Have We Expanded Our Use of CRT for Heart Failure Patients?

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Potential Conflicts of Interest

- I receive research funding from the National Heart, Lung and Blood Institute and from the Agency for Healthcare Research and Quality.
Cardiac Resynchronization Therapy

MIRACLE (n=453)
CONTAK-CD (n=490)
COMPANION (n=1520)
CARE-HF (n=813)
REVERSE (n=610)
MADIT-CRT (n=1820)
RAFT (n=1798)

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Potential Benefits from CRT

- Survival
- HF hospitalizations
- Quality of life
- Functional status
- Reduction in MR
- Improvement in LVEF
- Reduction in VT/VF
- Reduction in AF (??)
COmparison of Medical Therapy, Pacing, ANd DefibrillatION in Heart Failure (COMPANION Trial)

- CRT vs. OPT: RR = 19%, p=0.014 (Adjusted p-value = 0.015)
- CRT-D vs. OPT: RR = 20%, p=0.010 (Adjusted p-value = 0.011)

CArdiac REsynchronisation in Heart Failure (CARE-HF) Study (N=813)

HR 0.63 (95% CI 0.51 to 0.77)

P < 0.0001

Cleland JGF et al. NEJM 2005;352:1539-1549
ACC/AHA 2008 Guidelines for CRT Implantation

- Class I indication in patients with:
  - LVEF less than or equal to 35%
  - NYHA Class III or ambulatory Class IV heart failure symptoms despite optimal medical therapy
  - QRS duration greater than or equal to 0.12 seconds
  - Sinus rhythm

- Class IIa indication in patients with all of the above but in atrial fibrillation
MADIT-CRT

- ICM NYHA I/II and NICM NYHA II
- EF < 0.30; QRS > 0.13 sec
- Randomized 1,820 patients

ICD only N=731
CRT-D N=1,089

Resynchronization–Defibrillation for Ambulatory Heart Failure Trial (RAFT)

NYHA II or III EF < 0.30; intrinsic QRS ≥0.12sec

Randomized 1,798 patients

ICD only N=904

CRT-D N= 894

Update to ACC/AHA 2008 Guidelines

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

Comorbidities and/or frailty limit survival with good functional capacity to <1 y

Continue GDMT without implanted device

Acceptable noncardiac health

Evaluate NYHA clinical status

NYHA class I symptoms

NYHA class II, III, and ambulatory class IV symptoms

Class I
LBBB pattern, sinus rhythm, QRS duration ≥150 ms

Class IIA
LBBB pattern, QRS 120-149 ms

OR
Non-LBBB pattern, QRS ≥150 ms

Class IIb
Anticipated to require frequent ventricular pacing (>40%)

OR
Atrial fibrillation, if ventricular pacing is required or QRS criteria above are met and rate control will result in near 100% ventricular pacing with CRT

Class IIb
Non-LBBB pattern, QRS 120-149 ms

NYHA class IV (stage D)
Refractory symptoms or dependence on intravenous inotropes

Device not indicated except in selected patients listed for transplantation or with LV assist devices

If device already in place, consider deactivation of defibrillation
Update to the ACC/AHA 2008 Guidelines: What Has Not Changed?

- Class I indication in patients with:
  - LVEF less than or equal to 35%
  - NYHA Class III or ambulatory Class IV heart failure symptoms despite optimal medical therapy
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- Class Ila indication in patients with all of the above but in atrial fibrillation
Have We Expanded Our Use of CRT for Heart Failure Patients?

- I do not know!
- We certainly have new evidence and updated guidelines, but no decisions have been made by CMS regarding reimbursement
- What are you doing in your practice?
Remember that 30-40% of patients who receive a CRT device do not respond!

- Define response!!!
Determinants of Response to CRT

- Patient characteristics:
  - LBBB vs. non-LBBB (a word about RBBB)
  - Non-ischemic CMY vs. ischemic CMY
  - Women vs. Men
  - Older patients
  - Patients with multiple comorbidities
- Location of the CS lead
- Programming of the device
Effects of CRT-D by QRS Morphology in MADIT-CRT

- Non-LBBB
  - 534, 30%
- IVCD, 306, 17%
- RBBB, 228, 13%
- LBBB, 1281, 70%

Zareba et al. Circulation 2011;123:1061-1072
Cumulative Probability of Heart Failure Events or Death by Treatment in Patients with LBBB and Non-LBBB

**LBBB**

*Duke Clinical Research Institute*

**Non-LBBB**

Zareba et al. *Circulation* 2011;123:1061-1072

**HR=0.47**

*p<0.001*

**HR=1.24**

*p<0.257*
Cumulative Probability of Heart Failure Events or Death by Treatment in Patients with LBBB QRS in MADIT-CRT

