<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:00 – 08:30</td>
<td>Registration</td>
</tr>
<tr>
<td>08:30 – 09:15</td>
<td>Clinical Case Presentation 1</td>
</tr>
<tr>
<td>09:15 – 10:00</td>
<td>Clinical Case Presentation 2</td>
</tr>
<tr>
<td>10:00 – 10:30</td>
<td>Tea Break</td>
</tr>
<tr>
<td>10:30 – 11:15</td>
<td>Clinical Case Presentation 3</td>
</tr>
<tr>
<td>11:15 – 11:45</td>
<td>ESC Guidelines on Chronic Heart Failure</td>
</tr>
<tr>
<td>11:45 – 12:00</td>
<td>Questionnaire</td>
</tr>
<tr>
<td>12:00 – 14:00</td>
<td>Lunch</td>
</tr>
</tbody>
</table>
A case of ischaemic cardiomyopathy
The story starts with…..

(2010)

- 66 year old man
- Smoker
- Father underwent CABG in his 50’s
- Frequent NSAID use for back pain
- Not on any other medication
- Had an anterior STEMI – treated
- Re-admitted 3 months later with recurrent anterior myocardial infarction - PCI to LAD
Preservation of myocardium in order to prevent ischaemic left ventricular dysfunction is critical in preventing heart failure/death due to ischaemic cardiomyopathy

Good secondary prevention and lifestyle modification

Prevention is better than cure!
Back to our patient

- Discharged on:
- Atenolol 50 mg 2x/day
- Simvastatin 20 mg daily
- Aspirin 150 mg daily
- Clopidogrel 75 mg daily
- Perindopril 4 mg daily

- Did not return for completion of revascularisation.
Progress over the next 12 months

- Doing reasonably well
- Very infrequent angina on moderate exertion, readily treated with short-acting nitrates
- Manages to stop smoking
- Develops a cough on the perindopril – therefore this was stopped
- Clopidogrel stopped after 12 months
- Class 1 – 2 NYHA – manages to do be reasonably active
Sees his new general practitioner because he finds that over the last 3 months he has become progressively more short of breath – now short of breath on walking even small distances.

He vehemently denies that he has had any chest pain recently.

Current medication:
- Atenolol 50 mg 2x/day
- Ecotrin 81 mg daily
- Simvastatin 10 mg daily
Clinical findings

- All pulses palpable
- Mild pedal oedema
- No pallor
- JVP raised – 8cm above sternomanubrial angle
- Apex beat displaced – dyskinetic
- Soft pansystolic murmur
- S1 and S2 normal, no S3 heard
Echocardiography

- Quantification of LV function and regional wall motion abnormality (Our patient EF: 25%, global impairment of LV function)
- Rule out significant valvular heart disease which may contribute to the presentation (Our patient: mild mitral regurgitation only)
- Look for other abnormalities: e.g. LV clot (our patient: none)
BLOOD RESULTS

- CEU - Assess renal function and electrolytes as this can affect decisions re. drug therapy and can itself contribute to worsening cardiac failure (our patient: normal)
- FBC - Make sure the patient is not anaemic as this can make CCF symptoms worse (our patient: normal)
- TSH - If you do not check it, you cannot diagnose hypothyroidism (our patient normal)
What medication should this man be on?
First-up the therapy we know saves lives (and reduces heart failure recurrence!)
Pharmacological therapy

- Beta-blockers
- The only beta-blockers that have been tested in RCT’s are: metoprolol, bisoprolol and carvedilol
- These have been titrated to target dosages NOT target heart rates in the trials
Figure 2: Survival curves

Lancet 1999; 353: 9–13
<table>
<thead>
<tr>
<th></th>
<th>Starting dose (mg)</th>
<th>Target dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta-blocker</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bisoprolol</td>
<td>1.25 o.d.</td>
<td>10 o.d.</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>3.125 b.i.d.</td>
<td>25–50 b.i.d.</td>
</tr>
<tr>
<td>Metoprolol succinate (CR/XL)</td>
<td>12.5/25 o.d.</td>
<td>200 o.d.</td>
</tr>
<tr>
<td>Nebivolol</td>
<td>1.25 o.d.</td>
<td>10 o.d.</td>
</tr>
<tr>
<td><strong>ARB</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# Pharmacological interventions

