Heart Failure Patients
Diagnosis and Management

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Epidemiology

• Europe\(^1\)
  – Prevalence 3.9%
  – Annual incidence 1.3 cases per 1000 population age >25y
  – Rising to 11.6% cases in over 85 years

• In UK ~900,000 people living with HF
• Commonest cause for hospital admission in UK
  – 78% HF patients have ≥2 hospital admissions/y\(^2\)
    (20% 12 week readmission rate)

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\(^1\) Cowie et al *Eur Heart J* 1999
Economic burden of heart failure

- Cost of HF in the U.S. between $10-38 billion\(^1\)
- In UK ~900,000 people living with HF
- 1 million inpatient bed days (2% total NHS)
- Primary diagnosis in 5% of all hospital admissions
- Accounts for 1.2 - 2% all health care costs
  - 60-70% related to hospital admissions
  - May be as high as 2-4% NHS budget

\(^2\)English M and Mastream M. *Crit Care Nurse* 1995;18:1-6
What Medical Condition has the longest in patient stay?

Injuries and poisoning
Complications of pregnancy and childbirth
All GU system
All digestive system
All respiratory system
All nervous system
All cancer
Diabetes
Stroke
Heart failure
Acute MI
Angina
Coronary Heart Disease
All circulatory
All diagnoses

Average duration of hospital admission (days) – Year 2001

Prognosis

Severe heart failure:
- 10-50% mortality at 1 year
- 5-year survival rate for all NYHA classes estimated at 50%
  (American Heart Association, 2001 Heart and Stroke Statistical Update).

Cowie et al. *Eur Heart J* 1999;20:421-8
Annual absolute mortality in the E.U. for different pathologies

- Ovary cancer
- Bowel cancer
- Prostate cancer
- Breast cancer
- Colon/rectum cancer
- Lung cancer
- All cancers combined
- Heart failure
- Myocardial infarction
- Sudden cardiac death

Background slide
Aetiology – high output failure

- Sepsis
- Severe anaemia
- Massive AV fistula
- Thyrotoxicosis
- Severe Paget’s disease of bone
- Beri beri
Aetiology – poor cardiac output

- Coronary artery disease
- Valvular heart disease
  - Volume overload: Aortic / mitral regurgitation
  - Obstruction: Aortic stenosis
- Cardiomyopathy
  - Dilated
  - Hypertrophic
  - Alcohol
  - Drug induced – adriamycin, danorubicin, 5FU
- Hypertension
Aetiology - poor cardiac output

Infective
  • Myocarditis
Infiltrative
  • Amyloid, sarcoidosis, malignancy
Metabolic / Endocrine
  • Acromegaly, thyroid, phaeochromocytoma, haemochromatosis
Mechanical problems
  • Myocardial fibrosis - radiation
  • LV aneurysm
Arrhythmias
  • Incessant tachycardia
Aetiology

Coronary artery disease 52%
Idiopathic DCM 13%
Valve disease 10%
Alcohol 4%
Hypertension 4%
Atrial fibrillation 3%
Other 7%
Undetermined 10%

(332 cases over 15 months)

Fox KF et al Eur Heart J 2000
Symptoms

- Exertional dyspnoea
- Nocturnal cough
- Orthopnoea
- Paroxysmal nocturnal dyspnoea
- Ankle swelling
- Tiredness
- Anorexia, weight loss
- Cool peripheries
Signs

- Tachycardia
- Hypotension
- Raised JVP
- Third Heart sound, PSM of MR
- Bi-basal crepitations
- Pleural effusions
- Peripheral oedema
- Ascites
Severity: New York Heart Association Classification

• Asymptomatic – class I
  – no functional limitation despite the presence of heart disease

• Mild – class II
  – Breathless / fatigue on moderate exertion - slight limitation, normal lifestyle and employment

• Moderate – class III
  – Breathless / fatigue on minimal exertion / activities of daily living affected

• Severe – class IV
  – Symptoms at rest / minimal exertion, mostly housebound
Heart Failure - The Challenges

- Diagnosis of underlying cause
- Optimise treatment
- Reduce morbidity and mortality
- Prevent hospitalisation
- Identify patients who will benefit from revascularisation
- Risk stratification of patients
  - Identify patients who will benefit from complex therapy
- Primary prevention
  - Identification and treatment of risk factors and precipitants of heart failure
Investigations

