Chronic Heart Failure: Diagnosis and Modern Management

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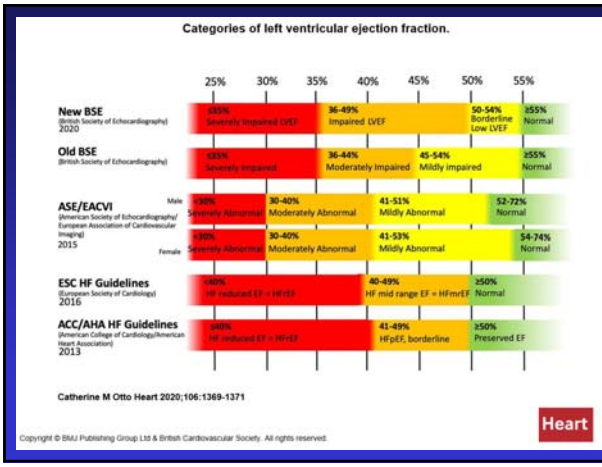

Definition of heart failure

Heart failure is a complex clinical syndrome of symptoms and signs that suggest impairment of the heart as a pump supporting physiological circulation. It is caused by structural or functional abnormalities of the heart.

Clinical syndrome characterised by symptoms such as breathlessness, fatigue, and signs such as fluid retention.

NICE 2010

HF- The size of the problem

- 2-4% of population
- Incidence in the UK is 63,000 cases PA.
- The prevalence of HF in the UK is 900,000 cases.
  - 1 in 35 65-74 yrs
  - 1 in 15 75-84 yrs
  - 1 in 7 >85
- Hospital admission likely to ↑ 50% over 25 yrs.
- Average GP will have ~ 30 cases

Definitions of HFrEF and HFpEF[1]

Classification	EF	Description
HFrEF	≤40%	• Also referred to as systolic HF • Randomized controlled trials have mainly enrolled patients with HFrEF
HFpEF	≥50%	• Also referred to as diastolic HF • Several different criteria have been used to further define HFpEF • Diagnosis of HFpEF is challenging, because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF
HFpEF, borderline	41%-49%	• These patients fall into a borderline or intermediate group • Their characteristics, treatment patterns, and outcomes appear similar to those of patients with HFpEF
HFpEF, improved	>40%	• It has been recognized that a subset of patients with HFpEF previously had HFrEF; these patients with improvement or recovery in EF may be clinically distinct from those with persistently preserved or reduced EF • Further research is needed to better characterize these patients

1. Yancy CW et al. J Am Coll Cardiol. 2013;62:e147-e239.

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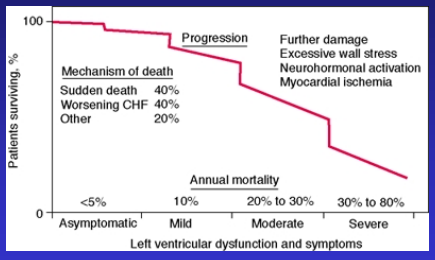
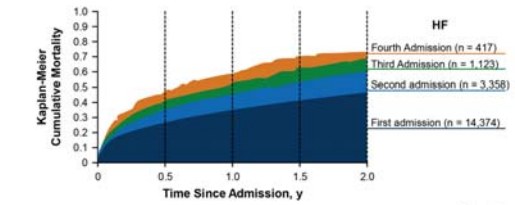
HF- Mortality



Repeat Hospitalizations Predict Mortality[1]



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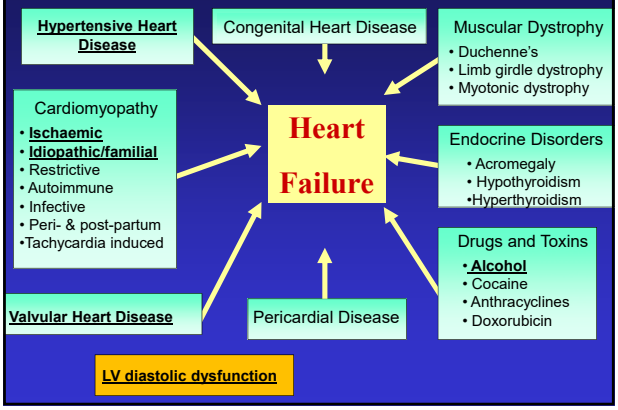
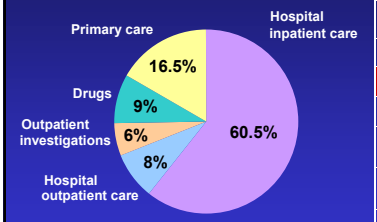
Causes of Heart Failure



Costs of HF to the UK NHS (2000)



Cost element	£ million
Primary care	103.8
Hospital inpatient care	378.6
Hospital day case care	0.45
Hospital outpatient care	51.25
Outpatient investigations	37.44
Drugs	54.08
Total	625.62

2011: £970

Coronary heart disease statistics: heart failure supplement., BHF 2002, http://www.heartstats.org, accessed 25.02.04.

General Practitioners – Key to Management of HF patients

- Identify signs and symptoms of HF
- Refer to secondary care to establish diagnosis.
- Work in partnership with cardiologist/heart failure team. Jointly optimise treatment with medication titration

Almost 75% of Patients With HF Have Additional Contributing Clinical Risk Factors[1-3]

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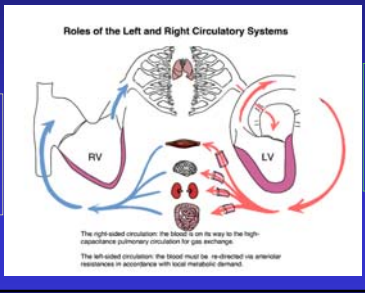
Heart Failure is Clinical Diagnosis – can be a challenge

- Difficult to diagnose on clinical grounds
- Diagnosis incorrect in approx. 30-40% of cases *
- Crepitations, oedema, tachycardia – not specific
- S3, ↑JVP, displaced apex – specific but insensitive, poor inter-observer agreement
- Therefore objective evidence of cardiac dysfunction mandatory: usually echocardiography, MRI, nuclear…….. but major resource issues

Wheeldon et al QJMed 1993:86:17-24

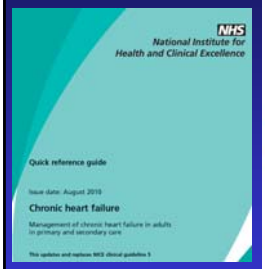
Heart Failure: CLINICAL PRESENTATION

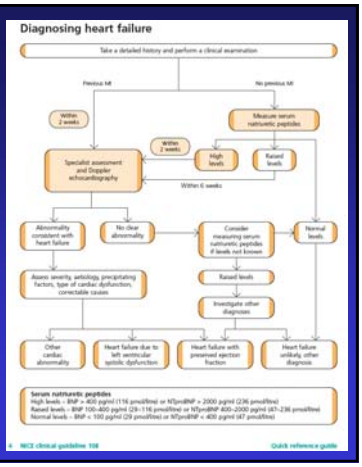
Left-Sided Congestion
-Crepitations
-Dyspnoea (Exertion > Rest)
-PND/orthoponea
-Interstitial oedema



Right-Sided Congestion
-Elevated JVP
-Oedema
-Ascites
-Hepatomegaly

Low Forward Output
-Fatigue
-Exercise Intolerance
-Pre-renal failure





Grading of heart failure

Table 2. New York Association (NYHA) classification for heart failure

NYHA class	Exercise tolerance	Symptoms
I	No limitation	No symptoms during usual activity
II	Mild limitation	Comfortable with rest or with mild exertion
III	Moderate limitation	Comfortable only at rest
IV	Severe limitation	Any physical activity brings on discomfort and symptoms occur at rest

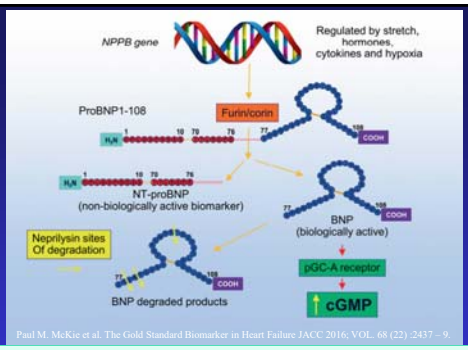
How effective are screening tests?

Investigations

- BNP/ NT-pro BNP
- Perform an ECG
- Chest X-ray
- Blood tests (electrolytes, urea and creatinine, eGFR, thyroid function tests, liver function tests, fasting lipids, fasting glucose, full blood count), urinalysis, and peak flow or spirometry.
- Cardiomyopathy screen: above + B12, Ferritin, ANA, CK, ACE
- Imaging: echocardiography, cardiac MRI

Are screening tests the answer?

- 12 Lead ECG
  - A normal ECG – helpful but low negative predictive value
  - Problems with confidence of interpretation in primary care, must be ***entirely normal*** or else loses reliability
  - LVH, LBBB, intraventricular conduction delays, non-specific ST-T wave changes, Q waves



BNP (brain (B-type) natriuretic peptide)/ NT- Pro BNP

- Amino acid peptide. Secreted from the ventricle
- Elevated in heart failure, therefore low BNP effectively excludes heart failure
- Can be useful as a diagnostic test

Treatment

BNP/NT-pro BNP as a screening test for heart failure

- Marker of structural heart disease rather than systolic dysfunction
- Low BNP/NT-pro BNP effectively rules out heart failure or LVSD, elevated BNP/NT-pro BNP indicates need for an echo/cardiac assessment

Selected Potential Causes of Elevated BNP Levels[1]

Cardiac	Noncardiac
• HF, including RV syndromes • Acute coronary syndromes • Heart muscle disease, including LV hypertrophy • Valvular heart disease • Pericardial disease • AF • Myocarditis • Cardiac surgery • Cardioversion • Toxic-metabolic myocardial insults (eg, cancer chemotherapy)	• Advancing age • Anemia • Renal failure • Pulmonary: obstructive sleep apnea, severe pneumonia • Pulmonary hypertension • Critical illness • Bacterial sepsis • Severe burns

Obesity may *reduce* BNP concentrations;
morbid obesity may reduce the sensitivity of BNP tests

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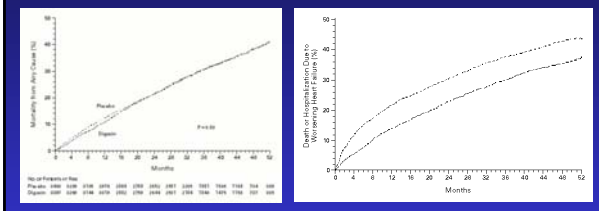
Dig Study

