HEART FAILURE

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F. RUSCHITZKA (Zurich, CH)

Conflicts of Interest
Aventis, Bayer, Biotronik, Cardiorentis, Merck, Novartis, Pfizer, SJM, Servier Interest in Conflict: none
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- Epidemiology
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- Ischemic Cardiomyopathy
  - STICH
  - CHART-1
- Diabetes
The AGES-Reykjavík study: Heart failure will more than double by 2040 and triple by 2060

The elderly in Iceland 2013-2060

Predictive relative increase in heart failure in individuals ≥ 70 years

R. Danielsen, (Reykjavik, IS), P5425
Patient with symptomatic\textsuperscript{a} HFrEF\textsuperscript{b}

\textbf{Therapy with ACE-I\textsuperscript{c} and Beta-blocker}
(Up-titratre to maximum tolerated evidence-based doses)

Still symptomatic and LVEF \leq 35%

\textbf{Add MR antagonist\textsuperscript{d,e}}
(Up-titratre to maximum tolerated evidence-based doses)

Still symptomatic and LVEF \leq 35%

Able to tolerate ACEI (or ARB)\textsuperscript{f,g}

ARNI to replace ACE-I

Sinus Rhythm, QRS duration \geq 130 msec

Evaluate need for CR\textsuperscript{h,i}

The above treatments may be combined if indicated

Resistant symptoms

\textbf{Consider digoxin or H-ISDN or LVAD, or heart transplantation}

\textbf{No further action required}
Consider reducing diuretic dose

\textbf{P. Ponikowski (Wroclaw, PL) FP 995}
## Implantable cardioverter-defibrillator in patients with heart failure

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Secondary prevention</strong>&lt;br&gt;An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients who have recovered from a ventricular arrhythmia causing haemodynamic instability, and who are expected to survive for &gt;1 year with good functional status.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td><strong>Primary prevention</strong>&lt;br&gt;An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA Class II–III), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than one year with good functional status, and they have:&lt;br&gt;  * IHD (unless they have had an MI in the prior 40 days – see below).&lt;br&gt;  * DCM.</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>ICD implantation is not recommended within 40 days of an MI as implantation at this time does not improve prognosis.</td>
<td>III</td>
<td>A</td>
</tr>
<tr>
<td>ICD therapy is not recommended in patients in NYHA Class IV with severe symptoms refractory to pharmacological therapy unless they are candidates for CRT, a ventricular assist device, or cardiac transplantation.</td>
<td>III</td>
<td>C</td>
</tr>
<tr>
<td>Patients should be carefully evaluated by an experienced cardiologist before generator replacement, because management goals and the patient’s needs and clinical status may have changed.</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>A wearable ICD may be considered for patients with HF who are at risk of sudden cardiac death for a limited period or as a bridge to an implanted device.</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>
PRIMARY PROPHYLACTIC ICD IN DILATED CARDIOMYOPATHY HF PATIENTS
Primary prophylactic ICDs in dilated cardiomyopathy - the DANISH study

- **Aim:**
  - to study if PP ICD reduces total mortality in HF pts with DCM

- **Method:**
  - RCT to ICD +/- CRT or no ICD +/- CRT

- **Primary endpoint:**
  - total mortality,
  - others: CV mortality and sudden cardiac death

- **Patients:**
  - ICD (n=556) Control (N=560), 64 years, NYHA II/III, LVEF 25%

All on OMT and 60 % had CRT
Follow up 5.6 years

- **PE: Total mortality**
  - Hazard Ratio = 0.87 (0.68 – 1.12)
  - p=0.28

- **Sudden cardiac death**
  - Hazard Ratio = 0.50 (0.31 – 0.82)
  - p=0.005

ICD reduced sudden cardiac death in pts with dilated cardiomyopathy but not total mortality

L. Kober (Copenhagen, DK), FP 1220
Mortality by age in DANISH

There was a survival benefit by ICD in younger patients

L. Kober (Copenhagen, DK), FP 1220
Remote Management of Heart Failure Using Implanted Devices and Formalized Follow-up Procedures (REM-HF)

- Multicentre, prospective, randomised, non-blinded, controlled trial comparing:
  - Usual care + weekly Remote Monitoring vs
  - Usual care alone

- **Primary outcome** – first event of death from any cause or unplanned CV hospitalisation

- Sept 2011 - March 2014: 1650 patients recruited from 9 English hospitals

M. Cowie (London, GB) FP 1223
REM-HF: First Event of Death from any Cause or Unplanned Cv Hospitalisation

**Mortality + CV hospitalizations**
Primary End Point

- HR 1.01
  - [0.87-1.18]
  - P = 0.87

**Mortality**

- HR 0.83
  - [0.66-1.05]
  - P = 0.12
More-Care: Effects of Remote Monitoring on Clinical Outcomes and Use of Healthcare Resources in Heart Failure Patients with CRT

HR: 1.02 (0.80-1.30)  
\( p = 0.889 \)

