Optimizing Timing of ICD Implant Post MI

Cynthia M. Tracy, MD
George Washington University
Washington, DC

No COI to declare
Reduction in Total Mortality: ICD vs Control

Boriani et al. PACE 2006;29
Decisions Regarding ICD Implants

• Secondary prevention- timing is simple
• Conditions at high risk for SCD (e.g.-familial syndromes)-
  – Timing elective but screening complex
• Unanswered questions regarding 1º prevention:
  – Optimal timing of ICD implant after MI or after the first diagnosis of HF
  – Optimal LVEF cut-off able to identify high-risk patients
• Data limited as RCTs typically not include:
  – Acute phase of an MI
  – Recent revascularization
  – NYHA class IV symptoms
  – Newly diagnosed HF
Cardiac Mortality EF and QRS Duration

- Most important risk parameter for all cause mortality and SCD is LVEF
  - Sensitivity, specificity and positive predictive accuracy of LVEF ≤40% predicting major arrhythmic events variable in different studies: 45–85%, 55–75% and 9–24% respectively
- Impact of QRS:
  - LVEF > 35% and QRS <150 msec - 17.9% mortality
  - LVEF ≤35% and QRD >150 msec - 39.4% mortality

Proportion of death attributed to specific causes of death across left ventricular ejection fraction groups

- Confounding risk assessment post MI is the fact that arrhythmic death occurs in all EF groups

Recovery of LV Function Post MI

- 261 patients in HEART (ramipril) trial, all with reperfusion therapy
- Day 1- **3.4%** (9/261) had normal LVEF $\geq 0.55$
- **66%** (171/261) had improvement in EF (0.05 0.10) with final EF 0.57 0.96
- Of 252 patients with EF <0.55:
  - **13%** complete recovery by day 14
  - **22%** complete recovery by day 90
  - **36%** had partial recovery by day 90

$\Rightarrow$ Early dysfunction often improves

Solomon et al.
Ann Intern Med 2001;134:451-8
Summary of Major ICD Trials

<table>
<thead>
<tr>
<th>Trial Name, Pub Year</th>
<th>Hazard ratio</th>
<th>LVEF, other features</th>
</tr>
</thead>
<tbody>
<tr>
<td>MADIT-I (192) 1996</td>
<td>0.46</td>
<td>0.35 or less, NSVT, EP positive</td>
</tr>
<tr>
<td>AVID (266) 1997</td>
<td>0.62</td>
<td>Aborted cardiac arrest</td>
</tr>
<tr>
<td>CABG-Patch (265) 1997</td>
<td>0.83</td>
<td>Aborted cardiac arrest</td>
</tr>
<tr>
<td>CASH* (643) 2000</td>
<td>0.82</td>
<td>Aborted cardiac arrest or syncope</td>
</tr>
<tr>
<td>CIDS (642) 2000</td>
<td>0.69</td>
<td>0.30 or less, prior MI</td>
</tr>
<tr>
<td>DEFINITE (648) 2004</td>
<td>0.65</td>
<td>0.35 or less, NICM and PVCs or NSVT</td>
</tr>
<tr>
<td>DINAMIT (152) 2004</td>
<td>1.08</td>
<td>0.35 or less, MI within 6 to 40 days and impaired cardiac autonomic function</td>
</tr>
<tr>
<td>SCD-HeFT (7a) 2005</td>
<td>0.77</td>
<td>0.35 or less, LVD due to prior MI and NICM</td>
</tr>
</tbody>
</table>

Zipes et al. JACC Vol. 48, No. 5, 2006 e249
When is it too early? Defibrillator in AMI Trial (DINAMIT) and Immediate Risk-Stratification Improves Survival (IRIS) study

- Evaluated effect of ICDs on survival early post MI
- **DINAMIT:**
  - MI 6-40 days
  - LVEF ≤ 30%
  - Decreased HRV
- **IRIS:**
  - MI 5-31 days
  - LVEF ≤ 40%
  - HR ≥ 90 BPM on first EKG and/or NSVT at ≥ 150 bpm day 5-31

Hohnloser et al. NEJM 2004;351:2481-2488
Steinbeck G, NEJM 2009; 361:1427-1436
Conclusions from DINAMIT and IRIS

- **IRIS:** During the 1st month after MI- ICD implantation does not offer survival benefit