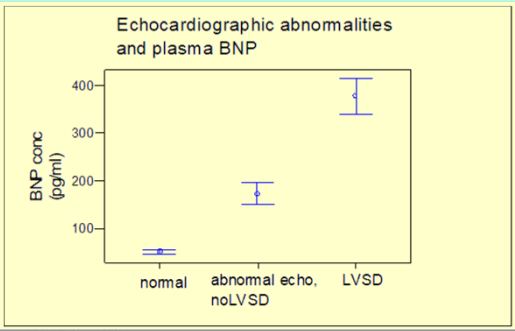


Mortality

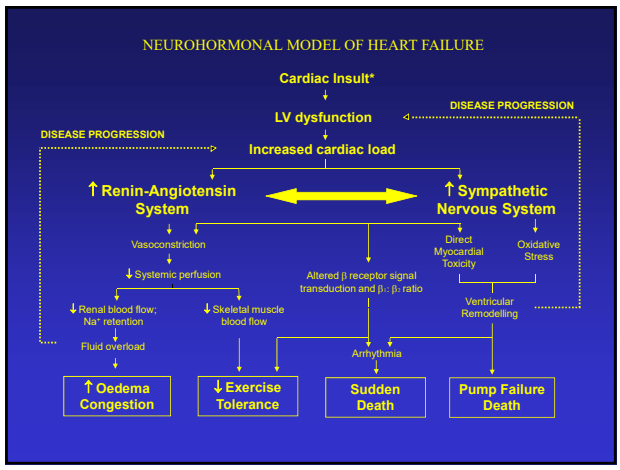
Death or Hospital Admission

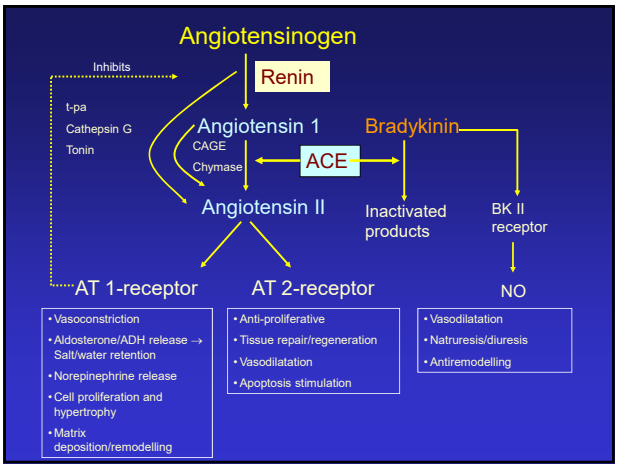
6800 patients in SR
N Engl J Med 1997;336:525-33

Relationship between BNP and echocardiographic abnormalities in 331 patients with suspected heart failure

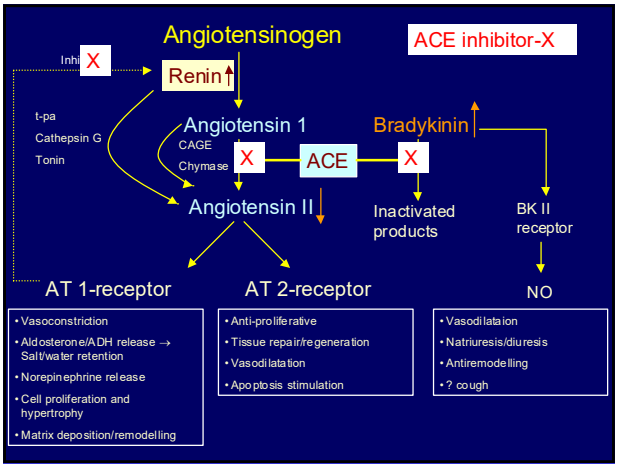


Serum natriuretic peptides
High levels – BNP > 400 pg/ml (116 pmol/litre) or NTproBNP > 2000 pg/ml (236 pmol/litre)
Raised levels – BNP 100–400 pg/ml (29–116 pmol/litre) or NTproBNP 400–2000 pg/ml (47–236 pmol/litre)
Normal levels – BNP < 100 pg/ml (29 pmol/litre) or NTproBNP < 400 pg/ml (47 pmol/litre)





ACE inhibitors are the cornerstone of therapy for heart failure due to LV systolic dysfunction



Practical Recommendations for Heart Failure Treatment:
Putting Guidelines into Practice

— ACE INHIBITORS —

ACE Inhibitors – Which and What Dose?

	Starting dose	Target dose
• captopril	6.25 mg tds	50–100 mg tds
• enalapril	2.5 mg bd	10–20 mg bd
• lisinopril	2.5–5 mg od	30–35 mg od
• ramipril	2.5 mg od	5 mg bd/10 mg od
• trandolapril	1 mg od	4 mg od
• Perindopril	2 mg od	4 mg od

od = once daily; bd = twice daily; tds = thrice daily

Major Trials of ACE-Inhibitors in HF

	Patients (n)	Mean Follow-up	NYHA Class	LVEF (%)	Effects on all-cause mortality
HF					
CONSENSUS	253	188 days	IV	N/A	All-cause mortality: At 6 months↓ 40%(p=0.002)
SOLVD-Treatment	2569	3.4yrs	II–III	≤35	All-cause mortality: ↓ 16% (p<0.0036)
SOLVD-Prevention	4228	3.1yrs	N/A	≤35	All-cause mortality ↓8% (p=0.30)
Post-MI HF					
SAVE	2231	3.5yrs	N/A	≤40	All-cause mortality: ↓ 19%(p=0.019)
AIRE	2006	1.25yrs	I–III	N/A	All-cause mortality: ↓ 27%(p=0.002)
TRACE	1749	2-4.2yrs	N/A	≤ 35	All-cause mortality: ↓ 22%(p=0.001)

The CONSENSUS Trial Study Group. N Eng J Med 1987; 316: 1429-1435., The SOLVD Investigators. N Eng J Med 1991; 325: 293-302. The SOLVD Investigators. N Eng J Med 1992; 327: 685-691., Pfeffer MA, Braunwald E, Moye LA et al. The SAVE Investigators. N Eng J Med 1992; 327: 669-677., The Acute Infarction Ramipril Efficacy (AIRE) Study Investigators. Lancet 1993; 342: 821-828., Kober L, Torp-Pedersen C, Carlsen JE et al. Trandolapril Cardiac Evaluation (TRACE) Study Group. N Eng J Med 1995; 333: 1670-1676.

Difficulties with ACE inhibitors

- Renal Failure
  - A 30% rise in creatinine is expected with diuretics and ACE inhibitors
  - A 50% rise in creatinine is acceptable
  - An even greater fall in GFR is expected
  - Only contra-indicated in bilateral RAS
  - Stop NSAIDs and other nephrotoxic drugs
  - If not fluid overloaded, reduce diuretic and observe patient and renal function
- Hypotension
  - Ignore if asymptomatic
  - If fluid overloaded (i.e. JVP elevated, oedema etc) refer secondary care
  - Stop drugs that drop BP, eg.Amlodipine, nitrates

Rarely necessary to stop ACE
- Cessation of ACE will cause major clinical deterioration
- Stop spironolactone first

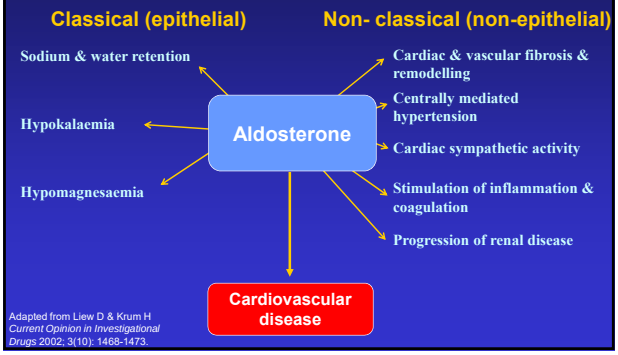
Betablockers in Heart failure

- 18 years ago – BB contraindicated in HF
- 1970s Sweden – small studies suggest benefit
- US carvedilol trials (1996)- NYHA I-III (IV)
  - n=1094, 4 separate trials, 65% RRR in mortality
- CIBIS II - bisoprolol - NYHA III
  - n=2647, mortality 11.8% v 17.3% ($p<0.0001$)
- MERIT - metoprolol CR/XL - NYHA II-III
  - improved mortality, morbidity and LVEF

Aldosterone receptor blockade

Betablockers are the second cornerstone of therapy for heart failure due to LV systolic dysfunction

The Role of Aldosterone in the Pathophysiology of CVD



Adapted from Liew D & Krum H *Current Opinion in Investigational Drugs* 2002; 3(10): 1468-1473.

Practical Recommendations for Heart Failure Treatment:
Putting Guidelines into Practice

— BETA BLOCKERS —

Beta Blockers – Which and What Dose?

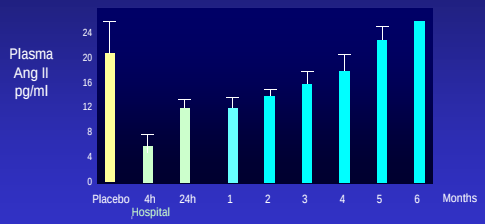
	Starting dose	Target dose
bisoprolol	1.25 mg od	10 mg od
carvedilol	3.125 mg bd	25–50 mg bd
metoprolol CR/XL	12.5–25 mg od	200 mg od
Nebivolol	1.25 mg od	10 mg od

NHS National Institute for Health and Clinical Excellence

Beta-blockers (first-line treatment with ACE inhibitors)

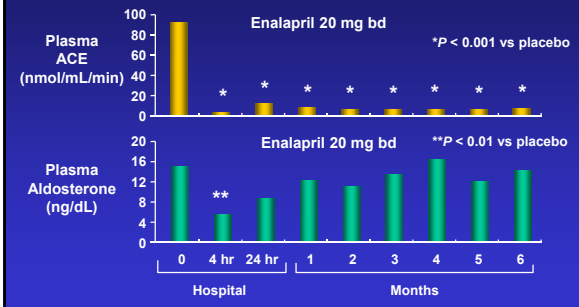
- Offer beta-blockers licensed for heart failure to all patients with heart failure due to left ventricular systolic dysfunction, including:
  - older adults **and**
  - patients with:
    - peripheral vascular disease
    - erectile dysfunction
    - diabetes mellitus
    - interstitial pulmonary disease
    - chronic obstructive pulmonary disease (COPD) without reversibility. *KPI*

ACE escape: Ang II levels increase over time despite ACEi



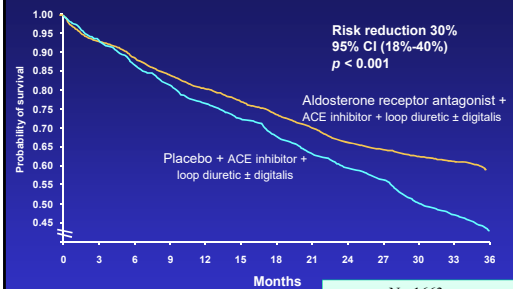
Biollaz et al. J Cardiovasc Pharmacol 1982;4:966

