Heart Failure, From an Electrophysiological Perspective
Device Therapy in the Failing Heart

Raffaele Corbisiero MD
Director of Electrophysiology
Deborah Heart & Lung Center
Fibrillation, especially atrial, has become important in the clinic. Since Ventricular fibrillation usually results in sudden cardiac death, it is, of course, of much less importance.
Expected Mortality Reduction with Drugs

1. Mean of major beta blocker trials
2. Mean of major ACE inhibitor trials

Reduction in Mortality (%)

Mean\(^1\) BB
Mean\(^2\) ACE-I
Aldactone RALES\(^3\)
Eplerenone EPHESUS\(^4\)

40%
30%
30%
21%

1. Mean of major beta blocker trials
2. Mean of major ACE inhibitor trials
This slide demonstrates that the benefits of medical therapy are clear, however, we must remember that compliance is an issue with these patients and is sometimes as low as 50%.

2 Connolly SJ. *Circulation.* 2000; 101; 1297-1302.
Mechanism of Death in HF


NYHA II
No. of deaths
n=103

SCD 64%
HF 12%
Other 24%

NYHA III
No. of deaths
n=232

SCD 59%
HF 26%
Other 15%

NYHA IV
No. of deaths
n=27

SCD 33%
HF 56%
Other 11%

HF = mortality secondary to worsening heart failure
SCD = sudden cardiac death
The MERIT-HF study evaluated the effects of metoprolol on mortality in patients with decreased ejection fraction and symptoms of HF.

A post-hoc analysis of the MERIT-HF study looked at the total mortality and mode of death relative to the NYHA functional classification.

The proportion of sudden cardiac deaths decreased with increasing severity of NYHA functional class.

Sudden death occurred in nearly 60% of patients.

The proportion of patients who died from worsening HF increased with increasing functional class.

Ventricular dysrhythmias, not controlled by medical therapy, are often the cause of SCD in HF.

Clearly, there are unmet needs in the management of patients with HF.

A summary of the major clinical trials showing the benefit of prophylactic ICD’s. The MADIT, MUSTT and MADIT II trial had patient populations with ischemic cardiomyopathy. Of note, around two thirds of these patients carried a diagnosis of CHF. The SCD HeFT trial included all etiologies of LV dysfunction.
Death or First Hospitalization for New or Worsening Heart Failure

- VVI-40 patients had fewer occurrences ($p \leq .03$)

- 1 year survival free of composite
  - VVI-40 83.9%
  - DDDR-70 73.3%
Clearly, ICD’s can help in sudden cardiac death risk prevention, however, the deleterious effects of ventricular pacing in an abnormal heart must be kept in mind.
## Cardiopulmonary Exercise Test Results

### Baseline to One month CPX

**Cardiopulmonary Exercise Test Results**

<table>
<thead>
<tr>
<th>Metric</th>
<th>Rest</th>
<th>Max</th>
<th>Pred</th>
<th>%Pred</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time Min/Min</td>
<td>0.4</td>
<td>3.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VO2 L/min</td>
<td>0.538</td>
<td>8.947</td>
<td>1.544</td>
<td>(61)</td>
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<tr>
<td>VO2/kg mL/kg/min</td>
<td>7.0</td>
<td>13.0</td>
<td>14.3</td>
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<tr>
<td>METS</td>
<td>1.0</td>
<td>5.6</td>
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<tr>
<td>VCO2 L/min</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>VO2/kg mL/kg/min</td>
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<td></td>
<td></td>
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<tr>
<td>VE(BTPS) L/min</td>
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</tr>
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<td>RR</td>
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<tr>
<td>RQ</td>
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<tr>
<td>VEO2</td>
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<tr>
<td>VECO2</td>
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<tr>
<td>PetO2</td>
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</tr>
<tr>
<td>PetCO2</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>SpO2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VD/Vt E</td>
<td></td>
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<td></td>
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<tr>
<td>VD/Vt A</td>
<td></td>
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</tr>
<tr>
<td>HR</td>
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<td>O2 Puls</td>
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</tr>
<tr>
<td>Speed</td>
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### Additional Metrics

<table>
<thead>
<tr>
<th>Metric</th>
<th>Value</th>
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<tbody>
<tr>
<td>VO2 L/min</td>
<td>0.244</td>
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<tr>
<td>VO2/kg mL/kg/min</td>
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<tr>
<td>METS</td>
<td>1.0</td>
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<tr>
<td>VCO2 L/min</td>
<td>0.201</td>
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<tr>
<td>VE(BTPS) L/min</td>
<td>10.3</td>
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<td>RR</td>
<td>16</td>
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<tr>
<td>RQ</td>
<td>0.82</td>
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<td>VEO2</td>
<td>42</td>
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<tr>
<td>VECO2</td>
<td>51</td>
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<tr>
<td>PetO2</td>
<td>105.9</td>
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<td>PetCO2</td>
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<td>SpO2</td>
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<td>VD/Vt E</td>
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<tr>
<td>VD/Vt ABG</td>
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<tr>
<td>HR RPM</td>
<td>107</td>
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Personal experience of first patient with biventricular pacemaker. Dramatic improvement in symptoms were noted, however, patient did die of VF.
Any Death

