Heart Failure

Definition of heart failure

HF is a clinical syndrome in which patients have the following features:

- Symptoms typical of HF
  (breathlessness at rest or on exercise, fatigue, tiredness, ankle swelling)

and

- Signs typical of HF
  (tachycardia, tachypnoea, pulmonary rales, pleural effusion, raised jugular venous pressure, peripheral oedema, hepatomegaly)

and

- Objective evidence of a structural or functional abnormality of the heart at rest
  (cardiomegaly, third heart sound, cardiac murmurs, abnormality on the echocardiogram, raised natriuretic peptide concentration)

Diagnosis

- According to the Working Group in Heart Failure, CHF is a syndrome where the diagnosis has the following essential components:
- A combination of:
  - Symptoms, typically breathlessness or fatigue
  - Cardiac dysfunction documented at rest
- The diagnosis is supported by:
  - Response to treatment directed towards heart failure

Incidence

- 4.8 million in the United States
- 400,000 new cases/year
- 20 million patients with asymptomatic LV dysfunction

Incidence continued

- 6-10% of patients over 65 y.o.
- #1 cause of hospital admission in patients over 65 y.o.
- Annual expenditure 20-40 billion/year

Mortality

- ♥ 250,000 patients die as a direct result of CHF per year

- ♥ 1-year mortality rate = 10%
- ♥ 5-year mortality = 50%

Contributors to Increased Incidence

- Improvements in:
  - Survival post-MI
  - Technologies (i.e.. PCI, stents etc.)
  - Medical Treatments for ischemic heart disease (statin, ACE-I, ASA)
  - Overall survival

Etiology of Chronic Heart Failure

- Coronary artery disease accounts for about 65%
- Non-ischemic Cardiomyopathy:
  - Idiopathic
  - Hypertension
  - Valvular Heart Disease
  - Thyroid
  - Toxic or drug-induced

Etiology of Acute Heart Failure

- ♥ Myocardial ischemia-infarction
- ♥ Ventricular systolic or diastolic dysfunction
- ♥ Mitral valve regurgitation
- ♥ Ventricular rupture
- ♥ Myocarditis
- ♥ Uncontrolled HTN
- ♥ Other PE, arrhythmia's, pulmonary HTN

Chronic Heart Failure

Systolic Failure

Diastolic Failure

Diastolic Heart Failure - Definition

- Signs and / or symptoms of CHF
- Normal or mildly reduced left ventricular systolic function (EF > 45%)
- Evidence of abnormal left ventricular relaxation, filling, diastolic distensibility and diastolic stiffness (age adjusted E/A ratio, DT, IVRT, pv-S/D, pvA)

European Study Group on Diastolic Heart Failure et al. Eur Heart J 1998

How Do You Find Patients With Diastolic Heart Failure?

- **Patients with hypertension** (25%) and especially if there is sign of left ventricular hypertrophy (90%)

- **Patients with diabetes** and especially in those with complications (neuropathy, nephropathy)

- **Patients with ischaemic heart disease** and angina and no previous myocardial infarction

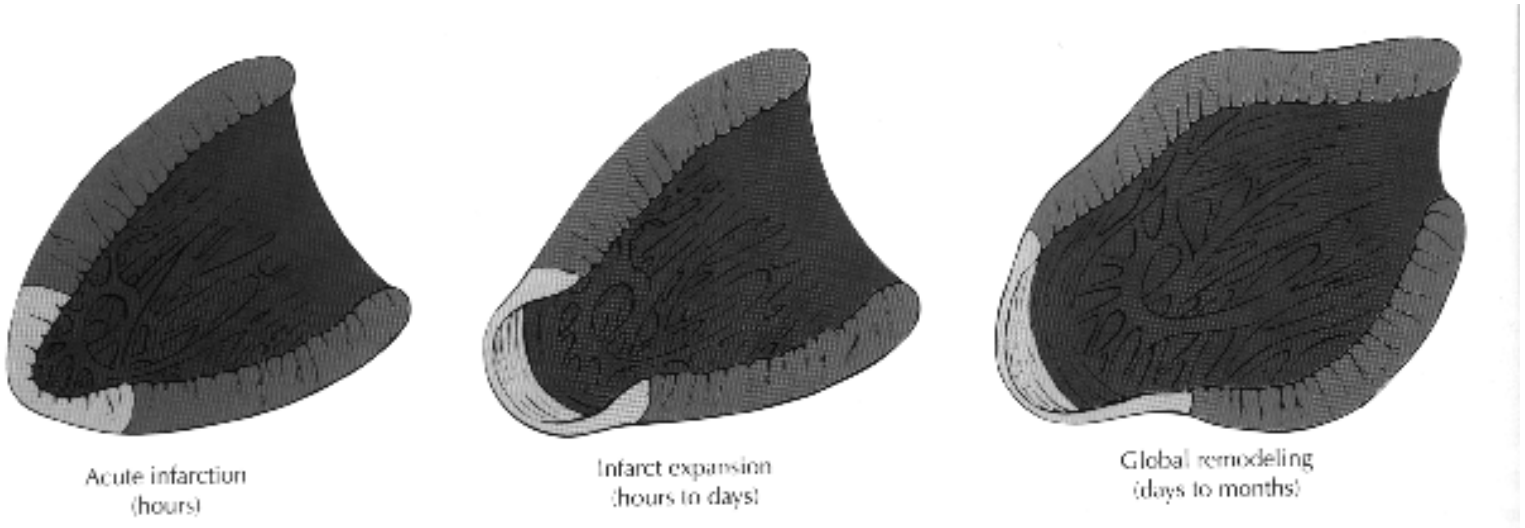
Epidemiological Aspects of Diastolic Heart Failure