Aldosterone not adequately suppressed by ACE Inhibitors



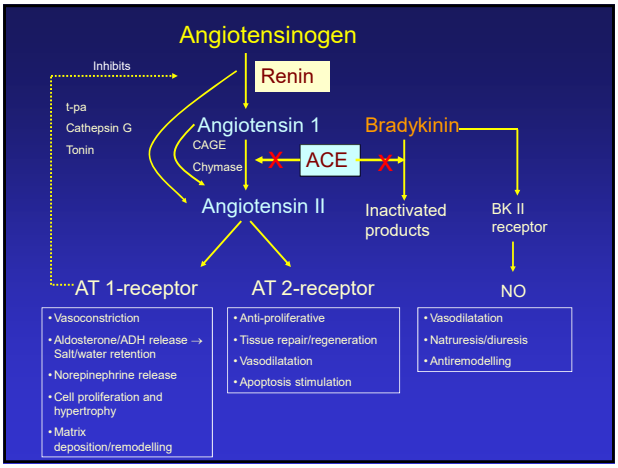
Biollaz J, et al. J Cardiovasc Pharmacol. 1982;4:966-972

RALES: All-Cause Mortality



N= 1663
NYHA IV (III)
ACEI 89%, Frusemide, digoxin 72%
27% RRR in mortality
Safe (hyperkalaemia excess 0.5%)

Pitt B et al, N Engl J Med 1999; 341: 709-717

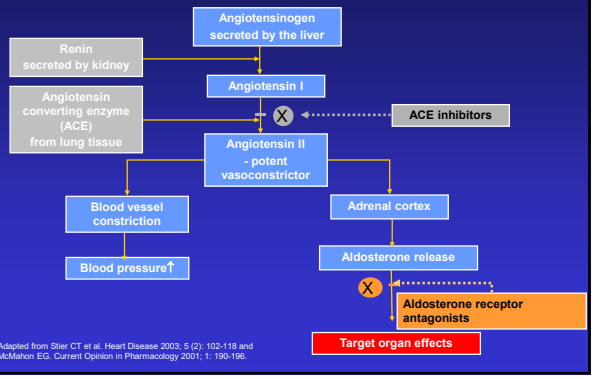


EPHESUS study – eplerenone post MI LVSD/HF

- 6642 patients
- LVEF<40%+HF or DM
- ACEI/AR2B 87%
- ***Betablockers 75%***
- Aspirin 88%
- Diuretics 60%
- Statin 47%

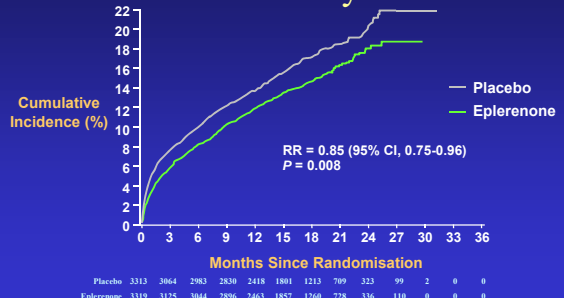
Pitt B et al. N Eng J Med 2003; 348: 1309-1321

RAAS Therapeutic Intervention Sites



Adapted from Stier CT et al. Heart Disease 2003; 5 (2): 102-118 and McMahon EG. Current Opinion in Pharmacology 2001; 1: 190-196.

Primary Endpoint: All-Cause Mortality



Pitt B et al. N Eng J Med 2003; 348: 1309-1321

EMPHASIS-HF

EMPHASIS-HF: Major results

Outcome	Eplerenone (%)	Placebo (%)	Adjusted hazard ratio (95% CI)	p
Cardiovascular death/heart-failure hospitalization	18.3	25.9	0.63 (0.54–0.74)	<0.001
Cardiovascular death	10.8	13.5	0.76 (0.61–0.94)	0.01
Heart-failure hospitalization	12.0	18.4	0.58 (0.47–0.70)	<0.001
Hospitalization for hyperkalemia	0.3	0.2	1.15 (0.25–5.31)	0.85

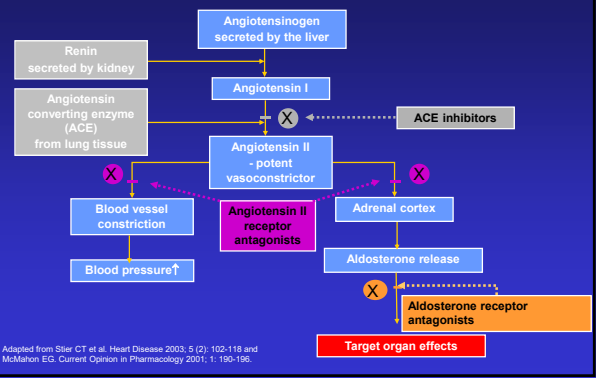
NYHA Class II HF (N=2737)
LV EF < 35%
Eplerenone 25-50mg QD vs. Placebo

Zannad et al. NEJM 2011;364:11-21

Angiotensin Receptor Blockers (ARBs)

Mineralocorticoid receptor antagonists (MRA) are the third cornerstone of therapy for heart failure due to LV systolic dysfunction

RAAS Therapeutic Intervention Sites



Adapted from Stier CT et al. Heart Disease 2003; 5 (2): 102-118 and McMahon EG. Current Opinion in Pharmacology 2001; 1: 190-196.

Practical Recommendations for Heart Failure Treatment:
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— SPIRONOLACTONE—

Spironolactone – Which Dose?
- Starting dose: 25 mg od or on alternate days
- Target dose: 25–50 mg od

Eplerenone
- Starting dose: 25 mg od
- Target dose: 25-50 mg od

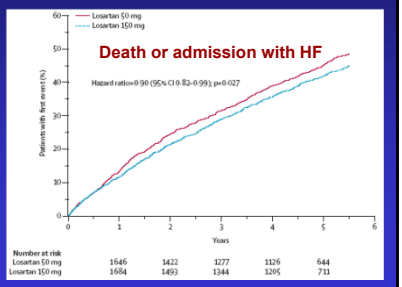
Angiotensin Receptor Blockers (ARBs) – why and when

- ELITE II – Losartan 50-75mg, (?150mg)
- Val-HeFT – Valsartan 160mgbd
- CHARM – Candesartan 32mg od

Effects of high-dose versus low-dose losartan on clinical outcomes in patients with heart failure (HEAAL study): a randomised, double-blind trial

Marvin A Konstam, James D Neaton, Kenneth Dickstein, Helmut Drexler,* Michel Komajda, Felipe A Martinez, Gunter A J Riegger, William Malbecq, Ronald D Smith, Sonali Guptha, Philip A Poole-Wilson, † for the HEAAL Investigators‡

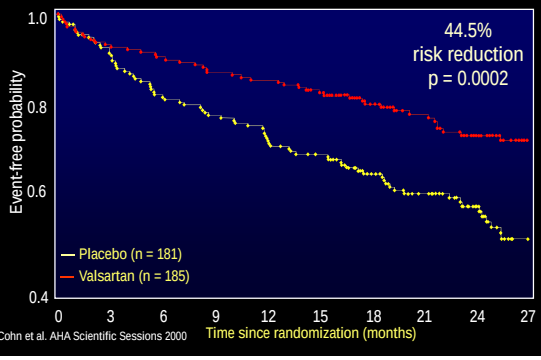
3856 pts. II-IV HF
EF<0.40
Intolerant to ACE



Lancet 2009;374:1840-48

Primary endpoint: greatest benefits in patients not on ACE inhibitor therapy

Combined all-cause mortality / morbidity

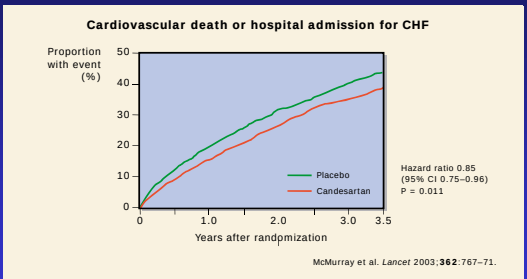


Cohn et al. AHA Scientific Sessions 2000

Valsartan Heart Failure Trial

- Chronic stable HF patients (NYHA II-III)
- Valsartan added to usual heart failure therapy (ACEi; diuretics; digoxin; β blockers)
  - 5,010 patients
  - 302 centers in 16 countries

CHARM Added: Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity

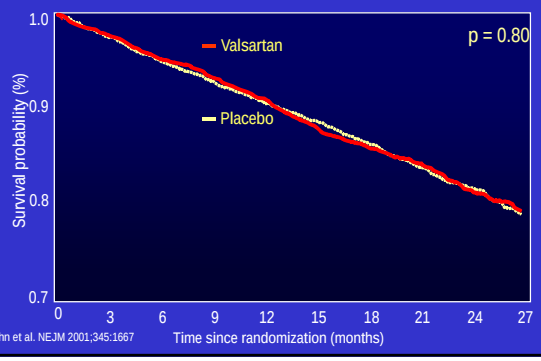


McMurray et al. *Lancet* 2003;**362**:767–71.

15% RRR in CV death or hospitalisation for HF

Lancet Sept 2003:362

Val-HeFT survival curves

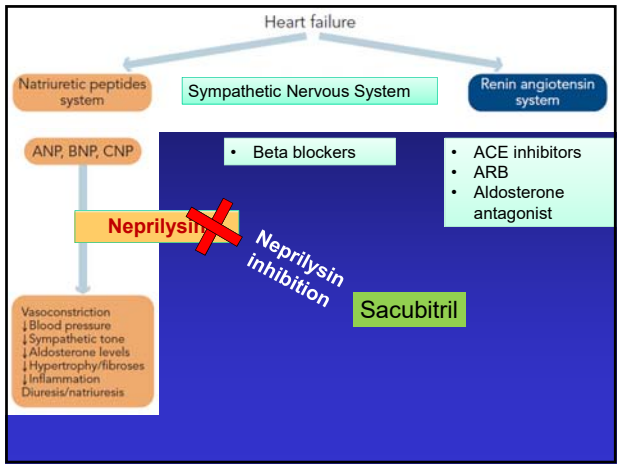


Cohn et al. NEJM 2001;345:1667

Use Angiotensin Receptor Blocker if unable to tolerate an ACEI

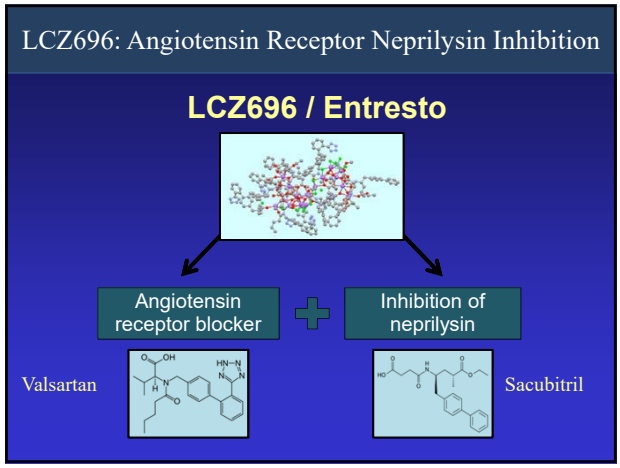
Let us Summarise - what we have learnt so far