- ECG
- Bloods
- CXR
- ABG
- Echocardiogram
- Cardiac catheterisation
- Non-invasive imaging:
  - stress echo, MUGA, MRI, thallium
- Functional assessment:
  - lung function, 6 min walk, MVO$_2$, QOL
Blood Tests

- FBC, U&Es, Cr
- Troponin / Cardiac enzymes
- Lipids
- TFT, Iron studies
- BNP
- ABGs - hypoxia, acidosis, CO$_2$ retention
Echocardiogram

Dimensions - LV, RV, LA
- dilated / hypertrophy / normal

Degree of LV impairment (EF)

Regional wall motion abnormalities

Valvular heart disease

Filling abnormalities

Pulmonary hypertension
Functional assessment

- Exercise testing
- Stress echocardiography
- Myocardial perfusion scanning
- Perfusion MRI scanning
- Pressure wire / coronary flow assessment
Myocardial perfusion scintigraphy

- Myocardial ischaemia: perfusion defect present during stress but not resting conditions
- Scar tissue: associated with a fixed perfusion defect seen at rest and stress
Cardiac catheterisation

Coronary artery disease
LV function
Heart pressures / sats
- valvular heart disease
- shunts
Valvular heart disease

- Early diagnosis
- Surveillance and monitoring
- Timely intervention to prevent irreversible HF
- Surgical or percutaneous approaches
  - AVR/MVR
  - TAVI
  - Mitraclipping
VICIOUS CYCLE OF HEART FAILURE

- Impaired LV function
- Outflow resistance
- Systemic vascular resistance
- Neurohormonal activation
- Cardiac output and stroke volume
- Ventricular dilatation
  - Increased wall stress

Preload
- Filling pressure
- Blood volume
- Sodium/water retention
- Renal perfusion
- Cardiac output and stroke volume

Sympathetic
- Renin-Angiotensin-Aldosterone
- Vasopressin
What are the treatment aims and considerations in heart failure?

1) Help Symptoms
2) Prevent Sudden Death
3) Improve Prognosis
4) Family Screening / ? Pregnancy
5) Community Follow Up and Care
6) Good palliative care provision
7) Referral to specialist units and departments
Treatment - Chronic Heart Failure

- Non-pharmacological
- BP control
- Diuretics: loop / thiazide
- ACE Inhibitors
- Spironolactone
- ß blockers
- Digoxin
Diuretics

• Promote renal excretion of salt and water
• Block tubular reabsorption of sodium and chloride
  – Loop diuretics: Ascending limb of loop of Henle
  – Thiazide diuretics: Distal convoluted tubule
  – Aldosterone blocking agents
Trials - ACE I Doses

- CONSENSUS STUDY 20mg* Enalapril
- V-HeFT II STUDY 10mg* Enalapril
- SOLVD STUDY 10mg* Enalapril
- SAVE STUDY 50mg** Captopril
  *twice daily   **three times a day

- ATLAS STUDY showed a significant decrease in mortality+hospital admissions in high dose versus low dose lisinopril
Primary endpoint: greatest benefits in patients not on ACE inhibitor therapy
Combined all-cause mortality / morbidity

Cohn et al. AHA Scientific Sessions 2000

44.5% risk reduction
p = 0.0002

Event-free probability

Time since randomization (months)

Valsartan (n = 185)
Placebo (n = 181)
Reduction in HF hospitalizations

- Event-free probability
- Time since randomization (months)
- Valsartan
- Placebo

27.5% risk reduction*  
p<0.001

Cohn et al. AHA Scientific Sessions 2000  
*Censored for death

Secondary endpoint: time to first HF hospitalization
Additional pharmacological agents

- Angiotensin II blockers
  - RESOLVD (candesartan cf enalapril)
  - Elite (losartan cf captopril)
  - Elite II (losartan cf captopril)
  - Val-HeFT (valsartan v placebo)
- Digoxin
- Nitrates / Hydralazine (VHeFT II)
- Inotropes
CKD patients: V Heft Trial

β Blockers

• Heightened sympathetic drive in CCF result in altered composition of β receptors on the myocardium.
  – Short term: Negative inotropic effect
  – 4-12 months: Ventricular remodelling

• Side effects
  – Hypotension
  – Bradycardia (conducting tissue disease)
  – Exacerbation of heart failure
  – (Reactive airways disease)
Carvedilol - US carvedilol heart failure study group