- Symptoms of heart failure with normal left ventricular function is synonymous with diastolic heart failure
- Based on different community studies the prevalence of heart failure with normal systolic function varies between 30-50%

Strong Heart Study (Arizona) et al. Am J Cardiol 2000
Framingham Offspring Study et al. JACC 1999
Hillingdon Study (UK) et al. Eur Heart J 1999
Olmsted County (Minnesota) et al. Circulation 1998

Pathophysiology of Heart Failure: Left Ventricular Remodeling

Left-ventricular (LV) remodeling is defined as a change in LV geometry, mass and volume that occurs over a period of time



Common Symptoms of Heart Failure

- Dyspnea on exertion
- Paroxysmal nocturnal dyspnea
- Orthopnea
- Fatigue
- Lower extremity edema
- Cough, usually worse at night
- Nausea, vomiting, anorexia, ascites
- Nocturia
- Sleep disorders

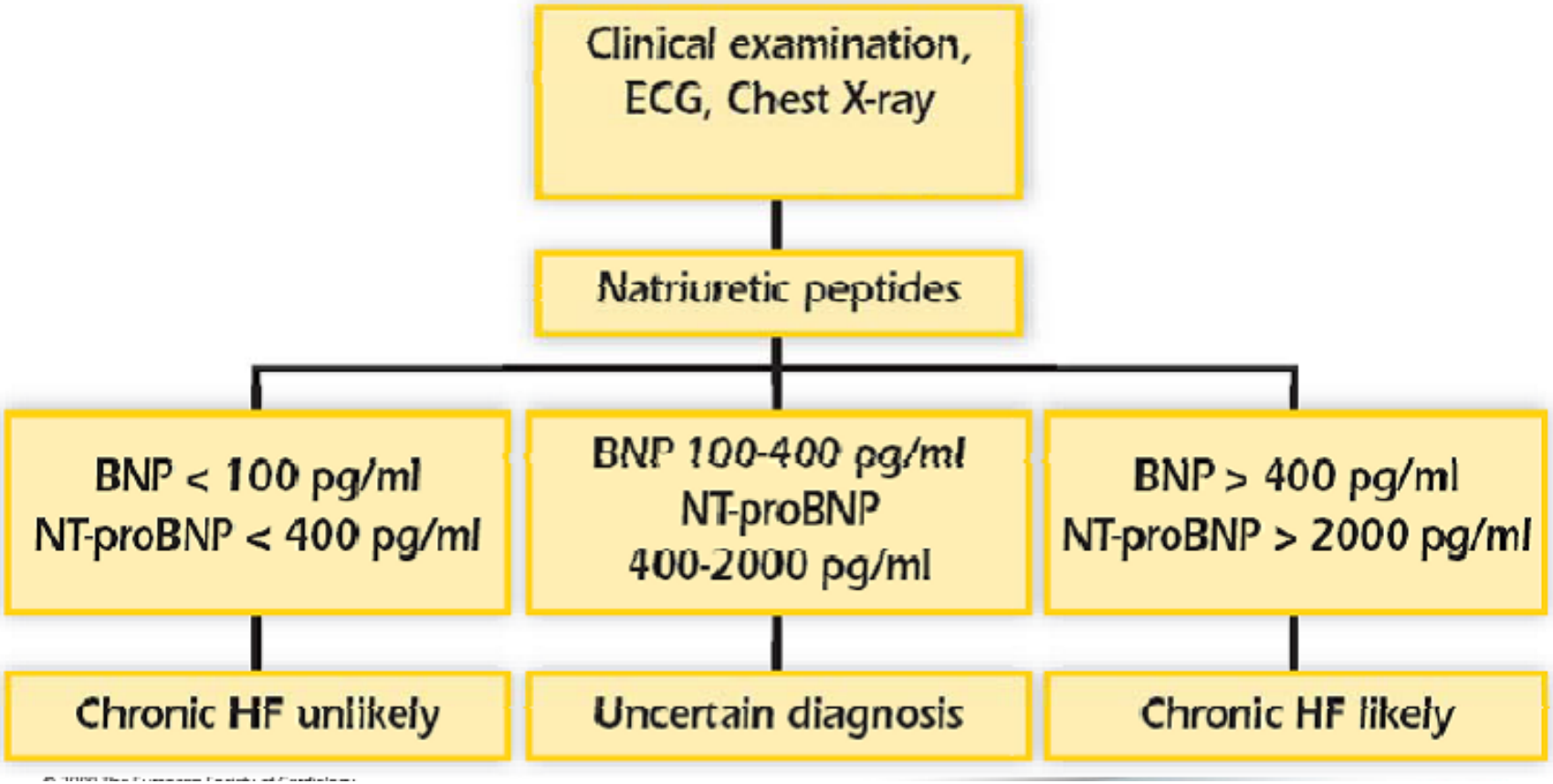
Common Physical Findings of Heart Failure

