Clips, Sparks & Implantable Monitors for HF

Anique Ducharme, MD, MSc
Director Heart Failure Clinic, Montreal Heart Institute
Professor of Medicine, University of Montreal
Montreal (Canada)

HF Update, Toronto,
Saturday May 13, 9:35 -9:55
Disclosures

I will discuss off label use and expanded indications for monitoring of the Cardiomems device in my presentation.

I have financial relationships to disclose:

Consultant/ Speaker for:

Novartis, Roche, Servier, St-Jude Medical (Abbott)

Stockholder in: None

Research grant/Steering Committee :

Edwards, Novartis, St-Jude Medical (Abbott)
Presence & severity of FMR & all-cause mortality + HF hospitalisation

FMR
- should not be considered just a mere consequence of ventricular remodeling
- but a major predictor of outcome

Mean follow-up 2.7±2.0 years

MitraClip Therapy in Heart Failure

- 50 high risk MR patients with severe LV dysfunction and LV dilatation treated with the MitraClip.
- Objectives:
  - clinical improvement;
  - functional status and
  - 6 minute walk,
  - degree of MR and
  - NT-proBNP.
MitraClip Therapy in Heart Failure Patients

In these high risk patients, treatment with the MitraClip was associated with a significant improvement in 6 min walk test and NT-proBNP.
Correction of Mitral Regurgitation in Nonresponders to Cardiac Resynchronization Therapy by MitraClip Improves Symptoms and Promotes Reverse Remodeling

Figure 1: Improvement Over Time of NYHA Functional Class and Mitral Regurgitation


Université de Montréal

ICM
When is a LVEF too bad to clip?
Clinical outcomes and economic impact of transcatheter mitral leaflet repair in HF patients

- 2 Phases:
  - 1) observational- patients with HF + MR treated medically or w MitraClip
  - 2) an economic model.

- MitraClip patients: propensity matched to a HF patients population, FU 22m

- Incremental cost: $52,500 & incremental cost-effectiveness ratio (ICER) of $32,300.00 per QALY gained.

22 months -All-cause mortality:
MC (21%) vs Medical (42%)  ($p = .007$).

SPARKS?

Dr. Howlett
President of the Canadian Heart Failure Society and Director of Heart Failure at the Labin Cardiovascular Institute of Alberta.
Original Article

Defibrillator Implantation in Patients with Nonischemic Systolic Heart Failure


for the DANISH Investigators

N Engl J Med
Volume 375(13):1221-1230
September 29, 2016
Severity of Heart Failure
Modes of Death

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

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

NYHA IV
- CHF: 33%
- Other: 56%
- Sudden Death: 11%
  n = 27
Sudden Cardiac Death-Heart Failure SCD-HeFT
Kaplan-Meier Estimates of Death from Any Cause:
NYHA Class II-III and LVEF ≤ 35%.

**Ischemic CHF**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Hazard Ratio (97.5% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone vs. placebo</td>
<td>1.05 (0.81–1.36)</td>
<td>0.66</td>
</tr>
<tr>
<td>ICD therapy vs. placebo</td>
<td>0.79 (0.60–1.04)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

**Non-Ischemic CHF**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Hazard Ratio (97.5% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amiodarone vs. placebo</td>
<td>1.07 (0.76–1.51)</td>
<td>0.65</td>
</tr>
<tr>
<td>ICD therapy vs. placebo</td>
<td>0.73 (0.50–1.07)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

**INDICATION:**

**Class 1A**

- Amiodarone 426 384 346 227 130 46
- Placebo 453 415 370 244 152 48
- ICD therapy 431 395 365 244 144 48

**Class 1B**

- Amiodarone 419 388 369 257 150 51
- Placebo 394 382 354 261 152 41
- ICD therapy 398 383 368 257 160 55

Bardy G et al. NEJM 2005; 352:3
**DANISH**

- **Trial design:** Patients with nonischemic CMP (LVEF≤35%) were randomized to ICD implantation (n = 556) versus usual care (n = 560).

**Results**

- **Younger patients** (<59 years) appeared to derive greater benefit from ICD implantation versus older patients (p for interaction = 0.009)
- **Sudden cardiac death:** 4.3% versus 8.2%; respectively, for ICD versus control (p = 0.005)

**Conclusions**

- In patients with a non-ischemic CMP, ICD did not reduce long-term mortality compared with usual care;
- suggestion of benefit among younger patients

Revisiting DANISH

• « Several important concerns about the possible “shocking” takeaway message from the DANISH trial may remain for the practicing clinician... »
Enrollment & Randomization of Patients. Concern # 1

- How many patients “assessed for eligibility”?  
  - Not mentioned despite trial reporting standards recommendation
- Important subgroups excluded  
  - atrial fibrillation (HR > 100)  
  - patients on dialysis
- How generally applicable the findings are to everyday practice?


