HF and CRT: CRT-P versus CRT-D

Andrew E. Epstein, MD
Professor of Medicine, Cardiovascular Division
University of Pennsylvania

Chief, Cardiology Section
Philadelphia VA Medical Center
Philadelphia, PA
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SCD Risks in HF Patients with LV Dysfunction

Total Mortality ~15-40%; SCD accounts for ~50% of total mortality.

* MADIT II control group total mortality at 24 months 22%.
Secondary Prevention Trials: AVID/CASH/CIDS Meta-analysis

Death

Arrhythmic death

MADIT II
Conventional versus ICD Therapy

Reduction in death rate with ICD Rx: 12% at 1 yr, 28% at 2 yrs, 28% at 3 yrs

Probability of Survival

Year

0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0

Conventional

Defibrillator

No. At Risk

Year

0 1 2 3 4

Conventional 742 502 (0.91) 274 (0.84) 110 (0.78) 9

Defibrillator 490 329 (0.90) 170 (0.78) 65 (0.69) 3

P = 0.007

SCD-HEFT
Mortality by Intention-to-treat

Amiodarone vs Placebo
1.06
.86, 1.30
.529

ICD Therapy vs Placebo
.77
.62, 0.96
.007

CRT Improves Quality of Life and NYHA Functional Class

Average Change in QoL Score (MLWHF)

NYHA: Proportion Improving 1 or More Class

1. NEJM 2002;346:1845-53
2. NEJM 2001;344:873-80
3. Eur Heart J 2002;23:1780-1787
5. JAMA 2003; 289:2685-94
MADIT CRT:
Changes in Mean LV Volumes and EF at 1 Year

Trials of CRT and ICDs

ICD

MADIT-CRT
RAFT

CRT-P

COMPANION
REVERSE
CeRtiTuDe

CRT-D
MADIT-CRT

Kaplan-Meier Estimates of the Primary Outcome

Death or Hospitalization for Heart Failure

Event-Free Survival

Years of Follow-up

No. at Risk

<table>
<thead>
<tr>
<th>Group</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
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<td>ICD/CRT</td>
<td>894</td>
<td>790</td>
<td>615</td>
<td>429</td>
<td>278</td>
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<td>ICD</td>
<td>984</td>
<td>770</td>
<td>572</td>
<td>384</td>
<td>214</td>
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</tbody>
</table>

HR (95% CI) 0.75 (0.64, 0.87)
P=0.0002

ICD-CRT (5-yr HF-free survival rate 0.576)

ICD (5-yr HF-free survival rate 0.487)
Kaplan-Meier Estimates of All cause Mortality

Death at Any Time During the Study

Event-Free Survival

Years of Follow-up

No. at Risk

<table>
<thead>
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</table>

HR (95% CI): 0.75 (0.62, 0.91)
P-value: 0.008

ICD-CRT (3-yr survival rate 0.714)

ICD (3-yr survival rate 0.694)
COMPANION:
Primary Endpoint: Mortality + Hospitalization

CRT vs OPT: RR = 20%, \( P = .008 \) (Critical boundary = .014)
CRT-D vs OPT: RR = 20%, \( P = .007 \) (Critical boundary = .022)

12-Month Event Rates
OPT: 68%
CRT: 55% (AR = 13%)
CRT-D: 56% (AR = 12%)

COMPANION:
Secondary Endpoint: All-Cause Mortality

CRT vs OPT: RR=24%, \( P=0.060 \) (Critical boundary=.014)
CRT-D vs OPT: RR=36%, \( P=0.003 \) (Critical boundary=.022)

REVERSE CRT "ON": Mortality CRT-P vs. CRT-D

Univariate Analysis
HR = 1.53 (0.82-2.85), p = 0.18

Multivariate Analysis
HR = 2.74, p = 0.009

Prospective Multicenter Cohort Study
  - Funded and Coordinated by the French Society of Cardiology

To evaluate the extent to which:
  - CRT-P patients differ from CRT-D patients in real life settings
  - CRT-P patients could have additionally benefited from a back-up defibrillator

Enrollment from Jan. 2008 to Dec. 2010

1,705 patients: 535 CRT-P and 1170 CRT-D

Follow-up at 6, 12, 18, and 24 months
  - Clinical / Echo / Rhythm
  - Completed in 1,611 (94.5%)
CeRtiTuDe - Overall Mortality

Among the 1,611 patients with complete follow-up, 286 deaths

CRT-D: 6.2 %/year

CRT-P: 12.2 %/year
Why Consider CRT-P without “D”?

