Program

• **Lecture 1**: Update on chronic heart failure – 2012 ESC/HeFSSA guidelines
• **Lecture 2**: Update on acute heart failure – 2012 ESC/HeFSSA guidelines
• **Lecture 3**: Update on the use of devices and end stage HF – 2012 ESC/HeFSSA guidelines
• **Lecture 4**: Diagnosis and management of right heart failure
Program

Lecture 3 :
UPDATE ON THE USE OF DEVICES AND END STAGE HF

• Background Information and ESC Guidelines on chronic heart failure 2012
Determinants of Cardiac Synchrony

Interventricular Synchrony

Determinants: Bundle branches

x = Right bundle
xx = Left anterior fasicle
xxx = Left posterior inferior fasicle
Determinants of Cardiac Synchrony

Interventricular Synchrony
Determinants: Mainly affects LV (scar etc)
Bundle Branch Patterns of Activation
Summary of Proposed Mechanisms Therapy

Cardiac Resynchronization

Intraventricular Synchrony

- ↑ dP/dt, ↑ EF, ↑ CO (↑ Pulse Pressure)

- ↓ LVESV

- ↓ LVEDV

Atrioventricular Synchrony

- ↓ MR

- ↓ LA Pressure

- ↑ LV Diastolic Filling

Interventricular Synchrony

- ↑ RV Stroke Volume

Reverse Remodeling

Ventricular Dysynchrony

**Electrical:** Inter- or Intra-ventricular conduction delays typically manifested as left bundle branch block

**Structural:** Disruption of myocardial collagen matrix impairing electrical conduction and mechanical efficiency

**Mechanical:** Regional wall motion abnormalities with increased workload and stress—compromising ventricular mechanics

Cardiac Resynchronization

Therapeutic intent of atrial synchronized biventricular pacing
- Modification of interventricular, intra-ventricular and atrial-ventricular activation sequences in patients with ventricular dysynchrony.
- Complement to optimal medical therapy

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1 Tavazzi L. Eur Heart J 2000;21:1211-1214
Achieving Cardiac Resynchronization

**Goal:** Atrial synchronous biventricular pacing

Transvenous approach for left ventricular lead via coronary sinus

Back-up epicardial approach
Benefits Sustained Through 2 Years

MIRACLE Study Program

Mean distance walked in 6 minutes (m)

- P<0.001
- P<0.001
- P<0.001
- P=0.01

Mean NYHA Functional Class

- P<0.001
- P<0.001
- P<0.001
- P<0.001

Mean QoL Score

- P<0.001
- P<0.001
- P<0.001
- P<0.001

Improvement

- 6 (N=1124)
- 12 (N=693)
- 18 (N=320)
- 24 (N=68)

Source: Abraham, WT et al. AHA 2003

Paired Data Displayed
CRT Effect on LV Structure at 6 Months in Moderate to Severe Heart Failure

<table>
<thead>
<tr>
<th></th>
<th>MIRACLE</th>
<th>MIRACLE ICD</th>
<th>Contak CD</th>
</tr>
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<tbody>
<tr>
<td>LVEDV Avg. Change (mL)</td>
<td>P&lt;0.001</td>
<td>P=0.06</td>
<td>Not Reported</td>
</tr>
<tr>
<td>LVEDD Avg. Change (mm)</td>
<td>P&lt;0.05</td>
<td>P=0.81</td>
<td>P=0.001</td>
</tr>
</tbody>
</table>

Data sources:
MIRACLE ICD: JAMA 2003;289:2685-2694
Contak CD: J Am Coll Cardiol 2003;2003;42:1454-1459
CARE-HF: CRT reduces death or unplanned hospitalisation for CV events in NYHA III/IV

No. at Risk

<table>
<thead>
<tr>
<th></th>
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<th>Medical Therapy</th>
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<tbody>
<tr>
<td>409</td>
<td>323</td>
<td>273</td>
</tr>
<tr>
<td>323</td>
<td>273</td>
<td>232</td>
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<td>273</td>
<td>232</td>
<td>166</td>
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<td>232</td>
<td>166</td>
<td>68</td>
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<td>166</td>
<td>68</td>
<td>48</td>
</tr>
<tr>
<td>48</td>
<td>7</td>
<td>3</td>
</tr>
</tbody>
</table>