JR Gimbel. PACE April 2017, Vol. 00
### Characteristics of the Patients at Baseline: Concern #2

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ICD Group (N = 556)</th>
<th>Control Group (N = 560)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (IQR) — yr</td>
<td>64 (56–72)</td>
<td>63 (56–70)</td>
</tr>
<tr>
<td>Female sex — no. (%)</td>
<td>151 (27)</td>
<td>156 (28)</td>
</tr>
<tr>
<td>Median blood pressure (IQR) — mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>123 (110–139)</td>
<td>124 (111–138)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>74 (65–81)</td>
<td>74 (66–82)</td>
</tr>
<tr>
<td>Median body-mass index (IQR) †</td>
<td>26.8 (23.9–30.5)</td>
<td>26.8 (23.8–30.1)</td>
</tr>
<tr>
<td>Median NT-proBNP level (IQR) — pg/ml</td>
<td><strong>1244 (616–2321)</strong></td>
<td><strong>1110 (547–2166)</strong></td>
</tr>
<tr>
<td>Median QRS duration (IQR) — msec</td>
<td>146 (114–166)</td>
<td>145 (110–164)</td>
</tr>
<tr>
<td>Median left ventricular ejection fraction (IQR) — %</td>
<td>25 (20–30)</td>
<td>25 (20–30)</td>
</tr>
<tr>
<td>Median estimated GFR (IQR) — ml/min/1.73 m²</td>
<td>74 (58–91)</td>
<td>73 (58–92)</td>
</tr>
<tr>
<td>NYHA class — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>297 (53)</td>
<td>300 (54)</td>
</tr>
<tr>
<td>III</td>
<td>252 (45)</td>
<td>253 (45)</td>
</tr>
<tr>
<td>IV</td>
<td>7 (1)</td>
<td>7 (1)</td>
</tr>
<tr>
<td>Median duration of heart failure (IQR) — mo</td>
<td>20 (8–72)</td>
<td>18 (8–60)</td>
</tr>
</tbody>
</table>

Slight imbalance only?

Rate of Death from Any Cause (Primary Outcome) in Prespecified Subgroups.

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>ICD Group</th>
<th>Control Group</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
<th>P Value for Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;59 yr</td>
<td>17/167</td>
<td>34/181</td>
<td>0.51 (0.29–0.92)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>≥59 to &lt;68 yr</td>
<td>36/173</td>
<td>50/202</td>
<td>0.75 (0.48–1.16)</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>≥68 yr</td>
<td>67/216</td>
<td>47/177</td>
<td>1.19 (0.81–1.73)</td>
<td>0.38</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>22/151</td>
<td>23/156</td>
<td>1.03 (0.57–1.87)</td>
<td>0.92</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>98/405</td>
<td>108/404</td>
<td>0.85 (0.64–1.12)</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>NT-proBNP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1177 pg/ml</td>
<td>32/266</td>
<td>74/268</td>
<td>0.59 (0.38–0.91)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>≥1177 pg/ml</td>
<td>57/292</td>
<td>88/290</td>
<td>0.99 (0.73–1.36)</td>
<td>0.96</td>
<td></td>
</tr>
</tbody>
</table>

Characteristics of the Patients at Baseline (#3)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>ICD Group (N=556)</th>
<th>Control Group (N=560)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medications — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACE inhibitor or ARB</td>
<td>533 (96)</td>
<td>544 (97)</td>
</tr>
<tr>
<td>Beta-blocker</td>
<td>509 (92)</td>
<td>517 (92)</td>
</tr>
<tr>
<td>Mineralocorticoid-receptor antagonist</td>
<td>326 (59)</td>
<td>320 (57)</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>34 (6)</td>
<td>32 (6)</td>
</tr>
<tr>
<td>CRT — no. (%)</td>
<td>322 (58)</td>
<td>323 (58)</td>
</tr>
<tr>
<td>Preexisting pacemaker or CRT pacemaker — no. (%)</td>
<td>56 (10)</td>
<td>46 (8)</td>
</tr>
</tbody>
</table>

There were no significant differences in any of the above between the study groups. ACE denotes angiotensin-converting enzyme, ARB angiotensin receptor blocker, CRT cardiac resynchronization therapy, GFR glomerular filtration rate, ICM implantable cardiac defibrillator, IQR interquartile range, NT-proBNP N-terminal pro–brain natriuretic peptide, and NYHA New York Heart Association.

CRT - / ICD + : median NT-proBNP (1,277 pg/ml)
CRT - / ICD - : median NT-proBNP (862 pg/ml)
(48% higher and > level (1177 pg /ml) for no benefit the subgroup analysis)

Whether or not this was statistically significant is not available (Table S3)
What’s the big fuss around BNP here?