1. Both appropriate and inappropriate shocks are avoided.
2. Some patients may not want “D”.
3. Some CRT-P indications are independent of ICD indications.
4. If LVEF is anticipated to improve, the benefit of “D” may be minimized.
5. CRT-P saves lives (COMPANION and CARE-HF)
6. Decreased cost.
CRT Indications Algorithm

Patient with cardiomyopathy on GDMT for ≥3 mo or on GDMT and ≥40 d after MI, or with implantation of pacing or defibrillation device for special indications

LVEF <35%
Evaluate general health status
Acceptable noncardiac health
Evaluate NYHA clinical status

NYHA class I
- LVEF ≤30%
- QRS ≥150 ms
- Ischemic cardiomyopathy
- Non-LBBB pattern

NYHA class II
- LVEF ≤35%
- QRS ≥150 ms
- Sinus rhythm
- Sinus rhythm
- Non-LBBB pattern
- LBBB pattern
- Non-LBBB pattern
- LBBB pattern
- LBBB pattern
- LBBB pattern
- LBBB pattern

NYHA class III & Ambulatory class IV
- LVEF ≤35%
- QRS ≥150 ms
- Sinus rhythm
- Sinus rhythm
- Non-LBBB pattern
- LBBB pattern
- Non-LBBB pattern
- LBBB pattern
- LBBB pattern
- LBBB pattern
- LBBB pattern

Special CRT Indications
- Anticipated to require frequent ventricular pacing (>40%)
- Atrial fibrillation. If ventricular pacing is required and rate control will result in near 100% ventricular pacing with CRT

Colors correspond to the class of recommendations in the ACCF/AHA Table 1.

Benefit for NYHA class I and II patients has been shown in CRT-D trials, and while patients may not experience immediate symptomatic benefit, late remodeling may be avoided along with long-term HF consequences. There are no trials that support CRT-pacing (without ICD) in NYHA class I and II patients. Thus, it is anticipated these patients would receive CRT-D unless clinical reasons or personal wishes make CRT-pacing more appropriate. In patients who are NYHA class III and ambulatory class IV, CRT-D may be chosen but clinical reasons and personal wishes may make CRT-pacing appropriate to improve symptoms and quality of life when an ICD is not expected to produce meaningful benefit in survival.
DBT Considerations Regarding Longevity and Comorbidities: What are the Patient’s Goals/Focus on the Elderly

- “Physicians, patients, and their families increasingly will be faced with decisions about device-based therapies (ICD and CRT) in elderly patients who meet conventional criteria for implantation. These decisions require … estimates of life expectancy, consideration of comorbidities and procedural risk, and patient preferences. Although these factors are important when device implantation is considered in any age group, they assume greater weight in clinical decision-making among the elderly.”

Survival vs QOL

Comorbidities and Survival

- Observational study of ICD outcomes in Canada
- 2,467 patients age ≥18 and ≤105 years
- Comorbidities associated with death
  - PVD
  - Pulmonary disease
  - CKD
  - HF
- HRs adjusted for age, gender, and HF
  - 1 noncardiac comorbidity: 1.72
  - 2 noncardiac comorbidities: 2.79
  - 3 noncardiac comorbidities: 2.98

Comorbidities and Survival

Risk and Mortality in MADIT II: U-shaped Curve of ICD Efficacy

- 5 risk factor model
  - Age
  - NYHA class
  - BUN
  - Atrial fibrillation
  - QRS duration
- Excluded VHR patients (BUN ≥50 and/or Cr ≥2.5 mg/dl [MADIT II exclusion BUN ≥70 and/or Cr ≥3.0 mg/dl]). N = 60

Mortality by Risk Score Quintile in Patients with ICDs

CARE-HF
Primary Endpoint
(All-cause Mortality or Unplanned Hospitalization for Major CV Event)

Event-free Survival

HR 0.63 (95% CI 0.51 to 0.77)

Number at risk

Summary

- CRT alone (CRT-P) or with an ICD (CRT-D) is highly effective therapy to decrease morbidity and mortality.
- Almost all patients with a CRT-P indication have an indication for and ICD at the time of implantation, and CRT-D is reasonable.
- The decision to implant a CRT-P or CRT-D requires discussion with the patient and their telling you what are their goals.
- CRT-P is appropriate when LVEF is relatively well-preserved and pacing is needed (CHB, AF/slow VR), but CRT-D is appropriate in borderline circumstances to avoid second operation/pocket opening.