- Elevated jugular venous pressure
- Hepatojugular reflux
- Displaced apical impulse
- S3 gallop
- Pulmonary rales
- Hepatomegaly
- Peripheral edema
- Ascites
- Signs of cardiac cachexia

Key features of the clinical examination in patients with heart failure

Appearance	Alertness, nutritional status, weight
Pulse	Rate, rhythm, and character
Blood pressure	Systolic, diastolic, pulse pressure
Fluid overload	Jugular venous pressure Peripheral oedema (ankles and sacrum) hepatomegaly, ascites
Lungs	Respiratory rate Rales Pleural effusion
Heart	Apex displacement Gallop rhythm, third heart sound Murmurs suggesting valvular dysfunction

Flow-chart for the diagnosis of HF in untreated patients with symptoms suggestive of HF using natriuretic peptides



Tests for diagnosis of heart failure

- ECG
- **Echocardiography**
- Chest X-ray
- Blood count
- Blood chemistry
- Exercise test
- **Natriretic peptides (BNP)**
- Cardiac cath.

New York Heart Association Functional Classification

I	No limitation of physical activity, no symptoms with ordinary activities
II	Slight limitation, symptoms with ordinary activities
III	Marked limitation, symptoms with less than ordinary activities
IV	Severe limitation, symptoms of heart failure at rest

Killip classification

Designed to provide a clinical estimate of the severity of circulatory derangement in the treatment of acute myocardial infarction.

Stage I	No heart failure. No clinical signs of cardiac decompensation
Stage II	Heart failure. Diagnostic criteria include rales, S3 gallop, and pulmonary venous hypertension. Pulmonary congestion with wet rales in the lower half of the lung fields.
Stage III	Severe heart failure. Frank pulmonary oedema with rales throughout the lung fields
Stage IV	Cardiogenic shock. Signs include hypotension (SBP <90 mmHg), and evidence of peripheral vasoconstriction such as oliguria, cyanosis and sweating

Classification of HF by structural abnormality (ACC/AHA) or by symptoms relating to functional capacity (NYHA)

ACC/AHA Stages of HF Stage of heart failure based on structure and damage to heart muscle		NYHA Functional Classification Severity based on symptoms and physical activity	
Stage A	At high risk for developing HF. No identified structural or functional abnormality; no signs or symptoms.	Class I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnoea.
Stage B	Developed structural heart disease that is strongly associated with the development of HF, but without signs or symptoms.	Class II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnoea.
Stage C	Symptomatic HF associated with underlying structural heart disease.	Class III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity results in fatigue, palpitation, or dyspnoea.
Stage D	Advanced structural heart disease and marked symptoms of HF at rest despite maximal medical therapy.	Class IV	Unable to carry on any physical activity without discomfort. Symptoms at rest. If any physical activity is undertaken, discomfort is increased.
ACC = American College of Cardiology; AHA, American Heart Association. Hunt SA et al. Circulation. 2005;112:1825-1852.		NYHA = New York Heart Association. The Criteria Committee of the New York Heart Association. Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels. 9th ed. Boston, Mass: Little, Brown & Co; 1994:253-256	

ACC / AHA Guidelines

Stage A
High risk for CHF
No structural heart disease
or CHF symptoms

Stage B
Structural heart disease
No CHF symptoms

Stage C
Structural heart disease
Prior or current CHF symptoms

Stage D
Refractory CHF requiring special interventions

Stage A

High risk for CHF
No structural
heart disease
or CHF symptoms

eg, Patients with:
hypertension, coronary artery disease, diabetes mellitus,
or patients using cardiotoxins or with CM

Therapy:
treat hypertension, encourage smoking cessation, treat lipid disorders, encourage regular exercise, discourage alcohol intake and illicit drug use, ACE inhibition in appropriate patients

Stage B

Structural heart disease
No CHF symptoms

eg, Patients with:
previous MI
LV systolic dysfunction
asymptomatic valvular disease

Therapy:
All measures under Stage A,
ACE inhibitors in appropriate patients, b blockers in appropriate patients

Stage C

Structural heart disease
Prior or current
CHF symptoms

eg, Patients with:
known structural
heart disease,
shortness of breath
and fatigue
reduced exercise tolerance

Therapy:
All measure under stage A,
drugs for routine use
(diuretics, ACE inhibitors,
b blockers, digitalis),
dietary salt restriction

Stage D

Refractory CHF requiring special interventions

eg, Patients who have marked symptoms at rest despite maximal medical therapy (eg, those who are recurrently hospitalised or cannot be safely discharged from the hospital without specialised interventions)

Therapy:
All measures under Stages A, B and C, mechanical assist devices, heart transplantation, continuous iv inotropic infusions for palliation, hospice care

Conditions associated with a poor prognosis in HF

Demographics	Clinical	Electrophysiological	Functional/Exertional	Laboratory	Imaging
Advanced age*	**Hypotension***	**Tachycardia**	**Reduced work,**	**Marked elevation of BNP/NT pro-BNP***	**Low LVEF***
Ischaemic aetiology*	**NYHA Functional Class III-IV***	**Q Waves**	**Low peak VO2***	**Hyponatraemia***	
Resuscitated sudden death*	**Recent HF hospitalization***	**Wide QRS***		**Elevated troponin***	
		LV hypertrophy		**Elevated biomarkers, neurohumoral activation***	
		Complex ventricular arrhythmias*			
Poor compliance	Tachycardia	Low heart rate variability	Poor 6 min walk distance	Elevated creatinine/BUN	Increased LV volumes
Renal dysfunction	Pulmonary rales	T-wave alternans	High VE/VCO2 slope	Elevated bilirubin	Low cardiac index
Diabetes	Aortic stenosis	Atrial fibrillation	Periodic breathing	Anaemia	High left ventricular filling pressure
Anaemia	Low body mass index			Elevated uric acid	Restrictive mitral filling pattern, pulmonary hypertension
COPD	Sleep related breathing disorders				Impaired right ventricular function
Depression					