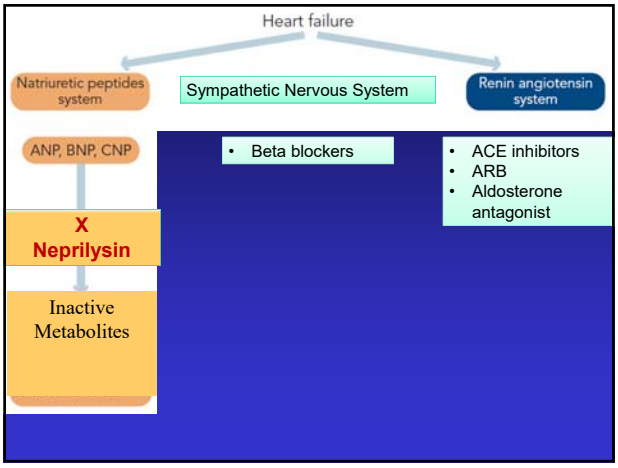
- ACEI or ARB if unable to tolerate an ACEI – 1st cornerstone
- Beta blockers – 2nd cornerstone
- Spironolactone/Eplerenone – 3rd cornerstone
- Endogenous Vasoactive Peptides
- SGLT2 inhibitors

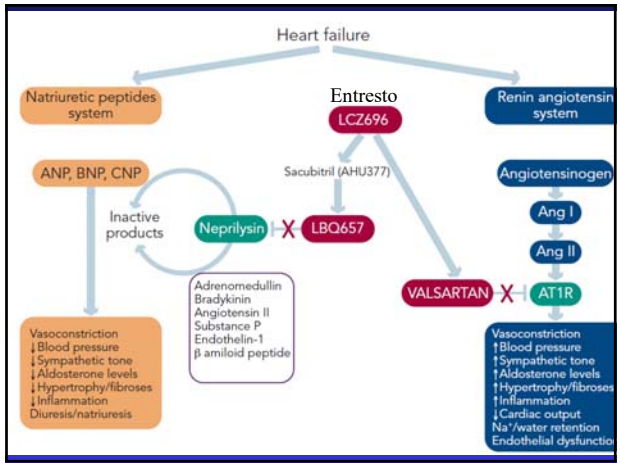


Tageting Endogenous Vasoactive Peptides That Counter Maladaptive Mechanisms in Heart Failure

LCZ696: Angiotensin Receptor Neprilysin Inhibition







The NEW ENGLAND JOURNAL of MEDICINE

CONCLUSIONS

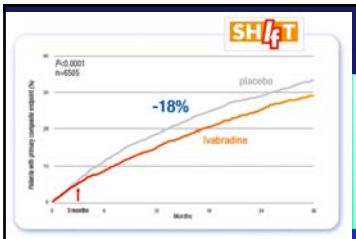
LCZ696 was superior to enalapril in reducing the risks of death and of hospitalization for heart failure. (Funded by Novartis; PARADIGM-HF ClinicalTrials.gov number, NCT01035255.)

20% relative risk reduction over median 27 months

Sacubitril valsartan for treating symptomatic chronic heart failure with reduced ejection fraction

NICE technology appraisal guidance [TA388] Published date: 27 April 2016

SHIFT



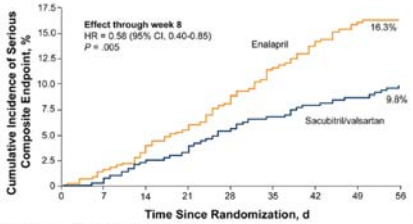
Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study
Karl Swedberg,

6558 patients
EF < 35% (isch. non isch.)
Class II-IV
Heart rate ≥ 70/min
Ivabradine 7.5mg BD vs Placebo

Swedberg et al Lancet 2010;376:875

PIONEER-HF: ARNI vs ACEi for Acute HF[1]

Composite of Death, HF Readmission, LVAD, and Listing for Cardiac Transplant[a]



PeerView.com

Drug Safety Update

MHRA

Latest advice for medicines users

The monthly newsletter from the **Medicines and Healthcare products Regulatory Agency** and its independent advisor the **Commission on Human Medicines**

Volume 8, Issue 5, **December 2014**

Contents

The NEW ENGLAND JOURNAL of MEDICINE

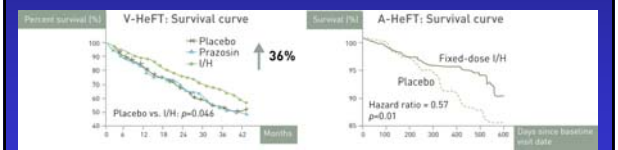
SEPTEMBER 18, 2014

Ivabradine in Stable Coronary Artery Disease without Clinical Heart Failure

Kim Fox, M.D., Ian Ford, Ph.D., Philippe Gabriel Steg, M.D., Jean-Claude Tardif, M.D., Michal Tendera, M.D., and Roberto Ferrari, M.D., for the SIGNIFY Investigators*

When To Use Nitrates + Hydralazine?

- Other HF patients unable to tolerate ACE inhibitors and ARBs (Class IIb, Level B)
- African-Americans with systolic dysfunction in addition to standard therapy (Class IIa, Level A)



Cohn et al. *N Engl J Med* 1986;314:1547-52. Taylor AL et al. *N Engl J Med* 2004;351:2049-57.

Arnold JMO, Liu P et al. *Can J Cardiol* 2006;22(1):23-45.

The SIGNIFY clinical trial[1] included a pre-specified subgroup analysis of 12,049 participants who had symptomatic angina. In this subgroup, there was a small but significant increase in the combined risk of cardiovascular death or non-fatal heart attack with ivabradine compared with placebo (3.4% vs 2.9% yearly incidence rates). The risk of bradycardia (17.9% vs 2.1%) and atrial fibrillation (5.3% vs 3.8%) was also increased in participants taking ivabradine compared with placebo.

Participants in the study were given higher doses of ivabradine than currently recommended in clinical practice. However, this did not fully explain the findings.

New advice for healthcare professionals:

When using ivabradine to treat the symptoms of chronic angina:

- only start ivabradine if the resting heart rate is at least 70 beats per minute
- do not prescribe ivabradine with other medicines that cause bradycardia, such as verapamil, diltiazem, or strong CYP3A4 inhibitors
- monitor patients regularly for atrial fibrillation. If atrial fibrillation occurs, carefully reconsider whether the benefits of continuing ivabradine treatment outweigh the risks
- consider stopping ivabradine if there is no or only limited symptom improvement after 3 months

We also remind you of the following:

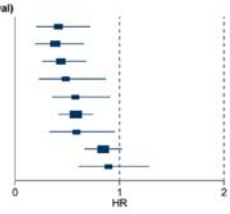
- Ivabradine is indicated to treat symptoms of chronic angina in patients unable to tolerate or with a contraindication to beta-blockers. It can also be used in combination with beta-blockers in patients for whom an optimal beta-blocker dose is not enough
- the recommended starting dose is 5 mg twice daily
- do not exceed the maximum maintenance dose of 7.5 mg twice daily
- down-titrate the dose if resting heart rate decreases persistently below 50 beats per minute or if the patient experiences symptoms of bradycardia. The dose can be down-titrated to 2.5 mg twice daily if necessary
- stop ivabradine treatment if the resting heart rate remains below 50 beats per minute or symptoms of bradycardia persist

MHRA Regulating Medicines and Medical Devices

Article citation: Drug Safety Update volume 8 issue 5, December 2014: A1.

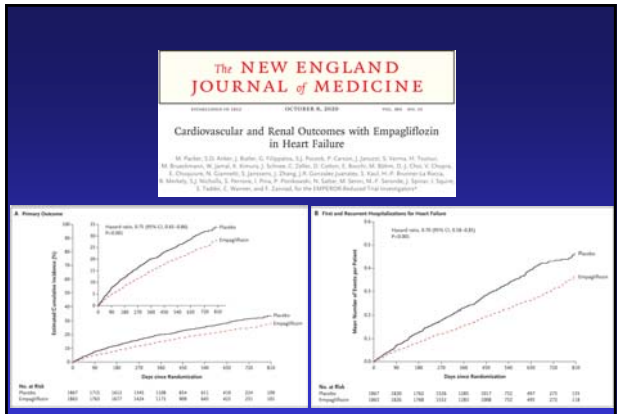
Guideline-Directed Medical Therapy Reduces HHF in HFrEF[1]

	HR (95% Credible Interval)
ACEI + BB + MRA + ivabradine + placebo	0.41 (0.21-0.70)
ARNI + BB + MRA vs placebo	0.38 (0.20-0.65)
ACEI + BB + MRA vs placebo	0.44 (0.27-0.67)
ARB + BB vs placebo	0.48 (0.24-0.86)
ACEI + MRA vs placebo	0.58 (0.34-0.95)
ACEI + BB vs placebo	0.58 (0.42-0.73)
BB vs placebo	0.58 (0.34-0.95)
ACEI vs placebo	0.84 (0.67-1.01)
ARB vs placebo	0.89 (0.61-1.27)

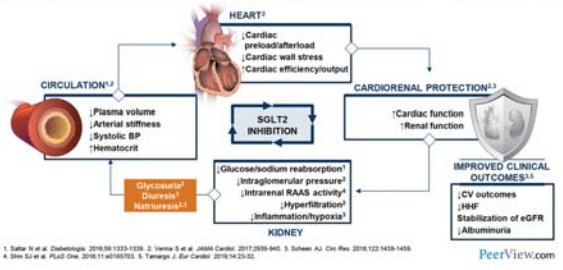


1. Komajda M et al. *Eur J Heart Fail*. 2018;20:1315-1322.

PeerView.com



SGLT2 Inhibition Improves Hemodynamic Parameters in Patients With T2DM, Leading to Cardiorenal Protection

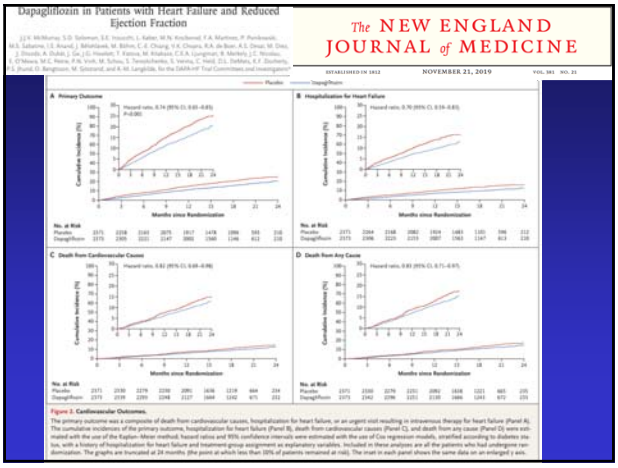


1. Satter N et al. *Diabetologia*. 2019;59:1333-1338. 2. Verma S et al. *JAMA Cardiol*. 2017;2939-940. 3. Scheen AJ. *Circ Res*. 2018;122:1459-1458. 4. Shin SJ et al. *PLoS One*. 2018;11:e0165753. 5. Tamargo J. *Eur Cardiol*. 2018;14:23-32.