HR 0.63 (95% CI 0.51 - 0.77)
37% Relative Risk Reduction
P < 0.001

MICD II: CRT therapy may reverse remodelling over 6 months in mild HF

Abraham et al Circulation 2004;110:2864-68
Grade II NYHA

P = 0.03  
Hazard Ratio = 0.47

% of Patients Hospitalised for HF

0%  5%  10%  15%  0  3  6  9  12

CRT OFF  CRT ON

Months Since Randomisation

Number at Risk

<table>
<thead>
<tr>
<th></th>
<th>CRT OFF</th>
<th>CRT ON</th>
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</thead>
<tbody>
<tr>
<td>0</td>
<td>191</td>
<td>419</td>
</tr>
<tr>
<td>3</td>
<td>187</td>
<td>415</td>
</tr>
<tr>
<td>6</td>
<td>181</td>
<td>411</td>
</tr>
<tr>
<td>9</td>
<td>176</td>
<td>409</td>
</tr>
<tr>
<td>12</td>
<td>119</td>
<td>251</td>
</tr>
</tbody>
</table>

53% reduction with CRT

Grade II NYHA

Baseline

12 Months

LVESVi (ml/mm²)

Δ = -1.3

Δ = -18.4

P<0.0001

n=487

Madit CRT

No. at Risk (Probability of Survival)

<table>
<thead>
<tr>
<th></th>
<th>CRT–ICD</th>
<th>ICD only</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1089</td>
<td>731</td>
</tr>
<tr>
<td>1</td>
<td>985</td>
<td>621</td>
</tr>
<tr>
<td>2</td>
<td>651</td>
<td>379</td>
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<tr>
<td>3</td>
<td>279</td>
<td>173</td>
</tr>
<tr>
<td>4</td>
<td>58</td>
<td>43</td>
</tr>
</tbody>
</table>

P<0.001

NEJM. Oct 2009
Changes in Echocardiographic Parameters

- **LVEDVI (ml/m2)**: Hypo-responder: -11.2, Responder: -26.5, Super-responder: -40.8
- **LVESVI (ml/m2)**: Hypo-responder: -12.6, Responder: -29.8, Super-responder: -43.1
- **LAVI (ml/m2)**: Hypo-responder: -7.9, Responder: -13.3, Super-responder: -16.2

**LVEF (%)**
## Predictors of LVEF Super-Response

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>1.96</td>
<td>1.32–2.90</td>
<td>0.001</td>
</tr>
<tr>
<td>QRS duration ≥150 ms</td>
<td>1.79</td>
<td>1.17–2.73</td>
<td>0.007</td>
</tr>
<tr>
<td>LBBB</td>
<td>2.05</td>
<td>1.24–3.40</td>
<td>0.006</td>
</tr>
<tr>
<td>Body mass index &lt;30 kg/m²</td>
<td>1.51</td>
<td>1.03–2.20</td>
<td>0.035</td>
</tr>
<tr>
<td>No prior myocardial infarction</td>
<td>1.80</td>
<td>1.20–2.71</td>
<td>0.005</td>
</tr>
<tr>
<td>Left atrial volume index, SD*</td>
<td>1.47</td>
<td>1.21–1.79</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Per 1-U SD below mean.*
Cumulative Probability of HF or Death, Death Alone and Death or ICD for VT/VF
Non-surgical device treatment of HF (CRT)

Recommendations for the use of CRT where the evidence is strong—patients in sinus rhythm with NYHA functional class III and ambulatory class IV heart failure and a persistently reduced ejection fraction, despite optimal pharmacological therapy.

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Classa</th>
<th>Levelb</th>
<th>Refc</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LBBB QRS morphology</strong></td>
<td>I</td>
<td>A</td>
<td>156, 157</td>
</tr>
<tr>
<td>CRT-P/CRT-D is recommended in patients in sinus rhythm with a QRS duration of ≥120 ms, LBBB QRS morphology, and an EF ≤35%, who are expected to survive with good functional status for &gt;1 year, to reduce the risk of HF hospitalization and the risk of premature death.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Non-LBBB QRS morphology</strong></td>
<td>Ila</td>
<td>A</td>
<td>156, 157</td>
</tr>
<tr>
<td>CRT-P/CRT-D should be considered in patients in sinus rhythm with a QRS duration of ≥150 ms, irrespective of QRS morphology, and an EF ≤35%, who are expected to survive with good functional status for &gt;1 year, to reduce the risk of HF hospitalization and the risk of premature death.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CRT-D = cardiac resynchronization therapy defibrillator; CRT-P = cardiac resynchronization therapy pacemaker; EF = ejection fraction; HF = heart failure; LBBB = left bundle branch block; NYHA = New York Heart Association.