ACE inhibitors

- An ACE inhibitor is recommended in all patients with symptomatic HF and an EF ≤40%
- Treatment with an ACE inhibitor improves LV function, patient well-being, reduces hospital admission for worsening HF and increases survival

Class of recommendation I, level of evidence A

- In hospitalised patients, treatment should be initiated before discharge

ACE Inhibitors: ESC Guidelines

- ACE inhibitors are recommended as first-line therapy in patients with a reduced LV systolic function (LVEF < 40-45%)
- In the absence of fluid retention ACE inhibitors should be given first, in the presence of fluid retention together with diuretics
- ACE inhibitors should be uptitrated to the dosages shown to be effective in large trials
- They should not be titrated based on symptomatic improvement

Management: Angiotensin-Converting Enzyme Inhibitors

- ACE inhibitors suppress conversion of angiotensin I to angiotensin II
- Benefits of ACE inhibitors
  - Reduce cardiac hypertrophy
  - Attenuate ventricular remodeling post MI
  - Cause peripheral vasodilation
  - Decrease sympathetic tone
  - Enhance activity of kinin

Clinical Use Of ACE Inhibitors

- ♥ Recommended for all patients with CHF and systolic dysfunction
- ♥ Recommended for patients with systolic dysfunction and no symptoms of CHF
- ♥ Prevents CHF in patients with preserved LV (EF > 40%) and CAD or risk factors (HOPE Trial)

Clinical Use Cont . . .

- Initiation of ACE inhibitor - Therapy should be initiated with low doses to avoid excessive hypotension

- Target doses - Doses should be slowly titrated to achieve targeted dose used in major clinical trials

ACE Inhibitors: Adverse Effects

- Severe hypotension, syncope, renal insufficiency, hyperkalemia and angioedema
- Some adverse effects can be avoided by initiating and titrating by low doses. Need to monitor BP, lytes and renal function
- Most frequent side effect is cough (5-15%) - cross sensitivity likely

ACE Inhibitors Cont . . .

- Contraindications
  - Allergic reaction
  - Pregnancy
  - Very low BP (<80mmHg)
  - Creatinine > 3
  - Bilateral renal artery stenosis
  - Potassium > 5.5

Angiotensin receptor blockers (ARBs)

- An ARB is recommended in all pts. with HF and an EF ≤40% who:
  - remain symptomatic despite optimal Rx with an ACE inhibitor and β-blocker
  - as an alternative in pts. intolerant of an ACE inhibitor
- Unless pts. are treated with an aldosterone antagonist
- Treatment with an ARB improves LV function, patient well-being and reduces hospital admission for worsening HF

Class of recommendation I, level of evidence A

- Treatment reduces the risk of CV death

Class of recommendation IIa, level of evidence B

- In hospitalised pts., treatment with an ARB should be initiated before discharge

Angiotensin Receptor Blockers (ARBs)

- ARBs could be considered in patients who do not tolerate ACE inhibitors
- It has been proven that they are as effective as ACE inhibitors in morbidity reduction
- In addition to ACE inhibition ARBs improve symptoms and reduce hospitalisations for CHF
- The addition of ARBs to ACE inhibition and β blockade can be recommended at present.

β-blockade

- A β-blocker should be used in all patients with symptomatic HF and an EF ≤40%
- β-Blockade improves ventricular function and patient well-being, reduces hospital admission for worsening HF and increases survival

Class of recommendation I, level of evidence A

- In hospitalised patients, treatment with a β-blocker should be initiated cautiously before discharge

β Blockade in CHF - ESC Guidelines

- β blocking agents are recommended for the treatment of all patients with stable mild, moderate and severe CHF from ischaemic and non-ischaemic origin… on standard treatment including ACE inhibition and diuretics

- β blocking agents are recommended in patients with LV dysfunction with/without CHF post-MI for survival benefit

ACC / AHA Practice Guidelines: β blockers

- β adrenergic blockade in all stable CHF patients, unless contraindicated
- Patients should have no or minimal evidence of fluid retention and should not have required treatment recently with an intravenous positive inotropic agent

Benefit Of Beta Blockers

- ♥ Improve symptoms and clinical status
- ♥ Increase LV ejection fraction
- ♥ Little effect on exercise tolerance
- ♥ Reduce frequency of hospitalizations for heart failure
- ♥ Decrease mortality

Clinical Use Of Beta Blockers

- Recommended for patients with NYHA class II-IV
- General contraindications:
  - Decompensated heart failure
  - Severe claudication
  - Bronchospasm
  - Advanced heart block
  - Use with caution if patient requires inotropes for support of circulatory function

Clinical Use Cont . . .

