HeFSSA Practitioners Program 2018
“Back to basics on heart failure treatment?”

• Co-morbidity in heart failure

• Arrhythmias in heart failure

• Special investigations in heart failure

• Heart failure with preserved EF, what is new?”
Atrial Fibrillation (AF)

- 2-fold increase in mortality
- 3-fold increase in heart failure
- 5-fold increase in stroke/systemic embolism
- Decrease in quality of life

Kannel et al. Am J Cardiol 1998
A vicious circle....

- Rapid and irregular rate -> decrease in cardiac output
- Loss of atrial kick

CHF

• Increases atrial filling pressures -> structural remodelling and electrophysiologic remodelling
• Functional MR

AF

Often co-exist

CHF is a clinical syndrome due to heterogenous diseases
AF and CHF: temporal relations

FRAMINGHAM DATA
“AF precedes CHF about as often as CHF precedes AF”
Incidence of CHF: 3-4% per year

Wang, Circulation, 2003
AF and CHF: temporal relations

ORBIT-AF DATA
6545 patients with no CHF at baseline
Contemporary population
Incidence of CHF: 1-2% per year
2/3 developed HFpEF

Pandey, JACC Heart failure, 2017
New onset AF is associated with an increase in all-cause mortality (HFrEF>HFpEF>no HF)

AF: marker or independent risk factor?

Verma et al., Circulation, 2017.
Atrial Fibrillation and CHF

AF causes a cardiomyopathy (AF-induced cardiomyopathy)

Treatment of AF will have benefit

AF is associated with CHF

Treatment of AF may or may not have benefit

Distinguishing which is the primary disturbance is challenging
AF and CHF

AF-induced cardiomyopathy (LV function improved)

Treatment

Redfield et al. 63 16 (25%) AV node ablation
Ozcan et al. 56 16 (29%) AV node ablation
Sohinki et al. (Europace 2014) 45 DCMO group (11.2%) ICMO (0.5%) CRT and AV node ablation
Management of AF and CHF (HFrEF)

- Control risk factors (hypertension, OSA...)

- Anticoagulation usually indicated (CHA$_2$DS$_2$-VASc score)

- Standard heart failure therapy
  - ACEi/ARB/MRA

- Rate control
  - Beta-blocker +/- Digoxin

- Rhythm control (Amiodarone and/or catheter ablation)
  - Severe symptoms
  - AF-induced cardiomyopathy suspected
RCT of rate versus rhythm control in patients with AF and CHF

1376 patients with AF and CHF (LVEF <= 35%)
- 33% paroxysmal
- 67% persistent

Rhythm control group:
- 82% Amiodarone
- 2% Sotalol
- <1% Dofetilide

No difference in cardiovascular mortality (HR 1.06; P=0.59)

Potential benefit of sinus rhythm may be neutralized by the toxic effects of AADS

AADs only successful in maintaining SR in 65-70%

Roy et al., NEJM, 2008
Rate versus Rhythm control?

Appropriate antithrombotic therapy

Clinical evaluation

Paroxysmal

Persistent

Long-standing persistent

Rhythm control

Remains symptomatic

Failure of rhythm control

Rate control

Camm et al. Europace, 2010
Rate control

- **Should be the default initial strategy**
- AV nodal blockers (beta-blockers, digoxin (measure digoxin levels))
- Avoid calcium channel blockers if LVEF<=40% because of negative inotropic effect
- Amiodarone can be used as a second-line agent if beta-blockers, digoxin fail

- AV node ablation and pacing is indicated in patients with permanent AF who have poor rate control despite drugs and who are considered not to be candidates for an AF ablation

2016 ESC AF guideline
Targets:
Resting HR<80bpm (IIA, B)
Resting HR<110bpm with no symptoms with normal LV function (IIB, B)

RACE II (Average resting heart rates)
Strict control: 75 bpm
Lenient control group: 85 bpm
Management of AF and CHF

- **Rhythm control**
  
  Persistent symptoms in AF
  
  First occurrence
  
  Failure to achieve adequate rate control
  
  Younger patients < 65 years
  
  Patients early in the natural history of AF
  
  AF-induced cardiomyopathy
  
  AF with a reversible disorder (e.g. Hyperthyroidism)
Role of catheter ablation in AF and CHF

ESC 2016 guidelines: No clear consensus on who should be offered catheter ablation
Basis for AF ablation

Aim:

1. Eliminate PV triggers
2. Alter arrhythmogenic substrate

⇒ Pulmonary vein isolation (PVI)
## Paroxysmal or Persistent AF with HFrEF
### Evidence from RCTs

<table>
<thead>
<tr>
<th>Study</th>
<th>Ablation (n)</th>
<th>Aetiology</th>
<th>Control (n)</th>
<th>Type of AF</th>
<th>Ablation success</th>
<th>Results</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>PABACHF</td>
<td>41</td>
<td>73% ICMO</td>
<td>CRT and AVNA</td>
<td>49% PAF</td>
<td>88%</td>
<td>Improved LVEF (6 months)</td>
<td>12%</td>
</tr>
<tr>
<td>MacDonald</td>
<td>22</td>
<td>50% ICMO</td>
<td>Rate control</td>
<td>100% Persistent</td>
<td>50%</td>
<td>No difference (12 months)</td>
<td>20%</td>
</tr>
<tr>
<td>ARC-HF</td>
<td>26</td>
<td>33% ICMO</td>
<td>Rate control</td>
<td>100% Persistent</td>
<td>88%</td>
<td>Improved exercise tolerance (12 months)</td>
<td>15%</td>
</tr>
<tr>
<td>CAMTAF</td>
<td>67</td>
<td>26% ICMO</td>
<td>Rate control</td>
<td>100% Persistent</td>
<td>73%</td>
<td>Improved LVEF, better exercise tolerance (12 months)</td>
<td>7.7%</td>
</tr>
<tr>
<td>AATAC</td>
<td>102</td>
<td>62% ICMO</td>
<td>Amiodarone (beta-blockers 78%)</td>
<td>100% Persistent</td>
<td>70%</td>
<td>Lower mortality and unplanned hospitalisations</td>
<td>2.9%</td>
</tr>
<tr>
<td>CAMERA-MRI</td>
<td>33</td>
<td>100% DCMO</td>
<td>Rate control</td>
<td>28% Persistent</td>
<td>75%</td>
<td>Improved LVEF</td>
<td>6.1%</td>
</tr>
</tbody>
</table>