aClass of recommendation.
bLevel of evidence.
cReferences.
**Non-surgical device treatment of HF (CRT)**

Recommendations for the use of CRT where the evidence is strong—patients in sinus rhythm with NYHA functional class II heart failure and a persistently reduced ejection fraction, despite optimal pharmacological therapy

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LBBB QRS morphology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRT, preferably CRT-D is recommended in patients in sinus rhythm with a QRS duration of $\geq 130$ ms, LBBB QRS morphology, and an EF $\leq 30%$, who are expected to survive for $&gt; 1$ year with good functional status, to reduce the risk of HF hospitalization and the risk of premature death.</td>
<td>I</td>
<td>A</td>
<td>154, 155</td>
</tr>
<tr>
<td><strong>Non-LBBB QRS morphology</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRT, preferably CRT-D should be considered in patients in sinus rhythm with a QRS duration of $\geq 150$ ms, irrespective of QRS morphology, and an EF $\leq 30%$, who are expected to survive for $&gt; 1$ year with good functional status, to reduce the risk of HF hospitalization and the risk of premature death.</td>
<td>IIa</td>
<td>A</td>
<td>154, 155</td>
</tr>
</tbody>
</table>

CRT-D = cardiac resynchronization therapy defibrillator; EF = ejection fraction; HF = heart failure; LBBB = left bundle branch block; NYHA = New York Heart Association.

*Class of recommendation.

*Level of evidence.

References.
Severity of Heart Failure
Modes of Death

NYHA II
- CHF: 12%
- Other: 24%
- Sudden Death: 64%
- n = 103

NYHA III
- CHF: 26%
- Other: 15%
- Sudden Death: 59%
- n = 103

NYHA IV
- CHF: 56%
- Other: 33%
- Sudden Death: 11%
- n = 27

Most Cardiac Arrests (70%-80%) Occur At Home

Prediction of Sudden Death from History Paris Study

Factors associated with sudden death during follow up (23 years):

- Resting heart rate.
- Systolic and diastolic blood pressure.
- Tobacco consumption.
- Body mass index.
- Diabetes.
- Serum cholesterol.
- Parental history of sudden death.
Inter-relationships between heart failure and arrhythmias

• This is a frequent occurrence
• Either can cause or aggravate the other
• **Arrhythmias can produce (or aggravate) heart failure by:**
  – Increasing heart rate (tachycardiomyopathy)
    • Uncontrollable atrial fibrillation, persistent SVT
  – Cause dyssynchronous contraction
• **Heart failure can produce or aggravate (or perpetuate) existing arrhythmias or be pro-arrhythmic**
  – Some antiarrhythmic drugs can produce or aggravate heart failure (or other arrhythmias) e.g. Sotalol and torsade des pointes, Flecainide etc.
Common Underlying Pathology for Arrhythmic Sudden Cardiac Death

• With heart failure
  – Ischaemic heart disease
  – Cardiomyopathy - dilated (NB: ARVC)
    - hypertrophic
  – Others (valvular disease, sarcoid, HIV etc)

• Without heart failure
  – Channelopathies (long QT, short QT, Brugada, early repolarisation syndrome)
  – Catecholaminergic polymorphic VT
  – Idiopathic ventricular fibrillation
Heart Failure and/or Decreased LV Function

• About one-half of all deaths in heart failure patients are characterized as sudden due to arrhythmias.

• The risk of SCA increases as left ventricular function deteriorates (low LVEF).

• Unexplained syncope has predicted SCA in patients in functional NYHA Class II - IV.

3 Stevenson WE. Circulation. 1993;88:2953-2961.
**Mortality in Placebo Arms of CHF Trials**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Mortality %</th>
<th>Study Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHF-SAT</td>
<td>22%</td>
<td>45 months</td>
</tr>
<tr>
<td>GESICA</td>
<td>15%</td>
<td>13 months</td>
</tr>
<tr>
<td>SOLVD</td>
<td>9%</td>
<td>41 months</td>
</tr>
<tr>
<td>V-HEFT I</td>
<td>19%</td>
<td>27 months</td>
</tr>
</tbody>
</table>

Underlying Causes of Fatal Arrhythmias

- 80% Coronary Artery Disease
- 15% Cardiomyopathy
- 5% Other*


* ion-channel abnormalities, valvular or congenital heart disease, other causes
Underlying Arrhythmias of SCA

- VT: 62%
- Bradycardia: 17%
- Primary VF: 8%
- Torsades de Pointes: 13%
Conclusions on SCA

• Post-MI patients with a low left ventricular ejection fraction are at risk for SCA.

