Treatment of Heart Failure

Management of chronic heart failure

New York Heart Association (NYHA) Classification of heart failure	
Class I	**No limitation.** Normal physical exercise does not cause fatigue, dyspnoea or palpitations
Class II	**Mild limitation.** *Comfortable at rest* but normal physical activity produces fatigue, dyspnoea or palpitations
Class III	**Marked limitation.** *Comfortable at rest* but gentle physical activity produces marked symptoms of heart failure
Class IV	**Symptoms of HF occur at rest** AND exacerbated by any physical activity

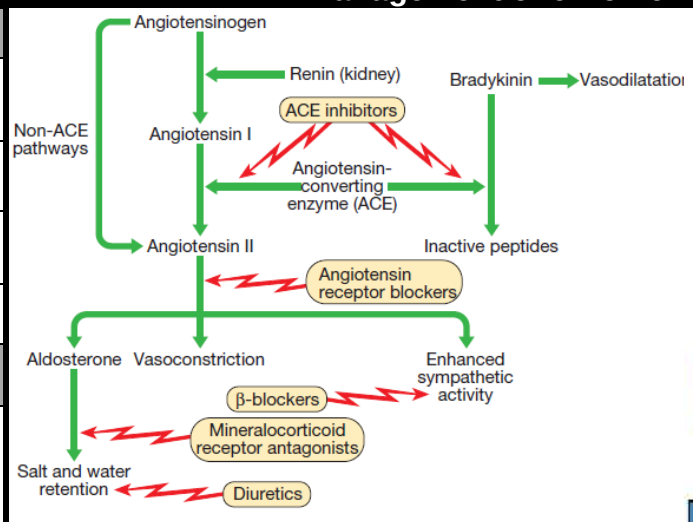
Diagnosis of heart failure (European Society of Cardiology guidelines)

Essential features (criteria 1 and 2)

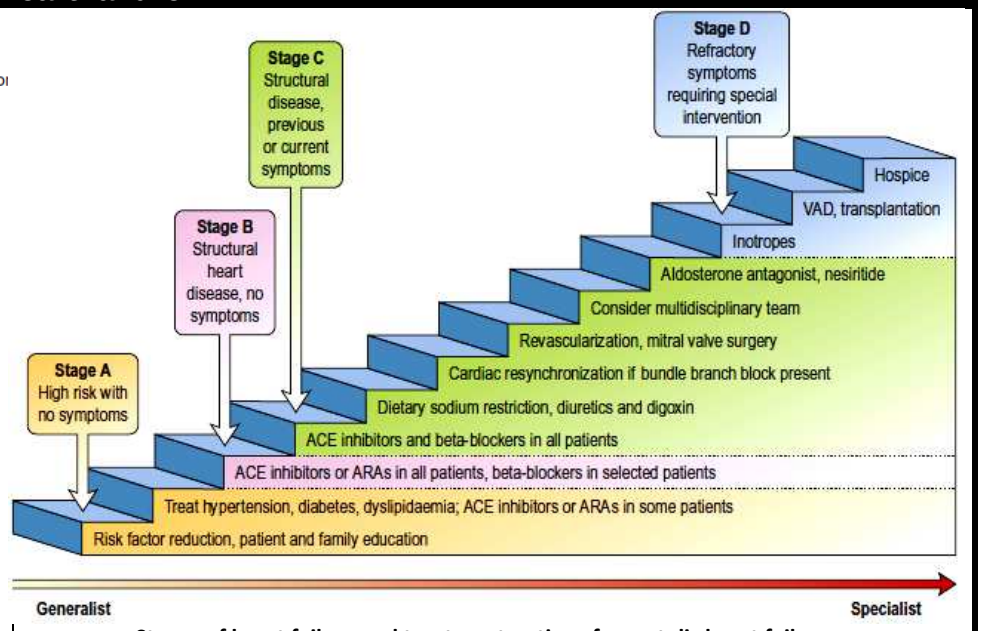
1. Symptoms and signs of heart failure (e.g. breathlessness, fatigue, ankle swelling)
2. Objective evidence of cardiac dysfunction (at rest, e.g. echocardiogram)

