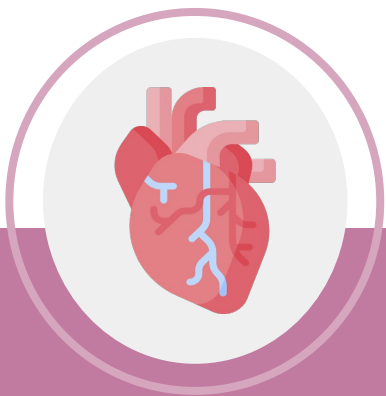




Editing file

Heart failure (2) (Management & Prognosis)

No.6



Objectives :

- ★ Know different classifications, clinical presentation, and diagnosis of heart failure.
- ★ Know the causes and precipitation factors for heart failure decompensation.
- ★ Describe the definition, pathophysiology, epidemiology, therapies that improve survival, and prognosis of heart failure.
- ★ To demonstrate and understand the most recent AHA/ACC and ESC HF guidelines and the literature supporting their recommendations.

Color index

Original text

Females slides

Males slides

Doctor's notes ⁴³⁸

Doctor's notes ⁴³⁹

Doctor's notes ⁴⁴²

New text in slides ⁴⁴²

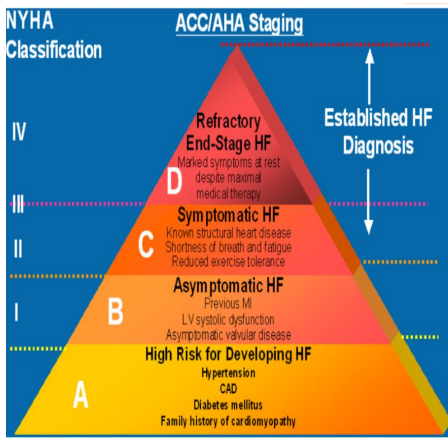
Text book

Important

Golden notes

Extra

Heart failure



| Definitions |
|--|
| <ul style="list-style-type: none"> • LVEF: Left Ventricular Ejection Fraction; Determined by Echocardiography • Heart failure with reduced Ejection Fraction (HFrEF) $\leq 40\%$ • Heart failure with mildly reduced Ejection Fraction (HFmrEF) 41-49% • Heart failure with preserved Ejection Fraction (HFpEF). $\geq 50\%$ |

| Forrester Classification (Especially acute HF) | | | |
|--|--------------------------------------|------------|------------|
| Important | Congestion (pulmonary edema) at Rest | | |
| | NO | NO | Yes |
| Low Perfusion At rest (BP) | NO | Warm & Dry | Warm & Wet |
| | Yes | Cold & Dry | Cold & Wet |

HF management tools

Correction of reversible causes (1st step in Tx)

e.g. Ischemia, VHD, thyrotoxicosis, anemia and other high output status, shunts, arrhythmias (e.g. Afib, atrial flutter, CHB), medications (e.g. CCB, antiarrhythmics, NSAIDS)

Lifestyle Modification

- Diet (Salt restriction: (2g of Na = 5 g NaCl = 1/2 table spoon) ¹)
- Fluid restriction (1.5 to 2 L / day) about 8 cups)
- Daily weight (tailor therapy)
- Smoke cessation
- Exercise: gradual exertion program (rehabilitation program, shows mortality benefit)

Pharmacological

- Oral medication
- Immunization (flu, pneumococcal and covid-19 (hopefully))

Surgical and device intervention

- Device therapy
- Assisting devices
- Transplant

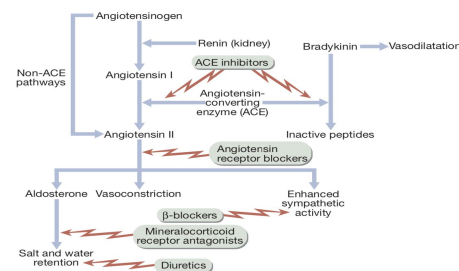
Management of Chronic HF

General Measures (EXTRA)

- **Education** of patients and families.
- **Physical activity:** reduce during exacerbations to reduce work of the heart. Encourage low-level (e.g. 20- to 30-min walks 3-5 times weekly) with compensated heart failure
- **Diet and social:** weight reduction if necessary (Daily weight "Tailor therapy"), no added salt diet (2g of Na=5g of NaCl), avoid alcohol (negative inotropic effects), stop smoking.
- **Vaccine** against pneumococcal disease influenza.
- **Correct aggravating factors**, e.g. arrhythmias, anaemia, hypertension and pulmonary infections
- **Driving:** unrestricted, except symptomatic heart failure disqualifies driving large lorries and buses
- **Sexual activity:** tell patients on **nitrates** not to take phosphodiesterase type 5 inhibitors.

Pharmacological Management

- 1 Diuretic
- 2 β -Blockers
- 3 ACEIs/ARBs
- 4 ARNi
- 5 Digoxin
- 6 Vasodilators
- 7 SGLT-2 inhibitors
- 8 MRAs



1- Total salt intake should be **2 grams per day**. We don't restrict the patient completely from salt. To describe ot to the patient, tell him "don't add any EXTRA salt, don't eat canned food and try to avoid cheese (any kind). And to stay away from restaurant. For fluid they should.t exceed fluids above 1.5 liters Typically, we begin with lifestyle modification by providing a booklet and speaking with the patient and his family in order to raise awareness .