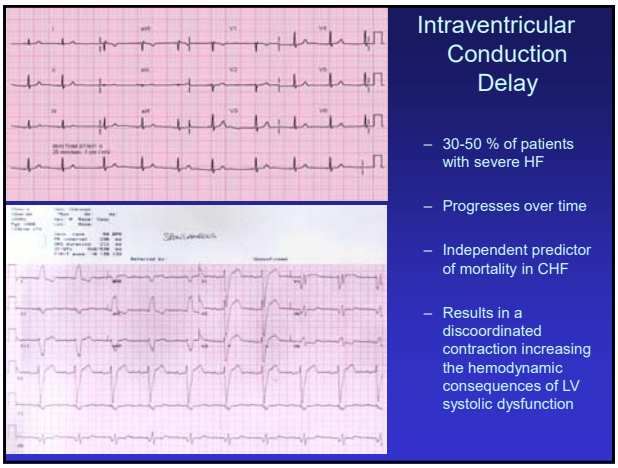
PeerView.com

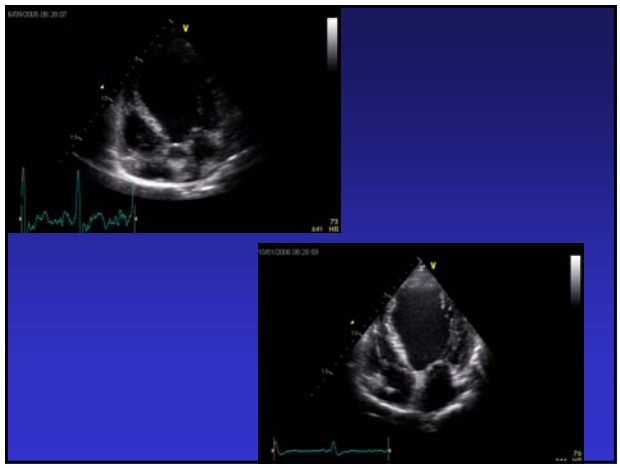
Drugs to avoid / stop in heart failure

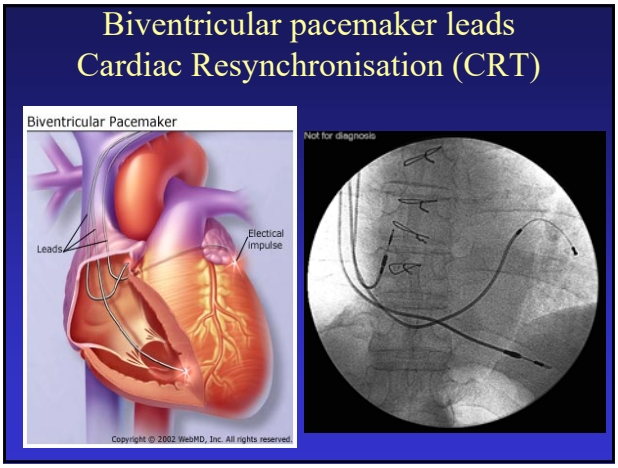
Drug	Effect
Calcium channel blockers (nifedipine, verapamil, diltiazem)	Negative inotropic effect
Thiazolidinediones (glitazones)	Cause fluid retention
Antiarrhythmic agents (especially flecainide, propafenone, disopyramide and calcium channel blockers, and less so for amiodarone, dofetilide and ibutilide) - dronedarone	Negative inotropic effect
Doxorubicin	Direct cardiotoxic effect
Nonsteroidal anti-inflammatory drugs, including cyclooxygenase-2 inhibitors (celecoxib)	Cause fluid retention
Steroids	**Causes fluid retention**

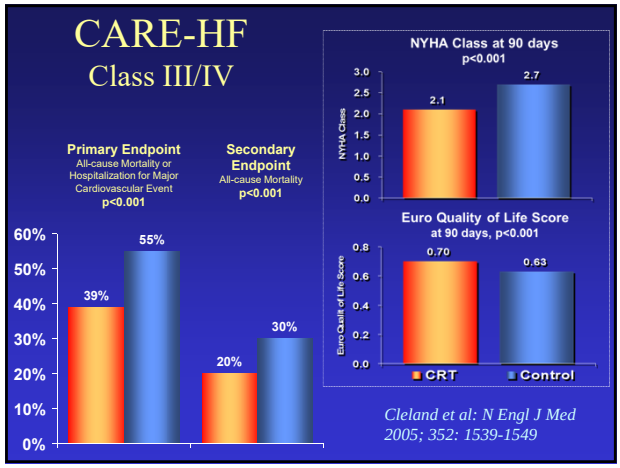


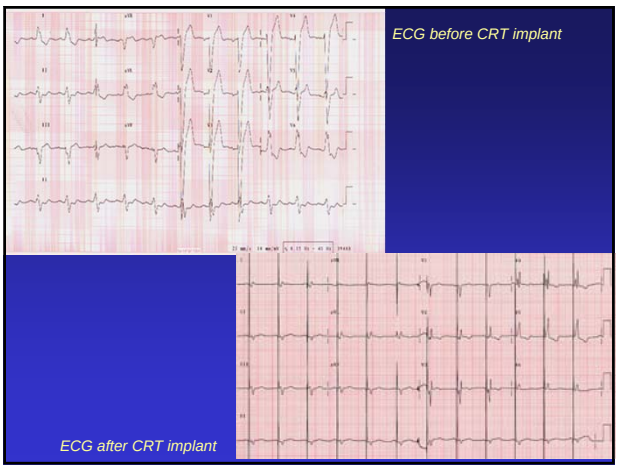
Device Therapy

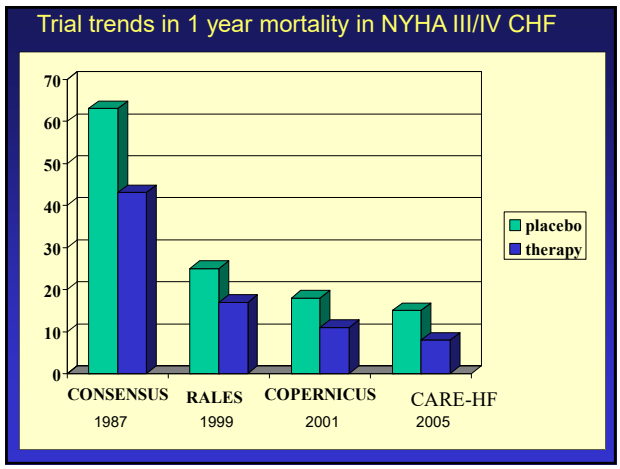

Intraventricular Conduction Delay
– 30-50 % of patients with severe HF
– Progresses over time
– Independent predictor of mortality in CHF
– Results in a discoordinated contraction increasing the hemodynamic consequences of LV systolic dysfunction




Biventricular pacemaker leads
Cardiac Resynchronisation (CRT)
Biventricular Pacemaker
Leads
Electical impulse
Copyright © 2002 WebMD, Inc. All rights reserved.
Not for diagnosis


CARE-HF
Class III/IV
Primary Endpoint
All-cause Mortality or Hospitalization for Major Cardiovascular Event
p<0.001
Secondary Endpoint
All-cause Mortality
p<0.001
60%
50%
40%
30%
20%
10%
0%
39%
55%
20%
30%
NYHA Class at 90 days
p<0.001
NYHA Class
3.0
2.5
2.0
1.5
1.0
0.5
0.0
2.1
2.7
Euro Quality of Life Score
at 90 days, p<0.001
Euro Qualit of Life Score
0.8
0.6
0.4
0.2
0.0
0.70
0.63
CRT
Control
Cleland et al: N Engl J Med 2005; 352: 1539-1549


ECG before CRT implant
ECG after CRT implant


Trial trends in 1 year mortality in NYHA III/IV CHF
70
60
50
40
30
20
10
0
CONSENSUS
1987
RALES
1999
COPERNICUS
2001
CARE-HF
2005
placebo
therapy

CRT/NICE guidelines

NICE National Institute for Health and Care Excellence

Implantable cardioverter defibrillators and cardiac resynchronisation therapy for arrhythmias and heart failure (review of TA95 and TA120)

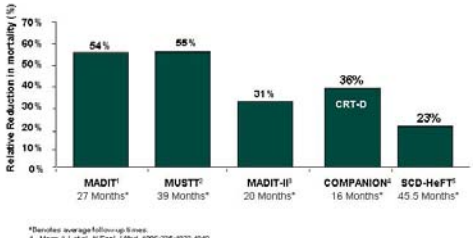
Issued: June 2014

NICE technology appraisal guidance 314

guidance.nice.org.uk/ta314

2014

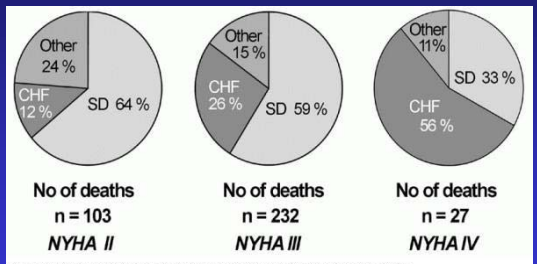
Reduction In All-cause Mortality with ICDs: Trials Summary



*Denotes average follow-up times.

1. Moss AJ, et al. *N Engl J Med*. 1996;335:1933-1940.
2. Buxton AE, et al. *N Engl J Med*. 1999;341:1882-1890.
3. Moss AJ, et al. *N Engl J Med*. 2002;346:877-883.
4. Bristow MR, et al. *N Engl J Med*. 2004;350:2140-2150.
5. Bardy GH, et al. *N Engl J Med*. 2005;352:225-237.

Mechanisms of death in CHF



Waagstein F Journal of Clinical and Basic Cardiology 2002; 5 (Issue 3): 215-223 ©

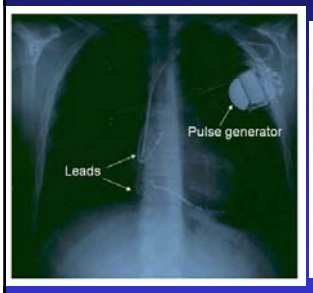
NICE National Institute for Health and Care Excellence

NICE 2014

	NYHA class			
QRS interval	I	II	III	IV
<120 milliseconds	ICD if there is a high risk of sudden cardiac death			ICD and CRT not clinically indicated
120–149 milliseconds without LBBB	ICD	ICD	ICD	CRT-P
120–149 milliseconds with LBBB	ICD	CRT-D	CRT-P or CRT-D	CRT-P
≥150 milliseconds with or without LBBB	CRT-D	CRT-D	CRT-P or CRT-D	CRT-P

LBBB, left bundle branch block; NYHA, New York Heart Association

Implantable Cardioverter Defibrillator



2. Typical of modern implantable cardioverter defibrillators (ICDs) and pacemakers are the Medtronic InSync II Marquis (left) and the InSync III (right).