- ♥ Start at very low dose with gradual increments (doubling every 2-4 weeks)
- ♥ Abrupt withdrawal can lead to dramatic deterioration

- ♥ Patient education paramount

Beta-Blockers: Adverse Effects

- ♥ Hypotension
- ♥ Bradycardia
- ♥ Worsening heart failure

Aldosterone antagonists

- The addition of an aldosterone antagonist is recommended in all patients with an EF ≤35%, severe symptomatic HF without hyperkalaemia or significant renal dysfunction

- Aldosterone antagonists reduce hospital admission for worsening HF and increase survival when added to existing therapy, including an ACE inhibitor

Class of recommendation I, level of evidence B

- In such hospitalised patients, treatment with an aldosterone antagonist should be initiated before discharge

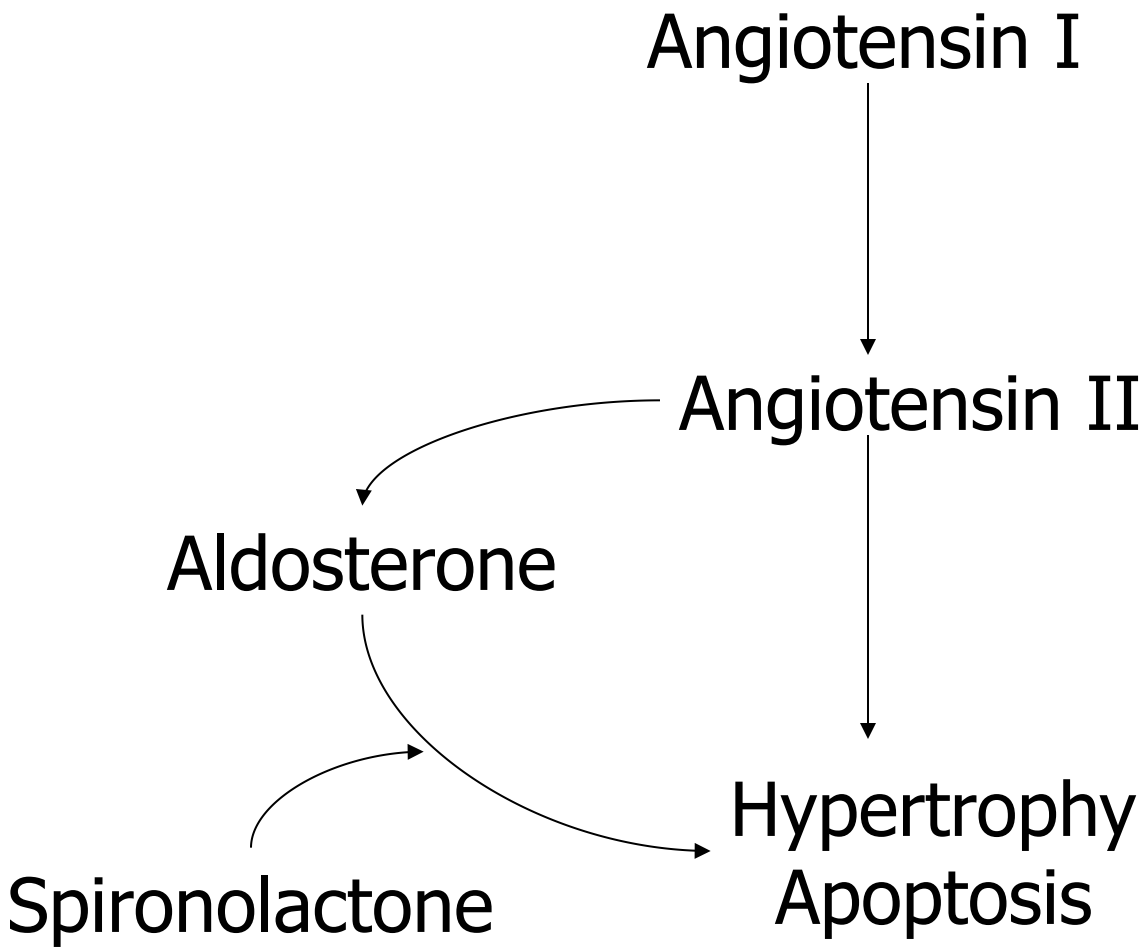
Spironolactone and eplerenon in Heart Failure: ESC Guidelines

Aldosterone antagonism is recommended in advanced CHF (NYHA III and IV) in addition to ACE inhibition to improve survival and morbidity

Aldosterone Antagonists

- ♥ Angiotensin II causes aldosterone production in the adrenal cortex
- ♥ Acts on the cortical collecting tubules to conserve sodium

- ♥ Originally thought to be blocked by ACE inhibitors. Now known that ACE I does not suppress production


Angiotensin I
Angiotensin II
Aldosterone
Hypertrophy
Apoptosis
Spironolactone

Aldosterone Antagonists

- ♥ Potassium-sparing diuretics
- ♥ Compete with aldosterone for receptor sites in the distal renal tubules
- ♥ Increase sodium and water excretion while conserving potassium and hydrogen ions
- ♥ Spironolakton and elprenenon

Aldosterone Antagonist

- Consensus Guidelines:
  - Use in Class III and IV heart failure
  - Should be given low dose

  (12.5mg - 25mg daily)

Aldosterone Antagonists: Averse Effects

- Arrhythmia, nervousness, dizziness, fatigue, rash, headache, breast tenderness, enlargement of breast in males, sexual dysfunction, increased hair growth in females
- May decrease effects of anticoagulants
- Use with caution in renal insufficieny