- ACE-inhibitors

<table>
<thead>
<tr>
<th>ACE inhibitor</th>
<th>Starting dose (mg)</th>
<th>Target dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Captopril\textsuperscript{a}</td>
<td>6.25 t.i.d.</td>
<td>50 t.i.d.</td>
</tr>
<tr>
<td>Enalapril</td>
<td>2.5 b.i.d.</td>
<td>10–20 b.i.d.</td>
</tr>
<tr>
<td>Lisinopril\textsuperscript{b}</td>
<td>2.5–5.0 o.d.</td>
<td>20–35 o.d.</td>
</tr>
<tr>
<td>Ramipril</td>
<td>2.5 o.d.</td>
<td>5 b.i.d.</td>
</tr>
<tr>
<td>Trandolapril\textsuperscript{a}</td>
<td>0.5 o.d.</td>
<td>4 o.d.</td>
</tr>
<tr>
<td>ARB</td>
<td>Starting dose (mg)</td>
<td>Target dose (mg)</td>
</tr>
<tr>
<td>------------</td>
<td>--------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>Candesartan</td>
<td>4 or 8 o.d.</td>
<td>32 o.d.</td>
</tr>
<tr>
<td>Valsartan</td>
<td>40 b.i.d.</td>
<td>160 b.i.d.</td>
</tr>
<tr>
<td>Losartan</td>
<td>50 o.d.</td>
<td>150 o.d.</td>
</tr>
</tbody>
</table>
ACE-inhibitors – special considerations

• Cough is no uncommon (~5%) – often well tolerated with reassurance but may have to switch to ARB

• Angio-oedema – serious complication but rare

• Expect a creatinine rise of up to ~20% - this does not mean one has to stop the drug

• May cause hyperkalaemia

• Postural hypotension a major problem especially with concurrent diuretic use – reduce dosage of diuretic as needed
Pharmacological interventions

• Aldosterone antagonists
• 2 available: spironolactone and eplerenone
• Problems of both: they can cause hyperkalaemia and for this reason are contraindicated in patients with renal failure
• Spironolactone: gynaecomastia
Figure 1. Kaplan–Meier Analysis of the Probability of Survival among Patients in the Placebo Group and Patients in the Spironolactone Group.

The risk of death was 30 percent lower among patients in the spironolactone group than among patients in the placebo group (P<0.001).
Aldosterone antagonists are now indicated in class 2 NYHA (not only class 3 NYHA) patients (evidence for class eplerenone)
A

Hazard ratio, 0.63 (95% CI, 0.54–0.74)
P<0.001

Hospitalization for Heart Failure or Death from Cardiovascular Causes (%)

Years since Randomization

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Placebo</th>
<th>Eplerenone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1373</td>
<td>1364</td>
</tr>
<tr>
<td></td>
<td>848</td>
<td>925</td>
</tr>
<tr>
<td></td>
<td>512</td>
<td>562</td>
</tr>
<tr>
<td></td>
<td>199</td>
<td>232</td>
</tr>
<tr>
<td>MRA</td>
<td>Starting dose (mg)</td>
<td>Target dose (mg)</td>
</tr>
<tr>
<td>----------------------</td>
<td>--------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>Eplerenone</td>
<td>25 o.d.</td>
<td>50 o.d.</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>25 o.d.</td>
<td>25–50 o.d.</td>
</tr>
</tbody>
</table>
• Started on:
  – Carvedilol 3.125 mg 2x/day gradually increased to 12.5 mg 2x/day (he did not tolerate a higher dose, felt “ill” on 25 mg 2x/day
  – Valsartan 80 mg 2x/day
  – Furosemide 40 mg 2x/day
  – Continued Aspirin and Simvastatin

• Advised to avoid NSAIDs
• Followed up after 1 month of above therapy
Did not feel better! STILL short of breath on minimal exertion
What next?

• Escalate therapy with one of the following:
  – Add an ARB
  – Ivabradine
  – Digoxin
  – Hydrallazine and long-acting nitrates
Ivabradine (SHIFT trial)

A

Placebo (937 events)
Ivabradine (793 events)

HR 0.82 (95% CI 0.75–0.90), p<0.0001

Patients with primary composite endpoint (%)

Number at risk

<table>
<thead>
<tr>
<th>Group</th>
<th>Number at Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>3264</td>
</tr>
<tr>
<td>Ivabradine</td>
<td>3241</td>
</tr>
</tbody>
</table>

Months

Heart Failure Society of Africa (HFSA)

Lancet 2010; 376: 875–85
What is Ivabradine?

• Slow down the discharge rate of the sinus node by inhibiting the If current
• It does NOT work for rate control in AF as it only works on the sinus node
• It is available in South Africa for patients with symptomatic heart failure who have resting heart rates >77 bpm
• Most notable side-effect: phosphenes
Figure 2: Kaplan-Meier cumulative event curves for primary outcome

Lancet 2003; 362: 767–71
<table>
<thead>
<tr>
<th>Cause of discontinuation</th>
<th>Candesartan (n=1276)</th>
<th>Placebo (n=1272)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension</td>
<td>58 (4.5)</td>
<td>40 (3.1)</td>
<td>0.079</td>
</tr>
<tr>
<td>Increase in creatinine</td>
<td>100 (7.8)</td>
<td>52 (4.1)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Hyperkalaemia</td>
<td>44 (3.4)</td>
<td>9 (0.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Any adverse event or laboratory abnormality</td>
<td>309 (24.2)</td>
<td>233 (18.3)</td>
<td>0.0003</td>
</tr>
</tbody>
</table>

Table 4: Permanent study-drug discontinuation for adverse events
THE EFFECT OF DIGOXIN ON MORTALITY AND MORBIDITY IN PATIENTS WITH HEART FAILURE

THE DIGITALIS INVESTIGATION GROUP*
Figure 1. Mortality in the Digoxin and Placebo Groups.
The number of patients at risk at each four-month interval is shown below the figure.