12 month event rate reductions:
CRT = 23.9%
CRT-D = 43.4%

p = .002, CRT-D vs. OPT
p = .12, CRT vs. OPT

12 month OPT Event Rate
(1-y) = 19.0%

Days from Randomization

% Patients Event-Free

CRT-D
CRT
OPT
The results of COMPANION, to date, are the most important resynchronization therapy trial.
Good News:
• Multiple studies show benefit in heart failure patients via device therapy
  - ICD
  - CRT

Bad News:
• Less than 20% indicated patients receive one
• 30% Non-responder rate
Despite the promising benefit of device therapy, we must keep in mind two key points:

1. In the USA, only one out of every five persons who need an ICD are receiving one.

2. The non-responder rate in CRT therapy is over 30%.
QRS duration is only weakly correlated with acute improvement \(^1,^2\)

However, change in QRS duration does not correlate with acute improvement\(^2\)

\(r = 0.51\)

\[\Delta\text{QRS (msec)}\]

\[\Delta\frac{dP}{dt}, \Delta\frac{dP}{dt}_{\text{max}}\]

1 Kadhiresan et al., PACE, 23:II12, 2000
2 Nelson et al., Circulation, 101:2703-9, 2001
The ECG is only the beginning in determining CRT candidate. The post CRT ECG is of little use or value.
Dyssynchrony

- ECG is only the start
- Post CRT ECG is of little value
- More direct measure of dyssynchrony is needed, such as echo or more sophisticated imaging, CT/MRI
- We are underutilizing CRT using a wide QRS as an diagnosis criteria. 40% of narrow QRS CHF patients may have dyssynchrony
Case study 2

Post-op PA / LAT
Once you have selected a patient for CRT, the most important area of concern is lead placement. Here we see a chest x-ray of a “responder”. Note the lateral lead position is important.
Case study 2

Follow-up PA / LAT
Spontaneous dislodgement of the lead is noted in the chest x-ray. The lead was still capturing the LV, however, the patient’s CHF symptoms worsened.
Pacing Site Matters:
Optimal Site For LV Lead is Generally the Lateral free Wall

Butter et. Al. Circulation 2001; 104:3026
Non-responders

1. Dyssynchrony
2. Lead placement
   - Lateral wall is good
   - Anterior wall probably not good
   - Specific site difficult to determine
   - Multiple site
There has been research to determine responders versus non-responders and optimal pacing site but little effort has looked into the efficiency of CRT based on a cellular and cardiac architecture perspective. Multiple studies have shown cardiac motion as a wringing out effect, such as simultaneous clockwise and counter clockwise rotation of the LV apex and base. Pacing from two locations in the LV is showing improved cardiac function in CT.
AV interval optimization:
Generally less critical than getting right site

Aortic PP

Aortic PPA
AV delay (0 to PR - 30 ms)

% change

0
4
8
12
16


dP/dt_{max}

dP/dt_{max}
AV delay (0 to PR - 30 ms)

AV delay (0 to PR - 30 ms)

% change

0
-4
-8
-12

AV interval optimization: AV interval optimization:
Generally less critical than getting right site

AV delay may not be as critical as LV lead placement, however, still needs to be addressed in non-responders. Many CHF patients have intra-atrial conduction abnormalities which sometimes lead to simultaneous left atrial and left ventricular contractions or biventricular pacemaker syndrome. In our experience, we have not found an ECG criteria that has helped in the programming of the AV delay. We used intracardiac electrogram with success.
Use of intra-cardiac electrograms for programming of optimal sensed and paced AV delays in CRT devices in an attempt to prevent “Bi-ventricular pacing syndrome.”

Raffaele Corbisiero, MD, David Muller RN, Leonard Polak

**BACKGROUND:** During participation in the RHYTHM Trial (St. Jude Medical), it was noted that some patients were non-respondent to CRT therapy. A subset was noted to have long intra-atrial conduction deficits with or without surface ECG evidence resulting in premature ventricular systole via pacing with shorter AV/PV cycles.

**METHODS:** Seven patients (7 men and 0 women) were studied with ages of 71.1 ± 14.1 years, NYHA class III (n = 6) and class IV (n = 1) heart failure, LV ejection fraction <30% (21.4 ± 4.6%) and a prolonged QRS duration of 151.85 ± 11.15 ms. These patients were implanted with a V-338 Epic HF (n = 6) or aV-340 Atlas+ HF (n = 1). An electrogram (A-tip to Can configuration) derived from the device was utilized to program AV/PV delays and LVOT Vti at this AV/PV delay was compared to that using echocardiography optimization via a General Electric Vivid 7 system.

**RESULTS:** The proposed AV/PV delay using the electrogram was in the range of 160–190 ms for 7 patients, and the Vti at this proposed AV/PV delay was 14.6 ± 4.6 ms; in comparison, optimized AV/PV delay and Vti using echocardiograph were 140–225 ms and 14.9 ± 4.3 ms, correspondingly. The correlation coefficient between Vti values obtained by these two methods was 0.99.