### Proof of concept trials
- Small numbers of patients (n=291)
- Heterogenous populations
- Soft endpoints with 1 trial showing no benefit
- Short follow-up with high ablation success rates
- High complications rates in expert centres

Liang et al., Cardiac Failure Review, 2018
Catheter Ablation for Atrial Fibrillation with Heart Failure

Nassir F. Marrouche, M.D., Johannes Brachmann, M.D., Dietrich Andresen, M.D., Jürgen Siebels, M.D., Lucas Boersma, M.D., Luc Jordaens, M.D., Béla Merkely, M.D., Evgeny Pokushalov, M.D., Prashanthan Sanders, M.D., Jochen Proff, B.S., Heribert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators*

CONCLUSIONS
Catheter ablation for atrial fibrillation in patients with heart failure was associated with a significantly lower rate of a composite end point of death from any cause or hospitalization for worsening heart failure than was medical therapy.
Repeat ablations in 25%
Major complication rate 9%

63% were in SR in ablation group at follow-up
22% were in SR in the medical group

Mortality difference occurred at 3 years when ½ of patients had exited the trial
Small number of expected endpoints (32% less than originally powered)

HR 0.62 for the primary endpoint and HR 0.53 for all-cause mortality is lower than any HF intervention to date

Large differences in effect with small number of events
e.g. CASTLE AF had only 11% of cardiovascular deaths compared to AF-CHF
Evolving evidence suggests an increasing role of catheter ablation in HFrEF

Small RCTs are “hypothesis generating”

CASTLE-AF has numerous limitations +++

Further trials needed
## Paroxysmal or Persistent AF with HFpEF Evidence from RCTs

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<tbody>
<tr>
<td>RAFT-AF (trial underway)</td>
<td>300</td>
<td>300</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
There is a cohort of HFrEF patients who likely will benefit from AF ablation.

AF-induced cardiomyopathy
Dilated cardiomyopathy
Ischaemic cardiomyopathy

For symptom relief, “hard” endpoints unclear

Individualised approach
Devices for CHF – Cardiac resynchronization therapy
More than 4000 patients enrolled in randomized controlled trials
Consistent improvement in quality of life, functional status, and exercise capacity
Strong evidence for reverse remodeling
  - ↓ LV volumes and dimensions
  - ↑ LV ejection fraction
  - ↓ Mitral regurgitation
Reduction in morbidity
Reduction in mortality
Diuretics

Hydralazine

β-blockers + ACE Inhib.

ACE Inhib.

Digoxin

Mortality

SOLVD CONSENSUS '96 to -31%

CIBIS II COPERNICUS - 35%

RALES 22%

CARE-HF 40%

Adapted from Ellenbogen KA et al.; J Am Coll Cardiol 2005;46:2199 –203
### Devices for CHF – Implantable cardioverter defibrillator (ICD)

#### ICD for the secondary prevention of sudden cardiac death and ventricular tachycardia

<table>
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<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
<th>Ref.</th>
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<tr>
<td>ICD implantation is recommended in patients with documented VF or haemodynamically not tolerated VT in the absence of reversible causes or within 48 h after myocardial infarction who are receiving chronic optimal medical therapy and have a reasonable expectation of survival with a good functional status &gt; 1 year.</td>
<td>I</td>
<td>A</td>
<td>151–154</td>
</tr>
<tr>
<td>ICD implantation should be considered in patients with recurrent sustained VT (not within 48 h after myocardial infarction) who are receiving chronic optimal medical therapy, have a normal LVEF and have a reasonable expectation of survival with good functional status for &gt; 1 year.</td>
<td>IIa</td>
<td>C</td>
<td>This panel of experts</td>
</tr>
<tr>
<td>In patients with VF/VT and an indication for ICD, amiodarone may be considered when an ICD is not available, contraindicated for concurrent medical reasons or refused by the patient.</td>
<td>IIb</td>
<td>C</td>
<td>155, 156</td>
</tr>
</tbody>
</table>

#### Implantable cardioverter defibrillator in patients with left ventricular dysfunction

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<tr>
<td>ICD therapy is recommended to reduce SCD in patients with symptomatic HF (NYHA class II–III) and LVEF ≤35% after ≥3 months of optimal medical therapy who are expected to survive for at least 1 year with good functional status:</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>– Ischaemic aetiology (at least 6 weeks after myocardial infarction).</td>
<td>I</td>
<td>A</td>
<td>63, 64</td>
</tr>
<tr>
<td>– Non-ischaemic aetiology.</td>
<td>I</td>
<td>B</td>
<td>64, 316, 317</td>
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