Figure 3. Incidence of Death or Hospitalization Due to Worsening Heart Failure in the Digoxin and Placebo Groups.
The number of patients at risk at each four-month interval is shown below the figure.
Hydralazine (225 mg) and long-acting nitrates (60 mg)

Figure 1. Kaplan–Meier Estimates of Overall Survival.
In our patient:

- Ivabradine was not readily accessible
- ARB not added as his potassium on spironolactone and ACE-inhibitor was already 5.2
- Digoxin added
Should he be on a statin?
Effect of rosuvastatin in patients with chronic heart failure (the GISSI-HF trial): a randomised, double-blind, placebo-controlled trial

GISSI-HF investigators*

Summary
Background Large observational studies, small prospective studies and post-hoc analyses of randomised clinical trials have suggested that statins could be beneficial in patients with chronic heart failure. However, previous studies have been methodologically weak. We investigated the efficacy and safety of the statin rosuvastatin in patients with heart failure.

Rosuvastatin in Older Patients with Systolic Heart Failure

John Kjekshus, M.D., Ph.D., Eduard Apetrei, M.D., Ph.D., Vivencio Barrios, M.D., Ph.D., Michael Böhm, M.D., Ph.D., John G.F. Cleland, M.D., Jan H. Cornel, M.D., Ph.D., Peter Dunselman, M.D., Ph.D., Cândida Fonseca, M.D., Assen Goudev, M.D., Ph.D., Peer Grande, M.D., Ph.D., Lars Gullestad, M.D., Ph.D., Åke Hjalmarson, M.D., Ph.D., Jaromir Hradec, M.D., Ph.D., András Jánosi, M.D., D.Sc., Gabriel Kamenský, M.D., Ph.D., Michel Komajda, M.D., Jerzy Korewicki, M.D., Ph.D., Timo Kuusi, M.D., Ph.D., François Mach, M.D., Vyacheslav Mareev, M.D., Ph.D., John J.V. McMurray, M.D., Naresh Ranjith, M.D., Maria Schaufelberger, M.D., Ph.D., Johan Vanhaecke, M.D., Ph.D., Dirk J. van Veldhuisen, M.D., Ph.D., Finn Waagstein, M.D., Ph.D., Hans Wedel, Ph.D., and John Wikstrand, M.D., Ph.D., for the CORONA Group*

Adjusted HR* 1·01 (99% CI 0·908–1·112); p=0·903
Unadjusted HR 1·02 (99% CI 0·923–1·130); p=0·594

Number at risk
Rosuvastatin 2285 1895 1669 1486 1358 1246 1126 879 620 319
Placebo 2289 1903 1697 1517 1362 1244 1121 877 631 308

Log-rank test p=0·594
• Patients with symptomatic heart failure despite good medical therapy should be considered for cardiac resynchronisation therapy (CRT)
• CRT is achieved by the implantation of a biventricular pacemaker
What is “CRT”?
Figure 1  The Kaplan–Meier estimates of the time to all-cause mortality.
The cause of death in many patients with cardiomyopathies is sudden cardiac death secondary to malignant ventricular tachyarrhythmias.

Anti-arrhythmics do NOT work to prevent these.

The only therapy available for this is implantation of an internal cardioverter defibrillator (ICD).
Severity of Heart Failure

NYHA II

- CHF: 12%
- Other: 24%
- Sudden Death: 64%

NYHA III

- CHF: 26%
- Other: 15%
- Sudden Death: 59%

NYHA IV

- CHF: 33%
- Other: 56%
- Sudden Death: 11%
Most Cardiac Arrests (70%-80%) Occur At Home

Figure 2. Kaplan–Meier Estimates of the Probability of Survival in the Group Assigned to Receive an Implantable Defibrillator and the Group Assigned to Receive Conventional Medical Therapy. The difference in survival between the two groups was significant (nominal P=0.007, by the log-rank test).
Our patient.....

- Received a combination device: biventricular pacemaker with ICD function
- He improved to the extent that we were able to increase the carvedilol to target dose
- He is now off diuretic completely
- Has had one ICD discharge – inappropriate, he had gone into AF which was then cardioverted by the ICD
- Has been initiated on warfarin for this episode of atrial fibrillation
Do not forget that some patients may qualify for heart transplantation/LV assist devices
HeFSSA Practitioners Program 2013

08:00 – 08:30 Registration
08:30 – 09:15 Clinical Case Presentation 1
09:15 – 10:00 Clinical Case Presentation 2
10:00 – 10:30 Tea Break
10:30 – 11:15 Clinical Case Presentation 3
11:15 – 11:45 ESC Guidelines on Chronic Heart Failure
11:45 – 12:00 Questionnaire
12:00 – 14:00 Lunch