- Non-selective β blocker
- Double blind RCT
- Mild-severe heart failure
- EF<0.35
- 1094 patients
- 65% risk reduction of death
- 27% risk reduction of hospitalisation

Packer et al, NEJM 1996;334: 1349-55
Bisoprolol – CIBIS II

- RCT double blind – bisoprolol v placebo
- >2500 patients
- NYHA III-IV, EF<0.35
- 50% IHD
- All on ACEI, 50% digoxin
- 34% risk reduction in mortality

Lancet 1999; 353:9-13
Spironolactone

• Potassium sparing diuretic – weak diuretic

• Competitive antagonist to aldosterone
  (retention of Na, loss K, sympathetic activation, parasympathetic inhibition, myocardial fibrosis)

• Side effects
  – Hyperkalaemia
  – Renal failure
  – Gynaecomastia
Spironolactone - ¹Rales

- Double blind RCT
- 1663 patients
- NYHA III-IV
- Risk of death 30% lower in spironolactone group as compared to placebo
- 35% reduction in risk of hospitalisation
- Improved NYHA

¹Pitt et al, NEJM 1999, 341: 709-17
Undertreatment of HF in Europe

Cardiovascular drug use 1999-2000

Cleland et al. Eur Heart J 2001; 22:494
Chronic heart failure

Implementing NICE guidance

August 2010

NICE clinical guideline 108
Treating heart failure

Heart failure

Heart failure with preserved ejection fraction

Manage comorbid conditions such as high blood pressure, ischaemic heart disease and diabetes mellitus in line with NICE guidance

Heart failure due to left ventricular systolic dysfunction

Offer both ACE inhibitors and beta-blockers licensed for heart failure as first-line treatment

Consider an ARB if intolerant of ACE inhibitors

Specialist assessment

Offer rehabilitation and education, and diuretics for congestion and fluid retention

If symptoms persist despite optimal first-line treatment, seek specialist advice and for second-line treatment consider adding:

- an aldosterone antagonist licensed for heart failure (especially in moderate to severe heart failure or MI in past month) or
- an ARB licensed for heart failure (especially in mild to moderate heart failure) or
- hydralazine in combination with nitrates (especially in people of African or Caribbean origin with moderate to severe heart failure)

Specialist assessment

Consider hydralazine in combination with nitrates if intolerant of ACE inhibitors and ARBs

If symptoms persist consider:

- CRT (pacing with or without a defibrillator)
- digoxin

Consider an ICD where appropriate
SHIFT trial Mortality

Ivabradine n=793 (14.5% PY) Placebo n=937 (17.7% PY)

HR = 0.82  p<0.0001

Cumulative frequency (%)

- 18%
SHIFT Hospitalisation

Ivabradine n=514 (9.4%PY) Placebo n=672 (12.7%PY)

HR = 0.74  p<0.0001

Cumulative frequency (%)

- 26%

Lancet. Online 29-08-2010
PARADIGM HF

- Sacubtiril (200mg bd) & Valsartan (max 160mg) vs Enalapril 10mg bd
- 8442 patients
- Class 2-4 NHYA HF
- LVEF <40%
- 1º end point: CV death, hospitalisation HF
- Trial premature termination at 27/12
PARADIGM HF (Entresto)

McMurray et al NEJM 2014
IV Iron therapy for HF: FAIR HF

- Double blind, placebo controlled
- 459 patients with iron deficiency, transferrin saturation <20% with or without anaemia randomised to
  - Weekly IV iron / saline for 24 weeks
- Primary end points: patients global assessment and NYHA class
FAIR HF Results

Anker et al, NEJM 2009; 361:2436-48
FAIR HF Results

6-minute walk test

KCCQ overall score

Anker et al, NEJM 2009; 361:2436-48
What to do if the patient is getting worse despite medical therapy?
Options During Decompensation

- Cardiology / Heart Failure input
- Change diuretic
  - Bumetanide (improved bioavailability)
  - IV Diuretics: intermittent or infusion
- IV Nitrates
- Fluid restriction
- Escalation of medical therapy
- Advanced heart failure therapy
Advanced Heart Failure Therapy

- Inotropic support
- Device Therapy
- Ultrafiltration
- Circulatory Support
- Cardiac Transplantation
- Palliative Care
Ultrafiltration remove fluid from blood at the same rate that fluid can be naturally recruited from the tissue.