HR = 0.47
p < 0.001

Zareba et al. Circulation 2011;123:1061-1072
Response to CRT: Patient Selection

**Ischemic versus Non-Ischemic**

![Graph showing survival rates for different patient selection criteria.](image)

- **Non-ischaemic CM** ($n = 380$)
- **Ischaemic CM** ($n = 190$)
- **Unsuccessful LV lead** ($n = 50$)

* $P < 0.001$ vs. ischaemic CM and ULV

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Adelstein et al. Eur Heart J 2011;32:93-103
From: Cardiac Resynchronization Therapy Is More Effective in Women Than in Men: Title and subTitle
BreakThe MADIT-CRT (Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy) Trial


Figure Legend:

Kaplan-Meier Estimates of Cumulative Probability of Heart Failure or Death Stratified by Sex and ICD or CRT-D Therapy

The 4 curves reflect the probability of heart failure or death, whichever comes first, over time in women and men having the device therapy—implanted cardioverter-defibrillator (ICD) or cardiac resynchronization therapy with defibrillator (CRT-D)—to which they were randomized. Women randomly assigned to CRT-D therapy (blue line) had the best result. The purple line indicates female ICD therapy; the black line indicates male ICD therapy; and the red line indicates male CRT-D therapy.
Figure Legend:
Kaplan-Meier Estimates of the Cumulative Probability of Death in Women and Men by Device Therapy
(A) Women had a significantly lower probability of death over time with CRT-D (red line) than with ICD (black line). (B) Men had similar probability of death over time with CRT-D therapy (red line) or with ICD therapy (black line). Abbreviations as in Figure 1.
Determinants of Response to CRT

- Patient characteristics:
  - LBBB vs. non-LBBB (a word about RBBB)
  - Non-ischemic CMY vs. ischemic CMY
  - Women vs. Men
  - Older patients
  - Patients with multiple comorbidities
- Location of the CS lead
- Programming of the device
LV Lead Location – MADIT-CRT

Unadjusted \( P = 0.052 \)

Unadjusted \( P = 0.014 \)

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LV Lead Location

- Echocardiography-guided LV lead placement targeting the site of latest LV mechanical activation
- Avoiding scar
Device Programming

- Do everything you can to achieve 100% biv-pacing.
- Make sure you have enough safety margin for the pacing output of the LV lead
- Optimizing the AV interval and the VV interval (random)
Gaps in Knowledge

- What is the best measure of dyssynchrony?
- Many echo tests have been proposed, but none has been proven to be accurate in distinguishing responders from non-responders
- These tests lack sensitivity, specificity, and reproducibility
Predictors of Response to CRT (PROSPECT)

- N= 426 patients
- Studied 12 echocardiographic methods for their ability to predict response
- All methods lacked sensitivity and specificity to affect clinical decisions
- These methods should not be used routinely in evaluating a patient for CRT
- Other methods are under investigation (eg, strain measurements, 3-dimensional imaging, scar location) that may be able to distinguish responders from non-responders with more accuracy
- However, before they can be recommended for general use, their applicability should be tested in a multi-center setting
Question # 1

- Which of the following patients is least likely to benefit from CRT?
  - A 64 yo woman with NYHA class III, LVEF of 20%, non-ischemic CMY, QRS width of 150 ms with LBBB morphology
  - A 50 yo man with NYHA class III, ischemic CMY with an EF of 25%, QRS width of 140 and LBBB
  - A 78 yo man with NYHA class II, ischemic cardiomyopathy with an LVEF of 10% and QRS width of 130 ms with non-LBBB
Question # 2

Which of the following is true:

- CRT is a Class I indication in patients with NYHA class I sx, LVEF < 30%, QRS of > 150 ms with LBBB and ischemic CMY

- CRT should be offered to all patients regardless of their burden of comorbidities or their life expectancy

- CRT has been shown to improve survival and reduce heart failure hospitalizations in patients with a QRS width of 110 ms

- The RCT that convincingly showed improved survival from CRT alone was CARE-HF
Conclusions

- Is the following statement true or false?
  - Echocardiography-guided LV lead placement targeting the site of latest LV mechanical activation has been shown to improve patient outcomes.
Conclusions

- CRT has been shown to improve survival and reduce heart failure hospitalizations in patients with an LVEF ≤ 35%, a wide QRS complex, NYHA class II, III and ambulatory class IV symptoms despite optimal medical therapy.
- Certain groups of patients are more likely to benefit from CRT than others.
- Uncertainties remain regarding the best measure of dyssynchrony and the best method for optimization.
- Imaging-guided LV lead placement will become more widespread.