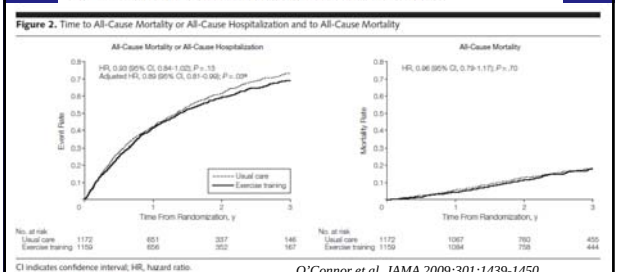
Lifestyle Changes

What	Why
•Eat a low-sodium, low-fat diet	•Sodium is bad for high blood pressure, causes fluid retention
•Lose weight	•Extra weight can put a strain on the heart
•Stay physically active	•Exercise can help reduce stress and blood pressure
•Reduce or eliminate alcohol and caffeine	•Alcohol and caffeine can weaken an already damaged heart
•Quit Smoking	•Smoking can damage blood vessels and make the heart beat faster
•Flu vaccination	

ORIGINAL CONTRIBUTION

Efficacy and Safety of Exercise Training in Patients With Chronic Heart Failure

HF-ACTION Randomized Controlled Trial



O'Connor et al. JAMA 2009;301:1439-1450

The modern HF patient

- Diuretic – if needed
- ACEI or ARB if ACEI not tolerated
- Entresto (Valsartan/Sacabutril)
- Beta blocker
- Spironolactone/Eplerenone
- SGLT2 inhibitors – with or without DM
- Hydralazine/nitrate (if ACEI/ARB intolerant -usually renal failure)
- Ivabradine (for heart rates >70 beats/min)
- Digoxin – selected patients
- CRTP or CRTD – selected patients
- Ventricular assist device – selected patients
- Cardiac transplant
- Cardiac rehabilitation

The last resort - Cardiac Transplantation

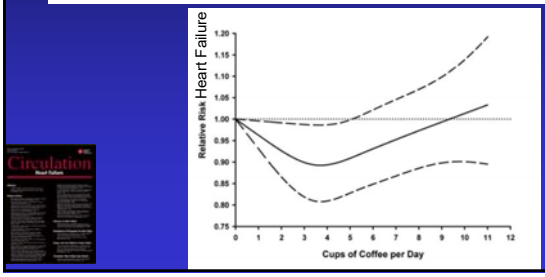
- Theoretically excellent treatment for patients with end-stage CHF
- Advantages:
  - Good medium-long-term outlook (up to 70% survival at 5years and 50% survival at 10 years)
- Problems:
  - 15-20% mortality in first year
  - Progressively fewer donors
  - Long list of disqualifying factors – therefore few patients suitable
  - Complex follow-up, immunosuppressive Rx
- <20 transplants carried out in Scotland last year

Coffee and Heart Failure

Habitual coffee consumption and risk of heart failure: a dose-response meta-analysis

Mostofsky E, Rice MS, Levitan EB, Mittleman MA.
Source: *Circ Heart Fail.* 2012 Jul 1;5(4):401-5. Epub 2012 Jun 26.
Abstract

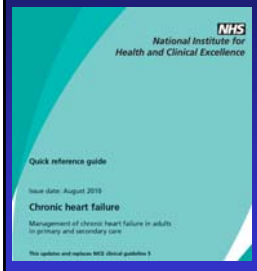
A meta-analysis was conducted of five independent prospective studies to assess the relationship between habitual coffee consumption and risk of heart failure. Results showed that moderate coffee consumption is inversely associated with risk of heart failure. Largest inverse association was found in those who consumed 4 servings a day

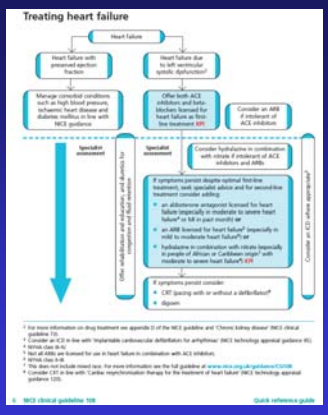


North Star Study
Heart Failure Congress May 2011

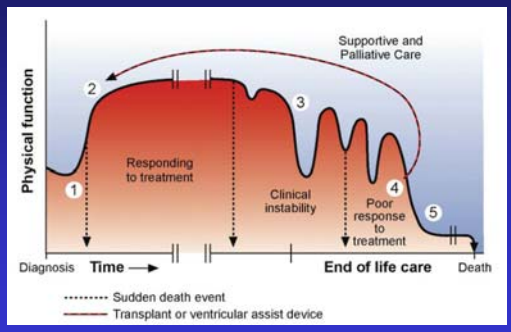
- 921 heart failure patients
- Clinically stable after attending a HF clinic
- Randomised to HFC or care by GP
- Primary endpoint of mortality or cardiovascular hospitaisation – no difference (p = 0.145)

Eur Heart J. 2013 Feb;34(6):432-42





Typical Course of Heart Failure



The End of Life Care Pathway

Managing Breathlessness
- Home oxygen
- Exclude infection
- Adaptive living
- Relaxation/deep breathing
- Oromorph
- OT/physio

Communication Issues
- Understanding of illness/prognosis
- When to seek help/call doctor
- Resuscitation issues
- Inactivate ICD but leave CRT
- Where to die – home, hospice or hospital?

Managing Oedema
- IV diuretics
- Skin care
- Footwear
- Support body image Δ

Pain
- Analgesia
- Palliative care

Managing Fatigue
- Nutrition/Dietician
- Daily activity/Exercise/Rehab.
- Sleep pattern
- Depression

Psychosocial issues
- Anxiety
- Depression
- Loneliness/social isolation
- Carer exhaustion/support
- Financial worries

CANCER
DIAGNOSTICS
HEART
LUNG
STROKE

NHS National End of Life Care Programme
Improving end of life care

NHS Improvement

End of life care in heart failure
A framework for implementation

The End of Life Care Pathway
- Discussions as end of life approaches
- Assessment, care planning and review
- Co-ordination of care
- Delivery of high quality services
- Care in the last days of life
- Care after death

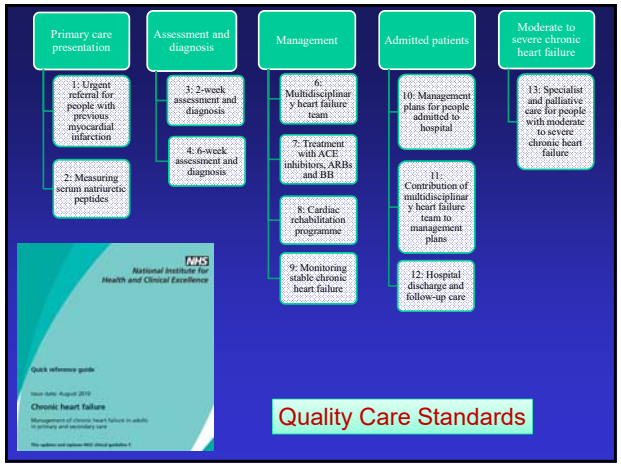
End of Life Care

- Gold Standards Framework
  www.goldstandardsframework.nhs.uk
- www.endoflifecareforadults.nhs.uk
- www.endoflifecare-intelligence.org.uk

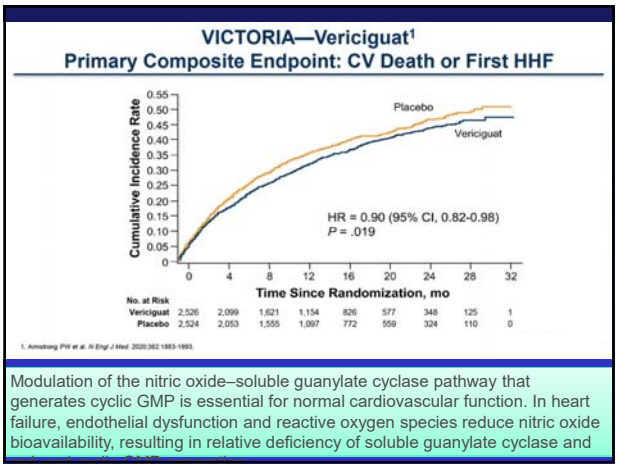
Signs, symptoms and markers of Advanced Heart Failure

- Marked Left Ventricular Dysfunction
- Arrhythmia
- Low sodium
- Frequent hospitalisations/HF reviews
- Resistant oedema

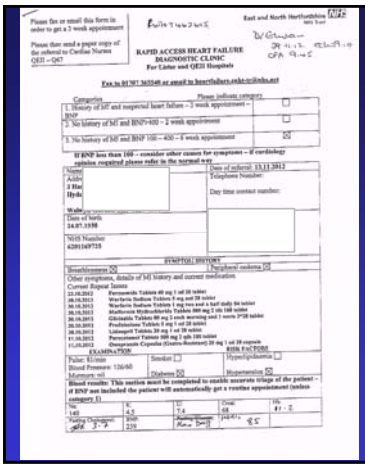
- Dyspnoea (NYHA 4)
- Abdominal discomfort
- Muscle cramp/neuropathic pain
- Cardiac cachexia
- Cognitive impairment
- Marked hypotension
- Worsening renal function
- Insomnia
- Multiple admissions



Quality Care Standards



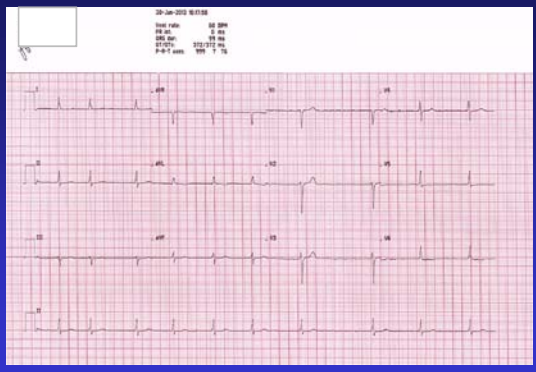
Modulation of the nitric oxide–soluble guanylate cyclase pathway that generates cyclic GMP is essential for normal cardiovascular function. In heart failure, endothelial dysfunction and reactive oxygen species reduce nitric oxide bioavailability, resulting in relative deficiency of soluble guanylate cyclase and