Non-essential features

3. Response to treatment directed towards heart failure(in cases where the diagnosis is in doubt)



Neurohumoral activation & sites of action of drugs used in TTT of HF



Stages of heart failure and treatment options for systolic heart failure

General measures

Education	Diet	Obesity control	Smoking	Exercise	Vaccination
• Explanation of : - Nature of disease - Treatment - Self-help strategies	• Large meals is avoided . • Weight reduction. • Salt restriction. • Severe HF→ fluid restriction.	• Maintain desired BMI	• Cessation	• For those with exacerbations of CHF → **bed rest , reduces the demands on the heart** • Regular moderate aerobic exercise within limits of symptoms.	• Consider : - influenza vaccination - pneumococcal vaccination

Drug therapy

Diuretics

Monitoring :
1- Serum electrolytes
2- Renal function tests

must be monitored regularly , for risk of : - **Hypokalaemia**
- Hypomagnesaemia

They may cause **hyperkalaemia**, particularly when used with an ACEIs.

Mechanism:

- Diuretics produce an **increase in urinary sodium & water excretion,**→ leading to **reduction in blood & plasma volume.**
  - It reduces preload → improves pulmonary & systemic venous congestion.
    ** Although a fall in preload (ventricular filling pressure) tends to reduce cardiac output, the 'Starling curve' in heart failure is flat, so there may be a beneficial fall in filling pressure with little change in cardiac output!!*
  - It may also reduce afterload & ventricular volume → leading to a fall in ventricular wall tension & increased cardiac efficiency.

Regimens :

1- Loop diuretics (e.g. furosemide) **or Thiazide diuretics** (e.g. bendroflumethiazide , hydrochlorothiazide) should be given in patients with fluid overload.
- **In some patients with severe chronic heart failure** *particularly if there is associated renal impairment, →oedema may persist, despite oral loop diuretic therapy :*
  a- Intravenous infusion of furosemide (5–10 mg/hr) may initiate a diuresis.
  b- Combining a loop diuretic with a thiazide diuretic (e.g. bendroflumethiazide 5 mg daily)

2- Aldosterone antagonists (spironolactone and eplerenone) :
- Potassium-sparing diuretics → particular benefit in patients with **: 1- Heart failure with severe left ventricular systolic dysfunction**. **2- Improve outcome in heart failure following acute MI.**

Angiotensin-converting enzyme inhibitors (ACEI)

S.E.- **Hypotension** :
introduced gradually with low initial dose with regular blood pressure monitoring
-**Hyperkalaemia** :
*Aldosterone should be discontinued .
*offset loop diuretic hypokalaemia
- **Renal dysfunction** : creatin. measured.

Mechanism:

- Angiotensin-converting enzyme (ACE) inhibition therapy interrupts the vicious circle of neurohumoral activation → by preventing the conversion of angiotensin I to angiotensin II, → thereby
  1- Preventing peripheral vasoconstriction 2- Activation of the sympathetic nervous system 3- Salt and water retention due to aldosterone release.
- These drugs also **prevent the undesirable activation of the renin–angiotensin system caused by diuretic therapy**.

Indications : *(Davidson's note 18.16 page: 551: ACE inhibitors in chronic heart failure due to ventricular dysfunction reduce mortality & re-admission rates)*
1- In moderate & severe heart failure : can produce a substantial improvement in *effort tolerance & in mortality*.
2- Asymptomatic heart failure following myocardial infarction : improve outcome & prevent the onset of overt heart failure.