Digitalis Glycosides

- Cardiac glycosides are recommended in atrial fibrillation and symptomatic CHF in order to improve cardiac function and symptoms
- A combination of digitalis and beta blockade appears superior to either agent alone
- In sinus rhythm digoxin may improve the clinical status in persisting CHF symptoms due to LV systolic dysfunction

Management: Digitalis

- Digitalis glycosides inhibit sodium-potassium adenosine triphosphatase. Inhibition of this enzyme in cardiac cells results in an increase in the contractile state of the heart
- Benefits of digitalis may be related to enzyme inhibition in noncardiac tissue

Clinical Use: Digitalis

- Therapy is initiated at dose of .25mg daily. Lower doses such as .125mg daily or every other day, particularly if the patient is elderly or has impaired renal function

- Use with caution in patients with significant sinus or atrioventricular block
- Not indicated for stabilization of acute decompensated heart failure

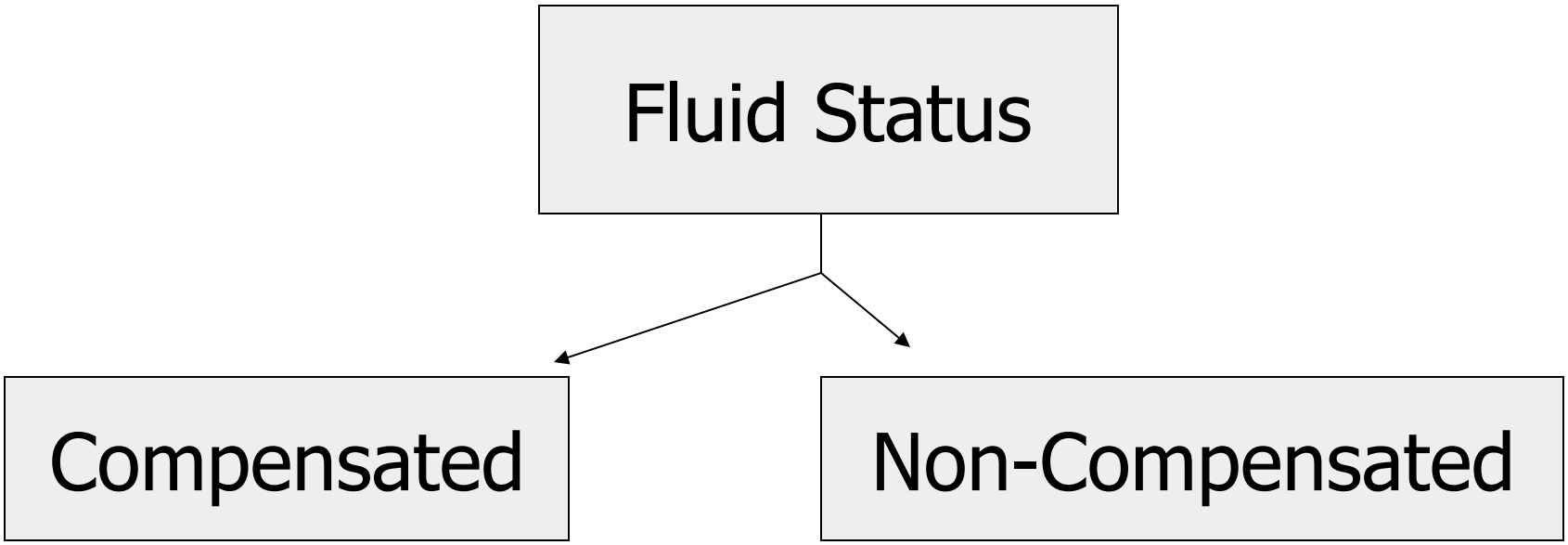
Digitalis: Adverse Effects

- ♥ Cardiac arrhythmia
- ♥ Gastrointestinal symptoms
- ♥ Neurologic complaints

- ♥ Side effects are usually associated with levels >2ng/ml

Management

Treatment: General Measures



Diuretics

- Diuretics are recommended in patients with clinical signs or symptoms of congestion
- Diuretics provide relief from the symptoms and signs of pulmonary and systemic venous congestion
- Diuretics cause activation of the renin-angiotensin-aldosterone system and should be used in combination with an ACE inhibitor/ARB

Class of recommendation I, level of evidence B

Adverse Effects: Loop Diuretics

- ♥ Electrolyte imbalance
- ♥ Higher incidence of mortality
- ♥ Hyperuricemia
- ♥ Ototoxicity
- ♥ Glucose intolerance

Lifestyle Measures

- ♥ Sodium restriction (2G/day)
- ♥ No salt substitutes
- ♥ Daily weight
- ♥ Fluid restriction

Lifestyle Measures Cont . . .

