>Required &gt; 3 months from PCI</td>
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<td>MUSTT 1999</td>
<td>ICM with EF &lt; 40%</td>
<td>84% &gt; 30 days out from AMI</td>
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<td></td>
<td>NSVT EPS</td>
<td>50% &gt; 3 years out from AMI</td>
</tr>
<tr>
<td>MADIT II 2002</td>
<td>ICM with EF &lt; 30%</td>
<td>Required &gt; 1 month from AMI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Required &gt; 3 months from revascularization</td>
</tr>
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</table>

NEJM 2002;346:877-83
NEJM 1996;335:1933-40
NEJM 1999;341:1882-90
### Remote Post-MI ICD Evidence

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<td>Required &gt; 1 month from AMI&lt;br&gt;Required &gt; 3 month from revasc</td>
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### Early Post-AMI Sudden Cardiac Arrest

Device Primary Prevention
Prophylactic Use of an Implantable Cardioverter-Defibrillator after Acute Myocardial Infarction

![Graphs showing risk of death over time for ICD and Control groups.](image1)

**DINAMIT 2004**

- 6-40 days post MI
- EF < 35%
- Abn HR variability

---

Defibrillator Implantation Early after Myocardial Infarction

![Graphs showing risk of death over time for ICD and Control groups.](image2)

**IRIS 2009**

- 5-31 days post MI
- EF < 40%
- NSVT
- Elevated resting HR

---

References:

NEJM 2004;351:2481-8

NEJM 2009;361:1427-36
### National Coverage Determination (NCD) for Implantable Automatic Defibrillators (20.4)

2. Patients with a primary diagnosis of AM and low EF must be considered for ICD unless:
   - AM within 40 days
   - Revascularization within 90 days
   - NYHA IV heart failure
   - Revascularization candidate

For these patients, the following criteria must be met:
- AM + Low EF = ICD unless
- AM within 40 days
- Revascularization within 90 days
- NYHA IV heart failure
- Revascularization candidate

JACC 2018;72(14)
NEJM 2009;361:1427-36
NEJM 2004;351:2481-8
Wearable Cardioverter-Defibrillator Use in Patients Perceived to Be at High Risk Early Post-Myocardial Infarction

8453 patients
1.6% received appropriate shocks
1.2% received appropriate shocks within 30 days of AMI
1.1% received inappropriate shocks
91% survived event to emergency room
  - Average of 2 shocks per event

Table 3. Primary, Secondary, and Other Outcomes.

<table>
<thead>
<tr>
<th>Event</th>
<th>Device Group (N=1524)</th>
<th>Control Group (N=778)</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrhythmic death</td>
<td>25 (1.6)</td>
<td>19 (2.4)</td>
<td>0.67 (0.37–1.21)</td>
<td>0.18</td>
</tr>
<tr>
<td>No. of patients (%)↑</td>
<td>9</td>
<td>0</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Death from any cause</td>
<td>48 (3.1)</td>
<td>38 (4.9)</td>
<td>0.64 (0.43–0.98)</td>
<td>0.04</td>
</tr>
<tr>
<td>No. of patients (%)</td>
<td>12</td>
<td>0</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Device worn at time of death or event leading to death — no.</td>
<td>12</td>
<td>0</td>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

- 1.4% received appropriate shocks
- 100% converted VT/VF
- 70% survived event (30% developed PEA, bradyarrhythmia, asystole)
- 65% survived to trial conclusion
- 0.6% received inappropriate shocks
- 4.5% aborted shock by pressing response button
LifeVest Wearable Defibrillator Reduces Total Mortality By 36 Percent At 90 Days

The Landmark VEST Trial Shows 90-Day Use of LifeVest WCD Reduces Total Mortality After Heart Attack

Recommendations for Wearable Cardioverter-Defibrillator
References that support the recommendations are summarized in Online Data Supplement S6.

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>RECOMMENDATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ea</td>
<td>B-NR</td>
<td>1. In patients with an ICD and a history of SCA or sustained VA in whom removal of the ICD is required (as with infection), the wearable cardioverter-defibrillator is reasonable for the prevention of SCD (S11.2.1–S11.2.4).</td>
</tr>
<tr>
<td>Eb</td>
<td>B-NR</td>
<td>2. In patients at an increased risk of SCD but who are not ineligible for an ICD, such as awaiting cardiac transplant, having an LVEF of 35% or less and are within 40 days from an MI, or have newly diagnosed NICM, revascularization within the past 90 days, myocarditis or secondary cardiomyopathy or a systemic infection, the wearable cardioverter-defibrillator may be reasonable (S11.2.1–S11.2.5).</td>
</tr>
</tbody>
</table>
Case 3: Inpatient consult

60M with HTN and T2DM admitted with syncope
Discharged on hospital day #3

Problem List
- Multivessel coronary disease awaiting surgical revascularization
- High risk syncope, cannot rule out ventricular arrhythmia
- HTN T2DM

Plan
- Asa, statin, BB, ARB
- WCD
- Follow up with cardiology in 3 days (at home in Texas)
Summary

• Sudden cardiac death is a messy clinical endpoint without autopsy

• The vast majority of SCD is attributed to ischemic heart disease

• Risk of SCD is highest in 1st month after AMI

• BB*, ACEi, ARB, and ARA* have best evidence for early post-AMI SCD prevention

• ICD therapy is mostly not available in early post-AMI period

Summary

• WCD requires patient participation

• WCD data is cloudy

• WCD successfully aborts lethal ventricular arrhythmias
  • Despite this 30% do not survive event

• WCD risks inappropriate shocks
  • 3 aborted shocks for every 1 appropriate shock

• WCD is assigned a class 2b recommendation ("may be reasonable") in ACC/AHA/HRS 2017 VA guideline
Sudden Cardiac Death After Myocardial Infarction

Minneapolis Heart Institute Grand Rounds
February 18, 2020

@RobFraserMD