Contraindications :
1- **Renal artery stenosis 2- Pregnancy 3- Previous angioedema**

Monitoring therapy : Renal function & serum potassium

	Starting dose	Target dose
ACE inhibitors		
Enalapril	2.5 mg twice daily	10 mg twice daily
Lisinopril	2.5 mg daily	20 mg daily
Ramipril	1.25 mg daily	10 mg daily
Angiotensin receptor blockers		
Losartan	25 mg daily	100 mg daily
Candesartan	4 mg daily	32 mg daily
Valsartan	40 mg daily	160 mg daily

Angiotensin II receptor antagonists (ARA)

- Same all side effects of ACE inhibitors.
- Unlike ACEI :
  - Don't affect bradykinin metabolism
  - **Don't produce cough.**

Mechanism :
Act by blocking the action of angiotensin II on : **Heart** → inhibit the sympathetic activity , resulting in bradycardia.
Peripheral vasculature → inhibit vasoconstriction , resulting in vasodilation.
Kidney → prevent aldosterone release , resulting in decrease salt & water retention.

Indications :
1- Alternative to ACEI as a second-line therapy in patients intolerant of ACEI. *(Compared with ACE inhibitors, ARBs are better tolerated and have similar efficacy in reducing cardiovascular events).*
2- Both ACEI & ARA two can be combined in patients with resistant or recurrent heart failure.

Vasodilators

Indications : When ACE inhibitor or ARB drugs are contraindicated (e.g. in severe renal failure) or intolerant.
Regimen : The combination of **Nitrates** → reduce preload **AND Hydralazine** → arterial dilators reduce afterload.

Beta-blockers

Bisoprolol

Mechanism :
- **Counteract the deleterious effects of enhanced sympathetic stimulation** AND **reduces the risk of arrhythmias** & **sudden death.**

Regimen : *(When initiated in standard doses, they may precipitate acute-on-chronic heart failure)*
- Given in small incremental doses (e.g. **bisoprolol** started at a **dose of 1.25 mg daily**, and **increased gradually over a 12-week period** to a **target maintenance dose of 10 mg daily**).

Effects :
1- Increase ejection fraction 2- Improve symptoms 3- Reduce the frequency of hospitalisation 4- Reduce mortality in patients with chronic heart failure .

Cardiac glycosides

Digoxin

Indications :
- Provide **rate control** in patients with **heart failure & atrial fibrillation**.
- Used as **add-on therapy** in **symptomatic heart failure patients already receiving ACEI & beta-blockers**
- **In patients with severe heart failure (NYHA class III–IV),** →digoxin reduces the **likelihood of hospitalisation for heart failure**, *although it has* ***no effect on long-term survival*.**

Inotropic & vasopressors

Indications :
- IV inotropes & vasopressor agents → are used in patients with chronic heart failure who are not responding to oral medication. *(they have not been shown to improve long-term mortality).*

Other medications

N.B. In patients with known ischaemic heart disease antiplatelet therapy (aspirin, clopidogrel) and statin therapy should be continued

Amiodarone

Indications :
1- It has little negative inotropic effect → may valuable in **patients with poor left ventricular function**.
2- It is only effective in the **treatment of symptomatic arrhythmias** (and should not be used as a preventative agent in asymptomatic patients).

Ivabradine

Mechanism : inhibits the *I*F channels in the SA node→ resulting in reduction if heart rate.
Indications : best suited to patients who cannot take β-blockers or in whom the heart rate remains high despite β-blockade.
It reduces *hospital admission & mortality rates* in patients with heart failure due to moderate or severe left ventricular systolic impairment.

Anticoagulants

Indications :
1- In hospital: all patients require prophylactic anticoagulation *(BECAUSE Heart failure is associated with a four-fold increase in the risk of a stroke).*
2-Patients with atrial fibrillation
3-Patients with sinus rhythm with a history of thromboembolism, left ventricular thrombus or aneurysm.