<table>
<thead>
<tr>
<th></th>
<th>Remote (n = 437)</th>
<th>Standard (n = 428)</th>
<th>HR (95% CI)</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death, first CV or device-related hosp.</td>
<td>130 (29.7)</td>
<td>123 (28.7)</td>
<td>1.02 (0.80-1.30)</td>
<td>0.889</td>
</tr>
<tr>
<td>HCU Type</td>
<td>Events (Patients with HCU)</td>
<td>2-year event rate per 100 patients (95%CI)</td>
<td>Adjusted IRR (95%CI)</td>
<td>p-value</td>
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<td>--------------------------------</td>
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</tr>
<tr>
<td></td>
<td>Remote arm N=437</td>
<td>Remote arm N=437 (707 FU years)</td>
<td>Standard arm N=428 (696 FU years)</td>
<td></td>
</tr>
<tr>
<td>Hospitalizations</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>for any reason</td>
<td>337 (165)</td>
<td>96 (86 - 106)</td>
<td>90 (80 - 100)</td>
<td>1.02 (0.83 - 1.26)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>197 (111)</td>
<td>56 (48 - 64)</td>
<td>58 (50 - 66)</td>
<td>0.91 (0.72 - 1.15)</td>
</tr>
<tr>
<td>related hospitalizations</td>
<td>111 (63)</td>
<td>32 (26 - 38)</td>
<td>30 (24 - 36)</td>
<td>0.97 (0.74 - 1.29)</td>
</tr>
<tr>
<td>Device related hospitalizations</td>
<td>24 (20)</td>
<td>6.8 (4.6 - 10.2)</td>
<td>6.2 (4.2 - 9.6)</td>
<td>1.16 (0.82 - 1.65)</td>
</tr>
<tr>
<td>a – Hospitalizations</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Emergency Department (ED)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>admissions not leading to hospitalization</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>for any reason</td>
<td>40 (27)</td>
<td>11.4 (8.4 – 15.4)</td>
<td>16.0 (12.4 - 20.0)</td>
<td>0.72 (0.53 - 0.98)</td>
</tr>
<tr>
<td>Cardiovascular ED</td>
<td>23 (15)</td>
<td>6.6 (4.4 – 9.8)</td>
<td>8.4 (5.8 - 12.0)</td>
<td>0.78 (0.55 - 1.09)</td>
</tr>
<tr>
<td>HF related ED</td>
<td>14 (8)</td>
<td>4.0 (2.4 – 6.6)</td>
<td>4.8 (3.0 - 7.8)</td>
<td>0.78 (0.54 - 1.12)</td>
</tr>
<tr>
<td>Device related ED</td>
<td>7 (7)</td>
<td>2.0 (1.0 – 4.2)</td>
<td>0.6 (0.2 - 2.2)</td>
<td>3.53 (2.19 - 5.68)</td>
</tr>
<tr>
<td>b – Emergency Department (ED)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>related visits</td>
<td>All visits 1114 (315)</td>
<td>316 (297-334)</td>
<td>538 (515-563)</td>
<td>0.59 (0.56-0.62)</td>
</tr>
<tr>
<td></td>
<td>Scheduled visits 867 (367)</td>
<td>246 (230-262)</td>
<td>514 (490-538)</td>
<td>0.48 (0.46 - 0.50)</td>
</tr>
<tr>
<td></td>
<td>Unscheduled visits 247 (140)</td>
<td>70 (62-80)</td>
<td>24 (19-30)</td>
<td>2.80 (2.16 - 3.63)</td>
</tr>
<tr>
<td>c – Out-patient visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
Reasons for failure?

1. Statistical power?
2. Patients characteristics?
3. Endpoints?
4. Adherence / Reactivity?
5. Signals?
# Implant based Telemonitoring in Heart Failure

<table>
<thead>
<tr>
<th>STUDY</th>
<th>N patients</th>
<th>F / V</th>
<th>RESULTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>IN TIME (2014)</td>
<td>664 CRT-D / ICD</td>
<td>1 y</td>
<td>Composite score</td>
</tr>
<tr>
<td>CHAMPION</td>
<td>550 Recent HF Hosp.</td>
<td>6 mo</td>
<td>HF Hospitalization</td>
</tr>
<tr>
<td>OPTILINK HF</td>
<td>1002 ICD / CRT-D</td>
<td>23 mo</td>
<td>NEUTRAL</td>
</tr>
<tr>
<td>MORE CARE</td>
<td>865 CRT-D</td>
<td>2 y</td>
<td>NEUTRAL</td>
</tr>
</tbody>
</table>
Respond-HF: SONR Versus AV&VV Echo-guided Optimization to Increase CRT Response

Assessed for Eligibility (N=1039) → CRT-D implantation with SonRtip (N=1009) → Randomization 2:1 (N=998)

- Echo AV & VV (N=328) → Lost to follow-up: n=1
- SonR (N=670) → Lost to follow-up: n=0