The transient removal of blood elicits a compensatory mechanism, called plasma or intravascular refill (PR), aimed at minimizing this reduction.\(^1,2\)

Freedom From Re-hospitalization for Heart Failure

Ultrafiltration vs Furosemide in HF

**Body Weight**

- Green triangle: Body Weight
- Purple circles: UF (n=8; 1710 ml)
- Yellow squares: Furosemide (n=8; 248 mg i.v.)

**Plasma Renin Activity**

- Y-axis: %
- X-axis: day

- *p<0.01 vs. day 0

Ultrafiltration vs. Furosemide in HF

Peak VO2

ml/kg/min

UF (n=8; 1710 ml)

Furosemide (n=8; 248 mg i.v.)

Tolerance Time

seconds

* p<0.01 vs. day -1
Sudden Death accounts for ~50% of mortality in advanced heart failure.
Electrocardiogram

Tachycardia, arrhythmia
Evidence of IHD / ACS / Underlying pathology
Conduction abnormalities
Biventricular pacing

- Severe refractory heart failure / ventricular dyssynchrony

- Reduces ventricular dyssynchrony
- Increased LVEF
- Increased CO
- Prolong diastole / LV filling & ejection time
- Reduced MR
- Reduced PCWP
- Decreased LVEDP / LVEDV
MIRACLE: Hospitalisation for worsening heart failure

Event Free Survival (%)

- Cardiac Resynchronization: p = 0.015
- Relative risk = 0.50;
- 95% CI (0.28, 0.88)

Patients At Risk

<table>
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<tr>
<th></th>
<th>Control</th>
<th>CRT</th>
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<tr>
<td>0</td>
<td>225</td>
<td>228</td>
</tr>
<tr>
<td>1</td>
<td>214</td>
<td>218</td>
</tr>
<tr>
<td>2</td>
<td>204</td>
<td>213</td>
</tr>
<tr>
<td>3</td>
<td>197</td>
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<td>4</td>
<td>191</td>
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<td>5</td>
<td>179</td>
<td>201</td>
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<tr>
<td>6</td>
<td>70</td>
<td>99</td>
</tr>
</tbody>
</table>

Abraham WT, et al. MIRACLE Trial Results; ACC 2001.
MIRACLE: Total Days Hospitalized for Heart Failure

Control N=225
363

CRT N=228
83

↓ 77%
p = 0.012

Abraham WT, et al. MIRACLE Trial Results; AHA 2001.
CARE-HF Mortality and Cardiovascular hospitalisations

N = 813
2.5y/FU

RRR 37%

Cleland et al NEJM 2005
CARE-HF Long-Term Follow-up
Effect of CRT on All-Cause Mortality
(Data censored for loss to Follow-up)

Hazard Ratio 0.77
(95% CI 0.63 to 0.93; p = 0.007)

Median Survival in CRT Group ~7 years
Minimum Duration of Follow-up 6.5 yrs

Cleland 2010
Companion randomisation

Randomization

- OPT Med Rx
- Resynchronization Therapy

N=2,200
Min F/U 1 year

1

2

+ +
Companion Study: All cause mortality

N=2,200
Min F/U 1 year
DCM 44%
IHD 56%

Any Death

12 month event rate reductions:
CRT = 23.9%
CRT-D = 43.4%
p = .002, CRT-D vs. OPT
p = .12, CRT vs.OPT

12 month OPT Event Rate
(1-y) = 19.0%

Days from Randomization
MADIT-CRT

n=1820

Death or HF RRR 34%
HF events RRR 41%

P<0.001

Moss et al NEJM 2009
MADIT - CRT

- **LVEDV**
  - ICD only (N=620): Change in Volume = 15 ml vs. 52 ml decrease from baseline
  - CRT–ICD (N=746): Change in Volume = 18 ml vs. 57 ml decrease from baseline

- **LVESV**
  - CRT–ICD (N=746): Change in Volume

- **LVEF**
  - CRT–ICD (N=746): Increase from baseline = 0.03 vs. 0.11
New NICE guidance: Broader indications

Summary of NICE TA314 guidance on “Implantable cardioverter defibrillators and cardiac resynchronisation therapy for arrhythmias and heart failure”:

<table>
<thead>
<tr>
<th>QRS</th>
<th>LBBB</th>
<th>NYHA I</th>
<th>NYHA II</th>
<th>NYHA III</th>
<th>NYHA IV</th>
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</thead>
<tbody>
<tr>
<td>&lt; 120 ms</td>
<td>n/a</td>
<td>ICD*</td>
<td>ICD*</td>
<td>ICD*</td>
<td>OMT</td>
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<tr>
<td>120-149 ms</td>
<td>without LBBB</td>
<td>ICD</td>
<td>ICD</td>
<td>ICD</td>
<td>CRT-P</td>
</tr>
<tr>
<td></td>
<td>with LBBB</td>
<td>ICD</td>
<td>CRT-D</td>
<td>CRT-P or -D</td>
<td>CRT-P</td>
</tr>
<tr>
<td>≥ 150 ms</td>
<td>with or without LBBB</td>
<td>CRT-D</td>
<td>CRT-D</td>
<td>CRT-P or -D</td>
<td>CRT-P</td>
</tr>
</tbody>
</table>

* If there is a high risk of SCD

- *Upgrade from ICD to CRT-D (and from OMT to CRT-D for non-ischaemic patients)*
- *New indicated population: non-ischaemic patients*
TAVI

TRANSZATHETER AORTIC VALVE IMPLANTATION (TAVI)

TRANSFEMORAL APPROACH
Severe MR: Mitraclip

• Based on the surgical Alfieri technique
• Less invasive, trans-septal approach
• Decreases distance between the anterior and posterior leaflets. Applies tension to the chordae, leaflets, and, potentially, the annulus
• More than 4000 procedures worldwide to date.
MitraClip

THE MIGHTY MITRACLIP

2. Clip is positioned above the damaged valve

3. Once in position, the clip is opened. Its two levers clamp the valve together

1. Clip is implanted via the femoral vein in the groin

Right atrium

Damaged mitral valve

Left atrium

Route of flexible delivery arm

Damaged valve

MitraClip
Mechanical support: LV Assist Devices

- Extracorporeal assist devices (Thoratec/Abiomed)
- Implantable LV assist devices
  - pulsatile (Heartmate)
  - axial flow pumps (Heartware)
- Totally implantable LVAD (Lion Heart)
- Total Artificial Heart (ABIOCOR)
Heartmate VAD
Heartmate VAD

n=129

**Quality of life**

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Medical-Therapy Group</th>
<th>LVAD Group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular dysfunction</td>
<td>50</td>
<td>1</td>
<td>51</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>Failure of LVAD</td>
<td>0</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Miscellaneous noncardiovascular causes</td>
<td>0</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Miscellaneous cardiovascular causes</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Cardiac procedure</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Perioperative bleeding</td>
<td>0</td>
<td>1</td>
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</tr>
<tr>
<td>Unknown</td>
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<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
<td>41</td>
<td>95</td>
</tr>
</tbody>
</table>

*LVAD denotes left ventricular assist device.*
NUMBER OF HEART TRANSPLANTS REPORTED BY YEAR

NOTE: This figure includes only the heart transplants that are reported to the ISHLT Transplant Registry. As such, the presented data may not mirror the changes in the number of heart transplants performed worldwide.

ISHLT

J Heart Lung Transplant. 2010 Oct; 29 (10): 1083-1141
Pulmonary vein isolation
AF ablation in Heart failure

Hsu et al. NEJM 2004
AF and CCF

Ferriera et al Europace 2008
Heart failure therapies

Stage A: High risk with no symptoms
- Risk-factor reduction, patient and family education

Stage B: Structural heart disease, no symptoms
- ACE inhibitors or ARBs in all patients; beta-blockers in selected patients
- Treat hypertension, diabetes, dyslipidemia; ACE inhibitors or ARBs in some patients

Stage C: Structural disease, previous or current symptoms
- ACE inhibitors and beta-blockers in all patients
- Dietary sodium restriction, diuretics, and digoxin
- Cardiac resynchronization if bundle-branch block present
- Consider multidisciplinary team
- Revascularization, mitral-valve surgery

Stage D: Refractory symptoms requiring special intervention
- Aldosterone antagonist, nesiritide
- Inotropes
- VAD, transplantation
- Hospice

Jessup NEJM 2003;348:2007-18
Terminal Heart Failure

- Anxiety and depression
- End of life palliative care
- DNR orders
- Turning off ICD devices
- Support for patient and families
Conclusions

- Accurate diagnose type of heart failure
- Establish recommended therapies
- Does patient have optimal medical treatment
- Need cardiology / heart failure team input?
- Involve palliative care when appropriate

- Good patient Mx involves primary, secondary and community linked services