Implantable Cardiac Defibrillators / and Cardiac Resynchronisation Therapy

1- Implantable cardiac defibrillator :
- Patients with **symptomatic ventricular arrhythmias AND heart failure** → Irrespective of their response to anti-arrhythmic drug therapy, all **should be considered for implantation of a cardiac defibrillator** *because it improves survival.*

2- Cardiac resynchronization therapy :
- In patients with **marked intraventricular conduction delay**, → **prolonged depolarisation** may lead to: **uncoordinated L.V contraction**. →When this is associated with **severe symptomatic heart failure**, **cardiac resynchronization therapy should be considered** : Here, both the LV and RV are paced simultaneously to generate a more coordinated left ventricular contraction and improve cardiac output. *This is associated with improved symptoms & survival.*

Coronary revascularisation

'Hibernating' myocardium can be defined as reversible left ventricular dysfunction due to chronic coronary artery disease that responds positively to inotropic stress and indicates the presence of viable heart muscle that may recover after revascularization. **It is due to reduced myocardial perfusion, which is just sufficient to maintain viability of the heart muscle.** ('hibernating' myocardium can be identified by : **stress echocardiography & specialized nuclear or MR imaging**).

1- **Coronary artery bypass surgery** or
2- **Percutaneous coronary intervention**

May improve function in areas of the myocardium that are 'hibernating' because of inadequate blood supply, **used to treat selected patients with HF & CHD.**

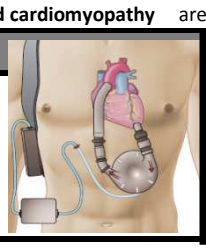
Heart transplantation 1-year survival over 90% / 5-year is 75%

Indications : treatment of choice for **younger** patients with : **Intractable heart failure whose life expectancy is <6 months→ 1- Coronary artery disease** & **2- Dilated cardiomyopathy** are the most common indications

Ventricular assist devices

Because of the limited supply of donor organs, ventricular assist devices (VADs) have been employed as:

• a bridge to cardiac transplantation • potential long-term therapy • short-term restoration therapy following a potentially reversible insult, e.g. viral myocarditis.
- VADs assist cardiac output by using a roller, centrifugal or pulsatile pump that, in some cases, is implantable and portable.
- They withdraw blood through cannulae inserted in the atria or ventricular apex and pump it into the pulmonary artery or aorta.
- They are designed not only to unload the ventricles but also to provide support to the pulmonary and systemic circulations.
- Their more widespread application is limited by high complication rates (haemorrhage, systemic embolism, infection), although some improvements in survival .



Source: **Davidson & Kumar.**

Management of acute heart failure (acute pulmonary edema)

The goals of treatment in a patient with AHF include:

1- **Immediate relief of symptoms** and stabilization of haemodynamics (short-term benefits).
2- **Reduction** in length of hospital stay & hospital readmissions.
3- **Reduction** in mortality from heart failure.

A) Patients with haemodynamic compromise , may require :

- Arterial lines (invasive blood pressure monitoring and arterial gases),
- Central venous cannulation (intravenous medication, inotropic support, monitoring of central venous pressure)
- Pulmonary artery cannulation (calculation of cardiac output/index, peripheral vasoconstriction and pulmonary wedge pressure).

B) Initial therapy :

1- Sit the patient up to reduce pulmonary congestion.
2- Give → a- Oxygen / Non-invasive positive pressure ventilation (continuous positive airways pressure (CPAP) of 5–10 mmHg).
b- Loop diuretic: furosemide (50–100 mg IV).
c- Vasodilator "Nitrates" : IV glyceryl trinitrate (10–200 µg/min) → until : 1- Clinical improvement occurs or 2- systolic BP falls to < 110 mmHg.
e- All patients require prophylactic anticoagulation with low molecular weight heparin, e.g. enoxaparin 1 mg/kg s.c. ×2 daily.

C) In patients who don't respond to the initial therapy : → Inotropic support : Dobutamine / Phosphodiesterase inhibitors / levosimendan can be added.
If blood pressure is low, use : noradrenaline (norepinephrine).

D) With acute cardiogenic pulmonary oedema & shock → Intra-aortic balloon pump may be beneficial.

E) Monitoring: regular measurements of temperature, heart rate, blood pressure and cardiac monitoring.