- Exercise
  - Avoid heavy lifting
  - Avoid temperature extremes

Class I recommendations for drugs in patients with symptomatic systolic dysfunction

ACE inhibitor	All patients*	Class I Level A
ARB	ACE intolerant/persisting signs or symptoms on ACEI/B-blokade*	Class I Level A
B-Blocker	All patients*	Class I Level A
Aldosterone antagonist	Severe symptoms on ACEI*	Class I Level A
Diuretic	All patients with signs or symptoms of congestion	Class I Level B

***unless contraindications or not tolerated**

Management: Devices

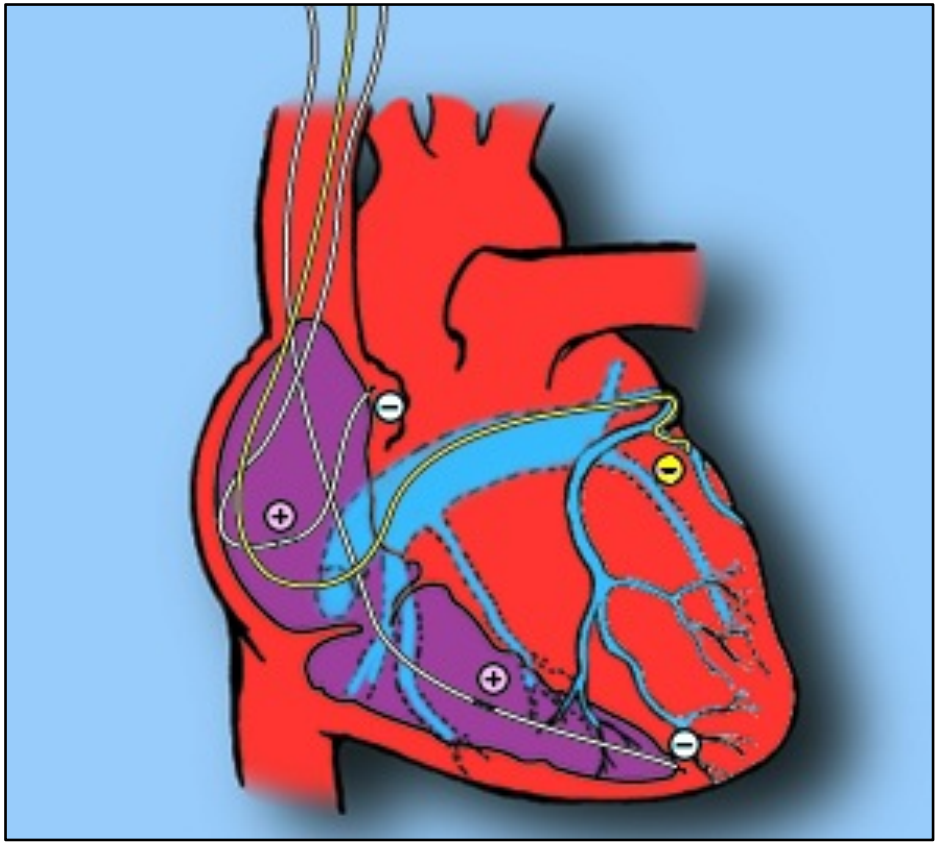
- ICD implantable cardioverter-defibrillator
- Cardiac resynchronisation therapy

Class I recommendations for devices in patients with LV systolic dysfunction

ICD	
Prior resuscitated cardiac arrest	Class I Level A
Ischaemic aetiology and >40 days of MI	Class I Level A
Non-ischaemic aetiology	Class I Level B
CRT	
NYHA Class III/IV and QRS >120 ms	Class I Level A
To improve symptoms/reduce hospitalization	Class I Level A
To reduce mortality	Class I Level A

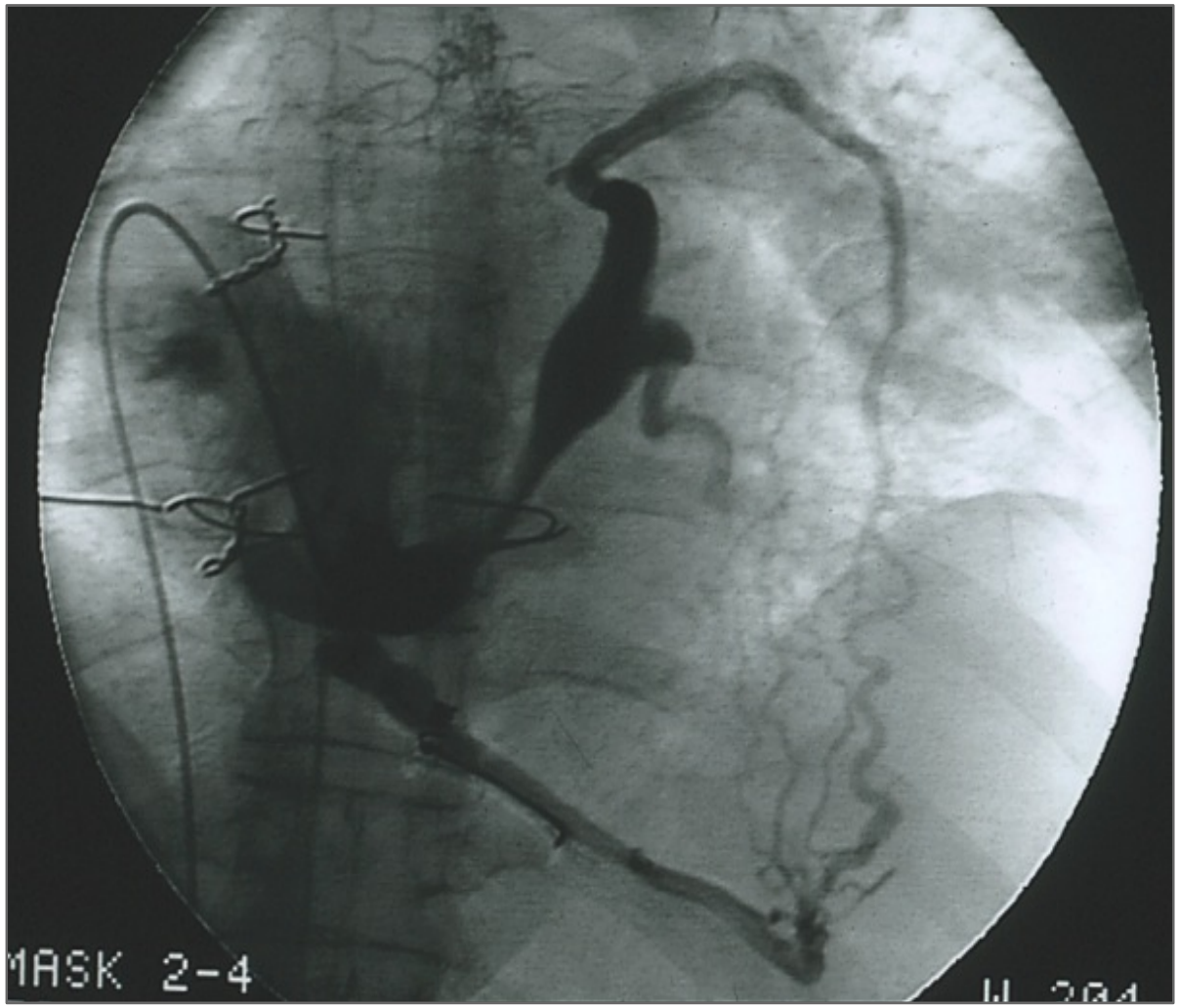
Resynchronization Therapy For Heart Failure