ITT M N=649

- Lost to follow-up: n=1
- Discontinued study early: n=9
- Adverse event or explant: n=4
- Withdrawn consent: n=3
- Other reasons: n=1

ITT M N=318

- Lost to follow-up: n=0
- Discontinued study early: n=2
- Adverse event and explant: n=0
- Withdrawn consent: n=2
- Other reasons: n=0

Primary analysis at 12 months

Secondary analysis at 18 months

Lost to follow-up: n=0
- Discontinued study early: n=2
- Adverse event and explant: n=0
- Withdrawn consent: n=2
- Other reasons: n=0

Lost to follow-up: n=0
- Discontinued study early: n=7
- Adverse event and explant: n=2
- Withdrawn consent: n=4
- Other reasons: n=1

ITT M N=316

ITT M N=642

J. Brugada (Barcelona, ES) FP 2235
**Respond-HF: Outcomes at Month 18**

**All-cause Death**

- **SonR**
  - No. at risk: 670, 645, 625, 603, 589, 583, 506

- **Echo**
  - No. at risk: 328, 318, 305, 295, 289, 288, 246

- **HR = 1.14, 95% CI: [0.69-1.87]**
- Log-rank: *p=NS*

**Heart Failure Hospitalisations**

- **SonR**
  - No. at risk: 670, 617, 588, 555, 534, 344, 189

- **Echo AV & VV**
  - No. at risk: 328, 304, 277, 260, 250, 155, 75

- **HR = 0.67, 95% CI: [0.48-0.93]**
- Log-rank: *p=0.02*

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J. Brugada (Barcelona, ES) FP 2235
EchoCRT: Left Ventricular Global Longitudinal Strain (GLS) is Associated with Poor Outcome in Heart Failure Patients with Narrow QRS
EchoCRT: CRT May Have a Detrimental Effect on Clinical Outcomes in Patients with Lowest Left Ventricular Global Longitudinal Strain (GLS)

**LV GLS** reflects LV systolic function and correlates inversely with the extent of LV myocardial scar and fibrosis
STICH: CABG Added to Medical Therapy has a More Substantial Benefit on All-cause Mortality in Younger Patients

Interaction P-value = 0.0064

E. Velazquez (Durham, US), FP 3935

All-cause Mortality

Hazard Ratio 0.84
Log-rank P-value 0.019
NNT=14

Patients at risk
MED 602 532 487 435 404 357 315 274 248 164 82 37
CABG 610 532 487 460 432 392 356 312 286 205 103 42

Years Following Randomization

Baseline Age in Years

Baseline Age in Years

10-Year Rate (%)
OBJECTIVE

To validate the efficacy and safety of cardiopoietic cells derived by cardiogenic specification of mesenchymal stem cells

- **Patients with ischemic heart failure with**
  - LVEF ≤35%
  - Heart failure hospitalization or worsening within last 12 months
  - On guideline-directed heart failure therapy

- **randomized to:**
  - **Active** group: cardiopoietic cell therapy
  - **Control** group: sham procedure

- **Cardiopoietic Cell Product:** C3BS-CQR-1, Celyad, Mont Saint Guibert, BE
- **Intramyocardial Delivery Catheter:** C-Cath, Celyad, Mont Saint Guibert, BE

*J. Bartunek (Aalst, BE) FP 1229*
Chart-1: Primary Efficacy Endpoint Neutral
Primary Outcome as a Function of HF Severity (Post-hoc)

Mann-Whitney Estimator (95% CI)

- Overall Study Population (n=271)
  - 0.54 (0.47, 0.61)
  - P=0.27

- Patients with baseline LVEDV 200-370 mL (n=162; post-hoc)
  - 0.61 (0.52, 0.70)
  - P=0.015
Sodium–Glucose Co-Transporter-2 (SGLT-2) Inhibitors in Patients With Heart Failure and Type 2 Diabetes Mellitus

Virtually all of the filtered glucose is reabsorbed in the proximal tubules through the sodium glucose co-transporters SGLT-2 and SGLT-1.
Sodium–Glucose Co-Transporter-2 (SGLT-2) Inhibitors in Patients With Heart Failure and Type 2 Diabetes Mellitus

SGLT-2 inhibitors reduce glucose reabsorption in the proximal tubule leading to glycosuria.

- Glycosuria
- Loss of calories
- BP reduction

SD. Anker (Gottingen, DE) FP 5123
Heart Failure Outcomes with Empagliflozin in Patients with Type 2 Diabetes at High Cardiovascular Risk: Results of the EMPA-Reg Outcome® Trial

Cardiovascular mortality

Hazard ratio, 0.62 (95% CI, 0.49–0.77)
P<0.001

Heart Failure Hospitalisations

Hazard ratio, 0.65 (95% CI, 0.50–0.85)
P=0.002


D. Fitchett (Toronto, CA) FP 2236
Heart Failure: rendez-vous with the future

Call for abstracts: November 3 – January 13