**CONCLUSION:** Vti obtained by the electrogram derived AV/PV delay is a good estimation of the Vti optimized by echocardiography. It may reduce time and expense related to echocardiography for CRT patients. Further analysis should be performed with a larger sample size.
Non-responders

1. Dyssynchrony
2. Lead placement
3. AV optimization
   - Echo – Ritter, VTi
   - Non - echo
Incidence of Atrial Fibrillation in Patients with LV dysfunction

<table>
<thead>
<tr>
<th>Predominant NYHA Type</th>
<th>Prevalence of AF, %</th>
<th>Study, y</th>
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<tbody>
<tr>
<td>I</td>
<td>4</td>
<td>SOLVD-prevention (1992)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CHF-STAT (1995)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MERIT-HF (1999)</td>
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<tr>
<td></td>
<td></td>
<td>Diamond (1999)</td>
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<td></td>
<td></td>
<td>Stevenson (1996)</td>
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<td></td>
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<td>GESICA (1994)</td>
</tr>
<tr>
<td>IV</td>
<td>50</td>
<td>CONSENSUS (1987)</td>
</tr>
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</table>

NYHA, New York Heart Association; AF indicates atrial fibrillation; SOLVD, Studies of Left Ventricular Dysfunction; CHF-STAT, Survival Trial of Antiarrhythmic Therapy in Congestive Heart Failure; MERIT-HF, Metoprolol CR/XL Randomized Intervention Trial in Congestive Heart Failure; GESICA, Grupo Estudio de la Sobrevida en la Insuficiencia Cardiaca en Argentina (V); and CONSENSUS, Co-operative North Scandinavian Enalapril Survival Study.
The optimal AV delays require sinus rhythm which is sometimes hard to maintain in the CHF patient. Studies are forthcoming that will shed light on the question of sinus rhythm and CHF patients. If beneficial, sinus can be maintained through a variety of methods including one of a combinations of drugs, pacing and ablation. If atrial fibrillation persists or is poorly controlled, AV node ablation with pacing (biventricular as per PAVE) is clearly an option.
Synchronous vs non-Synchronous BiV Pacing

Is RV-LV delay important?

Systolic Function (echo index)

RV preactivation ← S → LV preactivation

Sogaard P, et al; Circulation 2002; 106:2078
Timing between the ventricles is now available in certain CRT-D devices and is useful in non-responders.

- 45 patients classified as “non-responders” following implant

- A-V & V-V delay optimized using Echo TDI

- 85% of patients improved significantly after optimization as shown by QOL and EF
Van Gelder et al. “Effect of Optimizing the VV Interval on Left Ventricular Contractility in Cardiac Resynchronization Therapy” Am J Cardiol 2004; 93, 1500-1503

- 53 patients
  - 41 patients in sinus rhythm
    - 26 patients w/ischemic cardiomyopathy (IC)
    - 15 patients w/idiopathic dilated cardiomyopathy (IDC)
  - 12 patients in AF

Maximum dP/dT measured
- Baseline (prior to BiV implant)
- Simultaneous BiV pacing
- V-V Optimized

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Baseline</th>
<th>Simultaneous</th>
<th>% Increase</th>
<th>Optimized V-V</th>
<th>% Increase</th>
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<tbody>
<tr>
<td>AF</td>
<td>12</td>
<td>941 ± 240</td>
<td>1,142 ± 207</td>
<td>21</td>
<td>1,180 ± 196</td>
<td>25</td>
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<tr>
<td>Sinus Rhythm</td>
<td>41</td>
<td>814 ± 178</td>
<td>952 ± 271</td>
<td>17</td>
<td>1,027 ± 297</td>
<td>26</td>
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<tr>
<td>IDC</td>
<td>15</td>
<td>754 ± 220</td>
<td>890 ± 245</td>
<td>18</td>
<td>955 ± 267</td>
<td>27</td>
</tr>
<tr>
<td>IC</td>
<td>26</td>
<td>846 ± 249</td>
<td>987 ± 232</td>
<td>17</td>
<td>1,069 ± 252</td>
<td>26</td>
</tr>
<tr>
<td>All Patients</td>
<td>53</td>
<td>842 ± 231</td>
<td>995 ± 247</td>
<td>18</td>
<td>1,061 ± 259</td>
<td>26</td>
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</tbody>
</table>
Non-responders

- 1. Dyssynchrony
- 2. Lead placement
- 3. AV optimization
- 4. Atrial arrhythmia's
- 5. V-V optimization
Too Late
The chest x-ray represents a class IV CHF patient with little hope of benefit from CRT-D.
Can CRT inhibit or slow progression of LV dysfunction and heart failure in minimally symptomatic patients (NYHA I-II) with low ejection fraction and wide QRS?
Madit-CRT asks an extremely important questions here. Could devices be used prophylactically for CHF as they are for ICD’s.