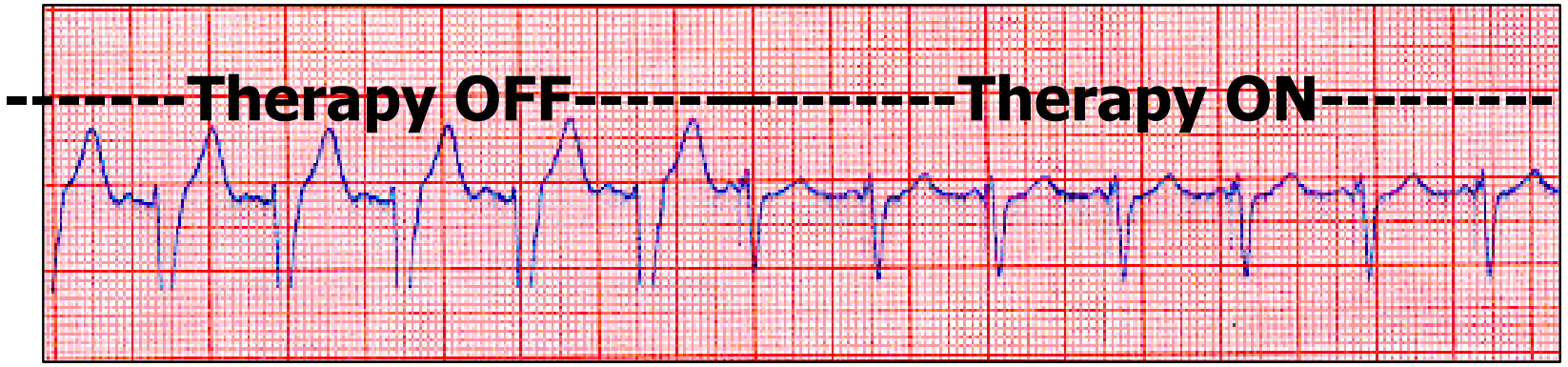
- Methods:
  - Epicardial Approach
    - Requires thoracotomy
    - Associated morbidity
  - Transvenous Approach
    - As practical established
    - Requires access to the coronary sinus
    - Requires leads developed for LV application



Goal: Pace Right and Left Ventricles

Venogram Image of Cardiac Venous System





Lead V3

QRS=160 ms **QRS=120 ms**


Diuretics to relieve symptoms/signs of congestion[a]
ACE inhibitor (or ARB if not tolerated)[a]
ADD a beta-blocker[b]
Still NYHA class II–IV?
Yes
No[c]
ADD a MR antagonist[b,d]
Still NYHA class II–IV?
Yes
No
LVEF ≤35%?
Yes
No
Sinus rhythm and HR ≥70 beats/min?
Yes
No
ADD ivabradine[e]
Still NYHA class II–IV and LVEF ≤35%?
Yes
No
QRS duration ≥120 ms?
Yes
No
Consider CRT-P/CRT-D[f]
Consider ICD[g]
Still NYHA class II–IV?
Yes
No[c]
No further specific treatment[c]
Continue in disease-management programme
Consider digoxin[h] and/or H-ISDN[i]
If end stage, consider LVAD and/or transplantation

Conclusions

- CHF is a very serious condition with a bad prognosis
- Diagnosis of CHF is based on objective evidence of cardiac dysfunction
- Symptoms as well as prognosis can be improved by appropriate therapy
- ACE inhibitors and β-blockers are very well documented and should be considered in all patients to improve survival, hospitalisation rates and QOL
- Dose levels should be titrated as in clinical trials to achieve maximum benefits
- Devices!