- **DINAMIT:** Pts who receive an ICD early post MI and who receive either shocks or ATP are at ↑risk for dying soon of nonarrhythmic causes

- **Possible explanations:**
  - Significant recovery LVEF occurred which diluted long-term ICD benefit
  - Some SCD early post MI due to recurrent ischemia
  - ICD implant imposed risk early post MI

- **Reduced heart rate variability may have selected a group of pts with a high mortality from nonarrhythmic causes**

- **OR.....**

Hohnloser et al. NEJM 2004;351:2481-2488
Steinbeck G, NEJM 2009; 361:1427-1436
ICD Shocks and Prognosis

SCD-HeFT (ICD group)
N=811 (269 pts received shocks: 128 only appr, 87 only inappr, 54 both)

Possible explanations:

- VT/VF - harbinger of end stage HF
- VT/VF - marker of progressive HD
- Independent impact of shocks (cell damage, negative inotroipoic effect, activation of signaling pathways)
- Other - post traumatic stress
- DINAMIT/IRIS - Perhaps early post MI pts more vulnerable to the negative effects of shocks

Another Variable: Timing of Implant Relative to Revascularization

- **CABG-Patch**: CBG alone vs CBG + ICD:
  - < 80 years + LVEF < 36% + Abnormal SAECG
- **Post-hoc analysis MADIT II- ICD**
  - Benefit seen only > 6 months after revascularization
- **Possible explanations for lack of benefit early post MI or revascularization**:
  - Heterogeneous populations including lower risk pts who’s EF ↑ with time and pts at high-risk with high mortality rates regardless of therapy

---

(N Engl J Med 1997;337:1569-75.) CABG PATCH
Paradox

• Risk of SCD after an MI is highest during the first weeks after the event
  – 14–24 % in the first month
  – Risk declines after 12 months
• BUT early post MI implant may reduce SCD but not overall mortality
• AND the benefit of ICD therapy increases as the time passes from the MI to ICD implantation

Predictors of sudden cardiac death change with time after myocardial infarction: results from the VALIANT trial MI

- Double-blind RCT (valsartan, captopril, or both)
- 14,703 patients with AMI with HF, LVEF < 40%
- Factors strongly associated with SCD differed over time:
  - HR and CrCl at baseline strongly associated with SCD in-hospital
  - Recurrent CV events (HF, MI, and rehosp) and LVEF < 40% more strongly associated with post DC SCD

Limitations of EF in Risk Stratification Post MI

- Limited sensitivity and poor specificity
- Cumulative incidence of SCD is greatest in post-MI pts with LVEF $\leq 30$
  - But incidence of SCD is greater in those with LVEF $\geq 40\%$ in the first 30 days compared with patients with an $\leq$ LVEF 30\% after 90 days
- The strength of the association between LVEF and SCD is greatest $> 6$ months post MI
  - Alternatively other factors important early post MI

**The Good News:** Benefit of ICD Appears Late and Persists Over Time (MADIT-II: post MI, LVEF < 30%)

Mortality rates (per 100 person-years of follow-up) in conventionally treated pts and ICD pts grouped by time from MI in quartiles

Survival curves comparing ICD and conventionally treated pts with recent MI and remote MI

Summary

• Risk stratification early post MI remains problematic
  – Competing importance of multiple variables (autonomics, scar formation, etc...)

• Too early ICD implant reduces SCD but does not improve mortality
  – Not all early post MI is SCD

• Importance of revascularization and optimizing EF
  – EF often increases after initiation of beta blockers and ACE inhibitors and after recovery from the acute event putting pt outside of risk category
  – Effects of OMT modify the organic and electrical substrate on which ICD therapy acts
  – Survival benefit of OMT suggests that treatments affecting remodeling impact on SCD and survival compared to treatments focused solely on treating arrhythmias

When/Who

• Best data supports: > 40 days post MI and >3 months post PCI or CABG
• **MADIT II** criteria (prior MI with an LVEF ≤30%)
  – No EPS
• **SCD-HEFT** criteria (LVEF ≤35% and NYHA II or III HF)
  – No EPS
• **MUSTT** and **MADIT I** criteria (LVEF ≤40% not meeting above criteria, we recommend periodic monitoring)
  – Consider EPS and if + ICD
• < 1 month post MI in high risk, can consider defibrillator vest but while this is likely to decrease SCD, it does not appear likely to decrease overall mortality for this group