• Increasing event rates occur with increasing NT-proBNP levels.
  – patients with predictably low event rates [NT-proBNP < 200 pg/mL] were excluded in DANISH.
  – while increasingly elevated NT-proBNP levels are associated with SCD, they are even more predictive of death from pump failure.

• In PARADIGM-HF:
  – patients who died from HF: median baseline NT-proBNP = 3,377 pg/mL versus
  – those who perished suddenly = NT-proBNP of 2,402 pg/mL

• “Is there a (significant?) mismatch in the ICD-only arm in NT-proBNP, creating a group of ICD patients who were simply “destined to die from HF,” thereby offsetting any benefit the ICD could play in reducing SCD?”

Too High expectations?
Concern #4 (& last)

- Design of DANISH (hypothesis):
  - # of ICD patients needed to reduce a single all-cause death :11 (Table III)
  - ICD benefit in other trials:
    - DEFINITE (NNT = 16; p=NS),
    - SCD-HeFT (NNT = 14), and
    - COMPANION (NNT = 33).

- “... it showed that in the population studied, a 25% reduction in all-cause mortality should not be expected statistically with ICD... - perhaps the bar for ICDs to show benefit was simply set too high.”

- “If we had done a trial twice as big and stopped after 4 years, I think we likely would have had a positive trial overall.”

L Køber, Interviewed at Medscape dec 2016
IMPLANTABLE MONITORS FOR HF
Disease Management Programs for HF
Results after 6 Months of follow-up

N = 230

Ducharme et al, CMAJ 2005; 173:40-45
Montreal Heart Institute Heart Failure Clinic

Growth of activity 2000-2016*

- By number of patients and age -

Mean age:
63.6
68.7
71.7
793
the aging Baby boomers ....
The Development of Acute Decompensation

Physiologic markers of the development of acute decompensation:

- Pressure Changes
- Autonomic Adaptation
- Impedance Changes
- Weight Changes, BP, HF Symptoms

Hemodynamic monitors

Remon CHF

CardioMEMS device with sensor in the pulmonary artery

chronic device with the sensor in right ventricle

HeartPOD device with the sensor in the left atrium

Adapted From: Singh B et al. Curr Treatment in CV Medicine 2012
CHAMPION: PAP-guided therapy on HF-related hospitalizations compared to standard of care

550 Pts
NYHA III
w/ CM Implants
All Pts Take Daily readings

Treatment
270 Pts
Management Based on PAP +Traditional Info

Control
280 Pts
Management Based on Traditional Info

PAP was managed to target pressures by physicians with appropriate titration of HF medications.

Target PAP:
- PAP Systolic 15 – 35 mmHg
- PAP diastolic 8 – 20 mmHg
- PAP mean 10 – 25 mmHg

- Days alive outside of hospital
- QOL


Safety: 98.6% freedom from device/system-related complications.
CHAMPION: PAP-guided therapy compared to usual care

N=550 patients, NYHA III, Randomized to specific target pressures levels

**PAP Mean Change from Baseline**

Compared to the control group, patients managed with PAP had lower mean PA pressures over 6 months

Ambulatory PAP Monitoring & Heart Failure Hospitalizations in “Real-World” Clinical Practice

- 1,114 Medicare patients w CardioMems
  - 1,020 HFHs in the 6 months prior versus
  - 381 HFHs, 139 deaths, and 17 VAD implantations
    and/or transplants in the 6 months after implant
    - HR: 0.55; 95% [CI]: 0.49 to 0.61; p < 0.001.

- 6-month HF cost ↓: $7,433/patient
- A subset (n=480) with data @ 12m showed similar results before/after
  - HR: 0.66; 95% CI: 0.57 to 0.76; p < 0.001.
Clips, Sparks and Implantable Monitors for HF

Conclusion

• Clips for MR are effective to ↓ hospital admission and ↑ quality of life.
  – Associated with superior survival and is cost-effective (retrospective)
  – Alternative therapies should be looked for in patients with LVEF ≤20%, including LVAD/ transplant.

• In non ischemic CMP, ICD for primary prevention remains debatable and it is reasonnable to optimize medical therapy first.
  – ICD is meant to prevent SCD !

• Implantable PAP monitor for HF
  – is the only remote monitoring strategy that works to reduce HF admission.
  – In real life setting, it is associated with lower HFH and is cost effective.
Thank you!

My expectations just get lower and lower.

That’s great!

Eventually I’ll be able to meet all of them!
Current treatments of myocardial infarction (MI) and heart failure have improved substantially over the last decades, and thus, the patient population at risk of SCD may have been altered as well.

Consequently, data on the high-risk patients after MI and with heart failure in the modern era are sparse and data from previous trials may no longer be applicable.