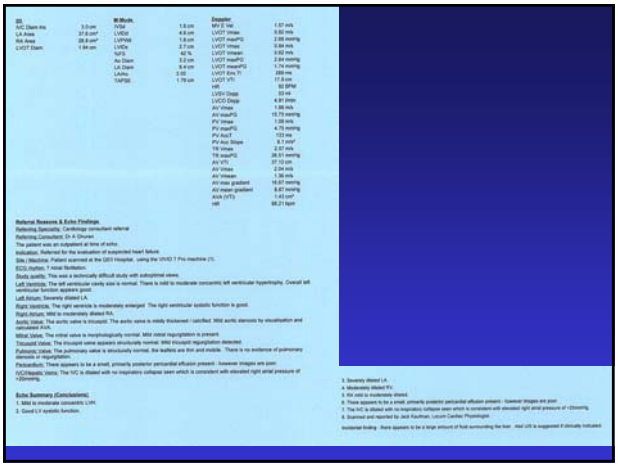
- Female 74 yrs.
- BMI 45
- SOBE
  - Stairs
  - 5 min walking
- No orthopnoea/pnd
- Chronic ankle swelling
- DM (II)
- ↑BP
- Atrial Fibrillation
- BNP 239 pg/ml

Summary

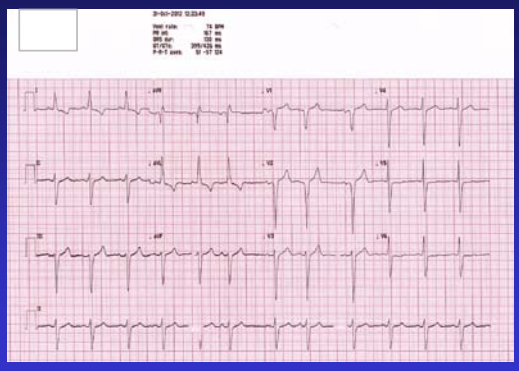
- Heart failure is a complex syndrome of symptoms and signs and requires an MDT approach in managing
- Coronary heart disease and hypertension are the commonest aetiologies
- Untreated it has a poor prognosis with high mortality and morbidity
- Pharmacological therapies are very effective and can improve prognosis with early and optimal treatment
- Device therapy (ICDs and CRTs) are increasingly utilised but reserved for selected patient groups
- A community based treatment is just as effective as secondary care in stable HF patients
- New drugs on the horizon may further improve prognosis

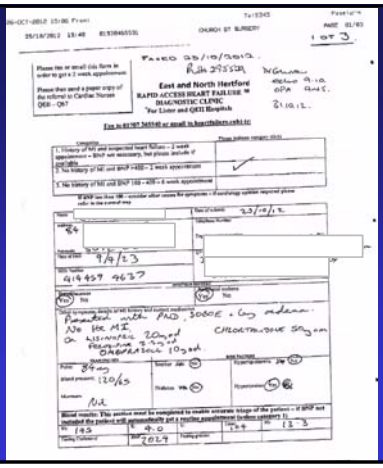


CASES



CASE 2

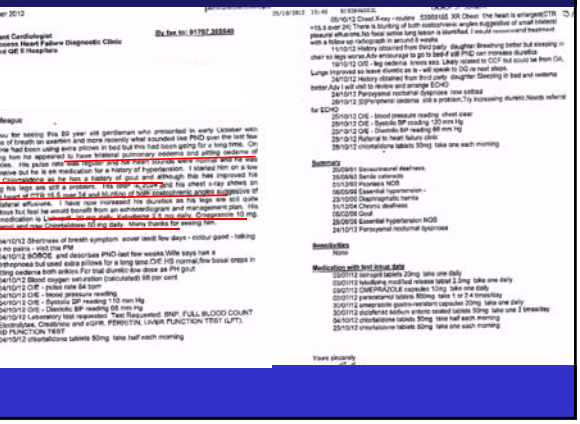


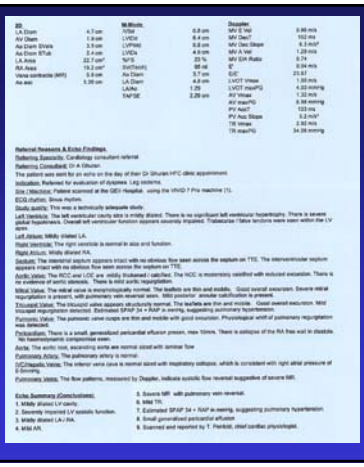


Male 89 yrs.

BNP 2024 pg/ml

Investigation/Test	Range	Units	Sample Collected 03 Oct 2012 13:53	16 Jul 2012	03 Jul 2012 13:35	23 Feb 2012	15 Dec 2010	05 Jul 2010
BNP	(0 - 100)	ng/L	*2024	-	-	-	-	-
C REACTIVE PROTEIN								
C Reactive protein	(0 - 5)	mg/l	-	*51	*182	-	-	-
CELL COUNT								
Hb	(13 - 17)	g/dL	13.3	-	*12.0	-	-	-
Hct	(0.4 - 0.5)	L/L	0.405	-	*0.357	-	-	-
MCH	(27 - 32)	pg	*32.4	-	*32.9	-	-	-
MCHC	(31.5 - 34.5)	%	32.8	-	33.6	-	-	-
MCV	(78 - 101)	fl	98	-	98	-	-	-
Platelets	(150 - 400)	10	*156	-	*133	-	-	-
RBC	(4.5 - 5.5)	10	*4.12	-	*3.65	-	-	-
WBC	(4 - 11)	10	8.5	-	9.2	-	-	-
EGFR CALCULATION								
eGFR (if patient is black)***		ml/min	-	-	-	-	56	-
eGFR (MDRD Calculation)***		ml/min	-	-	-	-	46	-
Serum Creatinine	(59 - 104)	umol/l	-	-	-	-	*127	-
ELECTROLYTES+CREAT								
Creatinine	(59 - 104)	umol/l	104	-	*156	-	*127	-
eGFR (if patient is black)***		ml/min	70	-	69	-	-	-
eGFR (MDRD Calculation)***		ml/min	58	-	57	-	-	-
Potassium	(3.6 - 5.2)	mmol/l	4.0	-	4.3	-	4.5	-
Sodium	(133 - 145)	mmol/l	145	-	141	-	141	-
ESR	(1 - 30)	mm/hour	-	-	28	-	*59	-
FERRITIN								
Ferritin	(20 - 298)	ng/ml	96	-	-	-	-	-
LIVER FUNCTION TEST								
Albumin	(35 - 52)	g/L	38	-	-	-	-	-
Alkaline Phosphatase	(30 - 115)	IU/l	94	-	-	-	-	-
ALT	(0 - 50)	IU/l	11	-	-	-	-	-
Bilirubin	(0 - 17)	umol/l	14	-	-	-	-	-
THYROID FUNCTION TEST								
Free T4	(7.8 - 14.4)	pmol/l	*18.0	-	-	-	-	-
Thyroid Stimulating Hormone	(0.3 - 5.6)	mIU/l	1.05	-	-	-	-	-
URIC ACID								
Urate	(0.1 - 0.425)	mmol/l	-	-	*0.442	-	-	-
URINE ALBUMIN (MICROALB)								
Random Urine Creatinine		mmol/l	-	-	-	6.5	-	17.1





Thank you very much for referring this 89-year-old gentleman to the Rapid Access Heart Failure Clinic. He was accompanied by his daughter who provided most of his history as Peter is deaf. He gives a two-month history of increasing shortness of breath on exertion, PND and orthopnoea. Since you commenced Chlorthalidone his symptoms have improved. You checked his BNP which was elevated at 2024.

His past medical history includes cataract operations, psoriasis, hypertension and gout. His current medication consists of Lisinopril 20 mg daily, Felodipine 2.5 mg daily, Omeprazole 10 mg daily, Chlorthalidone and Diclofenac sodium 50 mg tds. He lives with his wife and son and drinks up to one bottle of whiskey a week.

On examination pulse 76 beats per minute regular, JVP 4 cm, heart sounds S1 plus S2 plus a grade 3/6 pansystolic murmur at the apex that radiated to axilla. His chest was clear. He had moderate amount of leg oedema. His blood pressure was 142/86. His echocardiogram showed mildly dilated left ventricle (LVDD 6.4 cm, LVDS 4.9 cm) with severe global hypokinesia and significant LV systolic dysfunction. There was severe mitral regurgitation. The RVSP was estimated at 34 mmHg and the IVC was normal in size with normal inspiratory collapse. There was a small generalised pericardial effusion. ECG showed sinus rhythm with occasional supraventricular ectopics, left axis deviation and intraventricular conduction defect of left bundle-branch block pattern (QRS duration 130 milliseconds). He has T-wave inversion in leads I, aVL, V5 and V6 had assessed him.

His symptoms have improved, however he still has significant amount of leg oedema. Can I suggest to changing the Chlorthalidone to Furosemide 40 mg bd. We can always add Spironolactone at a later date if necessary. I would also suggest discontinuing his Felodipine which also can contribute to his ankle oedema. It was mentioned on his prescription that he is taking Diclofenac sodium and I would suggest changing this to an alternative analgesia as this can aggravate fluid retention. We need to also commence him on either Bisoprolol or Carvedilol and I will copy this letter to Heart Failure Team so that he can be reviewed in clinic with further optimisation of his medication.

I will review him again in two months' time and if he remains stable I think we can discharge him from clinic. Thanks very much for your referral and should you have any queries please do not hesitate to contact me.

Yours sincerely,

Dictated and verified by doctor but not signed.

Dr Azad Ghuran MB, ChB, MRCP, MD
Consultant Cardiologist

URGENT REFERRAL - Fax to 01707 365540 & Post

Rapid Access Heart Failure Diagnostic Clinic
QEII Hospital
Howlands
Welwyn Garden City
Herts AL7 4HQ

Dear Colleague

RE: [redacted] 52 Yrs

I would be most grateful if you could arrange to review this delightful 52 year old lady at your earliest convenience owing to her symptoms of breathlessness and ankle swelling. She says that her symptoms started suddenly on Friday 20th April and continued since. When I saw her the following Monday she was clearly having significant pitting oedema affecting both feet down to the lower legs on both sides. She was not breathless or tachypneic however she was complaining of shortness of breath as well as orthopnoea. She has no previous history of any heart or lung disease and she is usually fit and well. She is on no regular prescribed medication and has nothing significant in her past medical history. She does not smoke and does not drink.

On the day of examination I found her to be well, afebrile and not pale however her JVP was increased to 8 – 10 but her pulse on oximeter showed 99% oxygen saturation on air. She was slightly tachycardic at 110 bpm and her blood pressure was slightly up at 158/100. Her chest and cardiovascular system examination were all unremarkable. Subsequent to that I put her on a course of Furosemide 40 mg once a day which has been taking now for a fortnight feeling far much better with no further orthopnoea, significant improvement in her ankle swelling as well as her breathing.