• SCA can be prevented if high-risk patients are identified and referred to an Electrophysiologist (EP).
MADIT Survival Results

<table>
<thead>
<tr>
<th>Year</th>
<th>Probability of survival</th>
<th>Defibrillator</th>
<th>Conventional therapy</th>
</tr>
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<tbody>
<tr>
<td>0.0</td>
<td>1.0</td>
<td>95</td>
<td>101</td>
</tr>
<tr>
<td>0.2</td>
<td></td>
<td>80</td>
<td>67</td>
</tr>
<tr>
<td>0.4</td>
<td></td>
<td>53</td>
<td>48</td>
</tr>
<tr>
<td>0.6</td>
<td></td>
<td>31</td>
<td>29</td>
</tr>
<tr>
<td>0.8</td>
<td></td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td>1.0</td>
<td></td>
<td>3</td>
<td>0</td>
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</table>

**P-value = 0.009**

MUSTT Randomized Patient Results: Total Mortality

MADIT: ICDs Significantly Reduced Mortality

MADIT-II Survival Results

<table>
<thead>
<tr>
<th>Year</th>
<th>No. At Risk</th>
<th>Defibrillator</th>
<th>Conventional</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>742</td>
<td>502 (0.91)</td>
<td>329 (0.90)</td>
</tr>
<tr>
<td>1</td>
<td>502</td>
<td>274 (0.94)</td>
<td>170 (0.78)</td>
</tr>
<tr>
<td>2</td>
<td>274</td>
<td>110 (0.78)</td>
<td>65 (0.69)</td>
</tr>
<tr>
<td>3</td>
<td>110</td>
<td>9</td>
<td>3</td>
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</table>

P = 0.007

SCD-HeFT Mortality Rate Overall Results

<table>
<thead>
<tr>
<th></th>
<th>Hazard Ratio (97.5% CI)</th>
<th>P-Value</th>
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<tbody>
<tr>
<td>Amiodarone vs. Placebo</td>
<td>1.06 (0.86 - 1.30)</td>
<td>0.53</td>
</tr>
<tr>
<td>ICD vs. Placebo</td>
<td>0.77 (0.62 - 0.96)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>Amiodarone</th>
<th>Placebo</th>
<th>ICD</th>
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<tbody>
<tr>
<td>Months of Follow-Up</td>
<td>845</td>
<td>772</td>
<td>715</td>
</tr>
<tr>
<td>12</td>
<td>847</td>
<td>797</td>
<td>724</td>
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<td>24</td>
<td>715</td>
<td>724</td>
<td>505</td>
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<td>484</td>
<td>505</td>
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<td>280</td>
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<td>60</td>
<td>97</td>
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CD-HeFT Overall Mortality Results

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<tr>
<td>ICD vs. Placebo</td>
<td>0.77 (0.62 - 0.96)</td>
<td>0.007</td>
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</tbody>
</table>

ICDs reduce mortality by 23%

SCD-HeFT Mortality Rate
Ischemic CHF Patients

Mortality Rate

Hazard Ratio (97.5% CI)  P-Value
Amiodarone vs. Placebo  1.05 (0.91 - 1.36)  0.66
ICD vs. Placebo  0.79 (0.60 - 1.04)  0.05

No. at Risk
Amiodarone  Placebo  ICD
46  426  384  346  227  130
453  415  370  244  152  48
431  395  365  244  144  48

SCD-HeFT Mortality Rate
NYHA Class II Patients

<table>
<thead>
<tr>
<th></th>
<th>No. at Risk</th>
<th>Amiodarone</th>
<th>Placebo</th>
<th>ICD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone</td>
<td>601</td>
<td>563</td>
<td>536</td>
<td>378</td>
</tr>
<tr>
<td>Placebo</td>
<td>594</td>
<td>563</td>
<td>522</td>
<td>367</td>
</tr>
<tr>
<td>ICD</td>
<td>566</td>
<td>550</td>
<td>531</td>
<td>371</td>
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</tbody>
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<table>
<thead>
<tr>
<th></th>
<th>Hazard Ratio (97.5% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone vs. Placebo</td>
<td>0.85 (0.65 - 1.11)</td>
<td>0.17</td>
</tr>
<tr>
<td>ICD vs. Placebo</td>
<td>0.54 (0.40 - 0.74)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Hazard Ratio (97.5% CI)
P-Value
Amiodarone vs. Placebo 0.85 (0.65 - 1.11) 0.17
ICD vs. Placebo 0.54 (0.40 - 0.74) < 0.001