The result of her BNP has now come back at 1390 with a slightly increased free T4 but normal TSH, normal U+&E's, Ferritin, FBC with a broadly normal LFT despite an increase in the Bilirubin of 70.

It is still not clear as to the causes of this lady to go into bilateral heart failure state and therefore I would highly appreciate your expert advice and opinion about her further management.

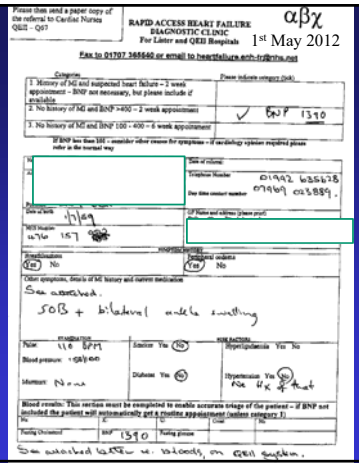
CASE 3

Thank you very much for referring this pleasant 52-year-old lady to the Rapid Access Heart Failure Clinic. She has been well in herself up until three weeks ago when she suddenly started getting increasingly short of breath on minimal exertion, ankle oedema, orthopnoea and paroxysmal nocturnal dyspnoea. There has been no history of chest pain. She also noticed that her heart rate had increased. Since you commenced furosemide 40 mg daily she feels a lot better. There is no history of any upper respiratory infection, arthralgia, rashes or connective tissue disease. Her only past medical history was adenoidectomy at 5 years of age.

She currently takes furosemide 40 mg daily. Her father has myasthenia gravis and is alive at age 80. Her mother is also alive at 80 and suffers with rheumatoid arthritis. She has a non-identical twin sister and an older sister who are both well. She does not smoke or drink alcohol. Systemic enquiry was unremarkable.

Examination: She was mildly icteric. Pulse 120 beats per minute and regular. JVP elevated at 6 cm. Heart sounds S1 plus S2. Her chest and abdomen were unremarkable. There was no ankle oedema. Her ECG showed a sinus tachycardia at a rate of 137 beats per minute. There was a **terminal** negative inflection in the P-wave in leads V1 suggesting left atrial enlargement. There was decreased R-wave progression across the precordial leads. She had normal axis.

Her echocardiogram showed a severely dilated left ventricle (LVDd 6.5 cm, LVDs 5.8 cm) with overall significant global hypokinesia. The left atrium was moderately dilated with a diameter of 4.1 cm and an area of 25 cm^2. The right ventricle was mildly enlarged with moderate function. The aortic valve was tricuspid. The mitral valve leaflet was morphologically normal and there was significant central mitral regurgitation present with pulmonary vein reversal seen. It is not clear whether this is primary or most likely functional in origin. There is mild tricuspid regurgitation and the RVSP was estimated at 36 mmHg. The inferior vena cava was normal in size with inspiratory collapse.


RAPID ACCESS HEART FAILURE DIAGNOSTIC CLINIC
For Lister and QEII Hospitals
Fax to 01707 365540 or email to heartfailure.enh-tr@nhs.net
αβχ
1st May 2012
BNP 1390
SOB + bilateral ankle swelling
Female 52 yrs.

This lady has a dilated cardiomyopathy with significant LV impairment and I have started her on ramipril 2.5 mg daily. I will appreciate if you can check her Us&Es in a week's time and increase her ramipril dose to 5 mg daily. Once on 5 mg I will appreciate if you can commence bisoprolol 1.25 mg daily. Both her ramipril and bisoprolol dose can slowly be titrated upwards keeping an eye on her Us&Es and blood pressure to the maximum tolerated dose of up to 10 mg daily. At a later stage I will add spironolactone. I have arranged a cardiomyopathy screen including thyroid function test, ferritin, B12, ACE level, lipids, glucose, CK and LDH amongst other routine biochemical tests. I will also arrange for her to have a coronary angiogram.

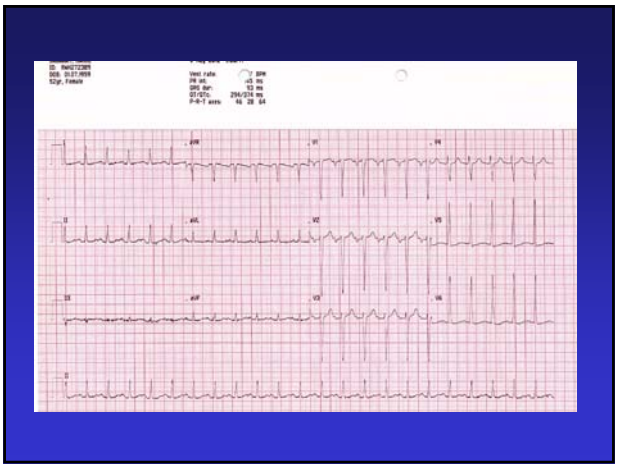
I will appreciate if you can forward me a copy of her chest X-ray report which was done at Cheshunt Community Hospital. I will arrange for her to have an ultrasound scan of her abdomen/liver. I will also arrange for her to have a cardiac MRI scan which may point to an underlying aetiology as well as provide information as to whether her mitral regurgitation is functional or primary in origin. I will ensure that her drug titration is monitored in our Heart Failure Clinic. I plan to review her again in four weeks' time. I will also book her angiogram when she next attends to ensure that she is a lot more stable and established on her medication.

Thanks very much for your referral and should you have any queries please do not hesitate to contact me.

Yours sincerely

Dictated and verified by Doctor but not signed

Dr Azad Ghuran MB ChB, MRCP, MD
Consultant Cardiologist



Clinic: 30/10/2013 (QEII Outpatients)
Typed: 01/11/2013

DRAFT

Diagnoses:

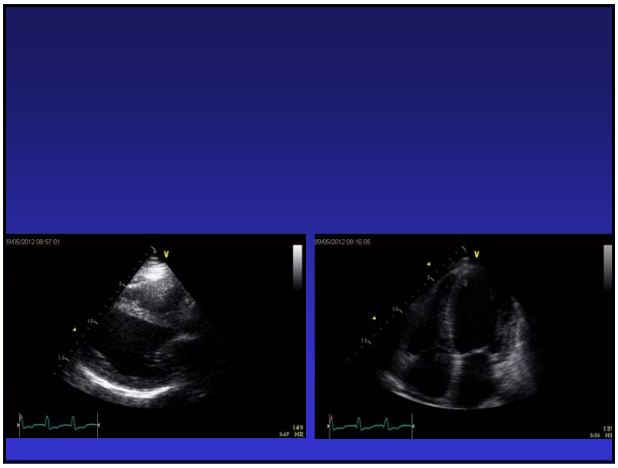
1. Previously dilated cardiomyopathy with significant LV impairment and severe functional regurgitation which has now recovered. Echocardiogram January 2013 showed normal LV cavity size with good LV systolic function with no significant valvular abnormalities
2. Cardiac MRI scan 12th June 2012 showed extensive fibrosis of the septum, inferolateral, lateral and basal-to-mid inferior walls
3. Normal alpha-galactosidase levels and creatinine kinase
4. Smooth unobstructed coronary arteries
5. Hyperlipidaemia total cholesterol previously 7 mmol/l now down to 5.2 mmol/l

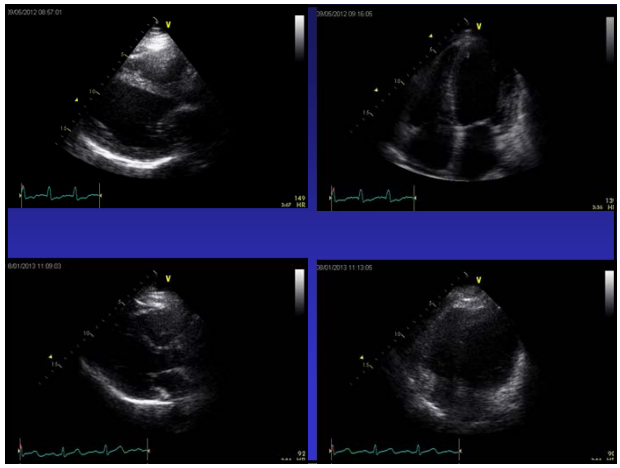
I reviewed Marie today in clinic. She remains well and asymptomatic from a cardiac point of view. Her pulse is 89 beats per minute and blood pressure 139/77.

Her current medication consists of ramipril 10 mg daily, bisoprolol 10 mg daily, atorvastatin 40 mg daily and spironolactone 25 mg daily. She is doing remarkably well compared to when she first presented and the main question at present is whether we should wean off any of her heart failure medication. I think it will be useful to repeat a cardiac MRI scan to see whether there has been resolution of fibrosis. If there is then I think we can consider weaning off medication, otherwise I will leave her medication unchanged. I plan to review her again in three months' time to go over the results of her repeat cardiac MRI scan.

Yours sincerely,

Dr Azad Ghuran MB ChB, MRCP, MD
Consultant Cardiologist





Date of Birth	01/07/1959	Weight kg	91
Referring Consultant	Dr. AV Ghuran	Surface Area m^2	2.00
Referring Hospital	Lister Hospital	Patient Type	NHS
Date of Study	12/06/2012	Date Of Report	14/06/2012

Indication Newly diagnosed DCM, unknown aetiology, significant LV impairment and MR on echo. CMR assessment.

Findings

Left ventricle: Raised indexed volumes. Moderate globally impaired LV function with impaired long axis function. Raised indexed mass although LV wall thickness normal (max wall thickness 10mm at basal septum in end-diastole).

Right ventricle: Normal indexed volumes and systolic function. No RV hypertrophy.

Valves: At least mild MR (by visual assessment) with 2 jets noted, most likely due to annular dilatation. Both leaflets appear mobile. The rest of the valves appear morphologically and functionally normal.

Other Findings: Mild biatrial dilatation. The aorta and pulmonary artery are of normal calibre. Normal pericardium, no pericardial effusion.

Gadolinium study: In the early phase after gadolinium injection, no LV/RV thrombus is seen. In the late phase there is extensive mid-wall gadolinium enhancement of the septum, and to a lesser extent, the inferior wall at basal to mid ventricular level. There is also more diffuse mid-wall enhancement in the inferolateral and lateral walls at basal and mid level.

Normal female ranges (RV ranges in brackets; see graphs for BSA indexed LV values)

	EDV (mL)	ESV (mL)	SV (mL)	EF (%)	Mass index (g/m^2)
LV	233	139	95	41	94
RV	151 (58-154)	52 (12-68)	99 (35-98)	66 (47-80)	

Conclusion

1. Dilated LV with moderately impaired global LV function.
2. At least mild MR, likely to be functional.
3. Extensive mid-wall fibrosis of the septal, inferior and lateral walls as described above.

In the absence of significant coronary artery disease, these findings are consistent with a DCM phenotype with extensive mid-wall fibrosis. In view of the pattern of enhancement and raised LV mass, Fabry's should be excluded.

Chronic Heart Failure: Diagnosis and Modern Management

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