- Salt intake restrictions محرم على HF pt
- Avoid heating food because it increases the salt content.
- Fluid restrictions
- Weight monitoring (increase of weight is due to fluid retention in the body which leads to shortness of breath) treated by diuretics

IMP:
you should know:
MOA + ADR

Management cont'

3 diuretics that we can use with HF pt

- Thiazides
- Loop diuretic
- K sparing diuretic spironolactone

Management of Chronic HF cont.

1-Diuretics (for fluid overload)

| Group | A- Loop diuretics Furosemide "Lasix"* (20-320 mg QD) Bumetanide "Bumex" (1-8mg) Torsemide (20-200mg) | B- Thiazide diuretic (Hydrochlorothiazides*, Chlorthalidone, Metolazone* most commonly used with furosemide) |
|-------|--|--|
| M.O.A | <ul style="list-style-type: none"> • Inhibit chloride reabsorption in ascending limb of loop of Henle results in natriuresis, kaliuresis and metabolic alkalosis • ↓Na⁺-Cl⁻-K⁺ cotransport in thick ascending limb of loop of Henle | <ul style="list-style-type: none"> • Block Na reabsorption in loop of henle and distal convoluted tubules • ↓Na⁺- Cl cotransporter in early distal convoluted tubule |
| Uses | <ul style="list-style-type: none"> • Most effective in controlling symptoms (Dyspnea & Peripheral+pulmonary edema), but have not been shown to reduce mortality or improve prognosis. • Most potent diuretics used in moderate/severe HF. | <ul style="list-style-type: none"> • Used for mild HF • Ineffective with GFR < 30 --/min. |
| ADR | <ul style="list-style-type: none"> • Pre-renal azotemia¹ • Hypokalemia² • Skin rash • Otototoxicity⁴ (single dose dependent, not accumulative) in long term use • Dehydration • Allergy (Sulfa) • Nephritis (interstitial) • Urate retention, causing gout. • Hypercalciuria leading to increased risk of calcium-based renal stones • Hypomagnesaemia • Decreased glucose tolerance hyperglycemia | <ul style="list-style-type: none"> • Pre-renal azotemia¹ • Skin rashes • Neutropenia • Thrombocytopenia • Hyperglycemia • ↑ Uric Acid³ • Hepatic dysfunction • Hyponatremia low sodium bcs of high excretion • Hypercalcemia |

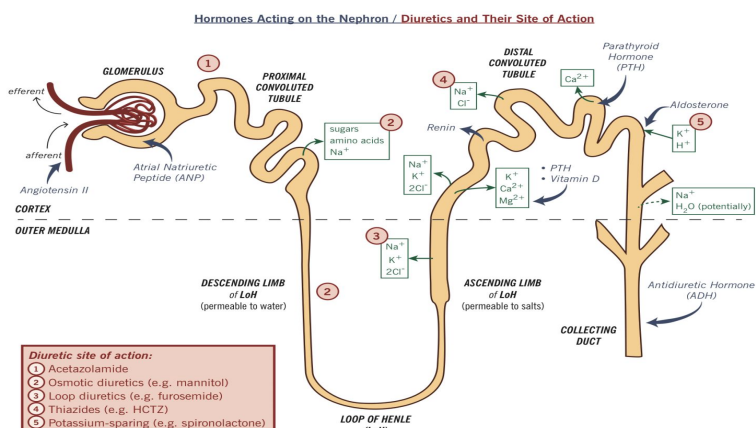
EXTRA

Diuretics benefits:

- Improves symptoms of congestion
- Can improve cardiac output
- Improved neurohormonal milieu
- No inherit nephrotoxicity

Diuretics limitations:

- Oral absorption unpredictable
- Excessive volume Depletion
- Electrolyte disturbance



© Cassandra Uy

1- in case of Chronic kidney disease they're ineffective Because diuretics deal with fluids, they can cause kidney problems. This can be resolved by lowering the dose or discontinuing the medication.

2- Monitor renal function and check for hypokalaemia and hypomagnesaemia Hypokalemia because of inhibiting Cl absorption that absorbs the K with it

3- Patient will come complaining of painful swelling in the big toe which indicates **hyperuricemia**

4- It affects the triple co-transporter that's located in the inner ear

Management of Chronic HF cont.

| Group | C- K+ sparing agents | | |
|--------------------|--|---|---|
| Drug name | Spironolactone (Aldosterone inhibitor) | Eplerenone | Triamterene, amiloride |
| General | <ul style="list-style-type: none"> Relatively weak diuretics with a potassium-sparing action | | |
| M.O.A ¹ | <ul style="list-style-type: none"> Acts at the collecting duct by competitive inhibition of cytoplasmic aldosterone receptors → ↑ Excretion of Na⁺, Cl & ↓ Excretion of K⁺, H⁺, NH₄ | <ul style="list-style-type: none"> Binds to the mineralocorticoid receptor and blocks the binding of aldosterone | <ul style="list-style-type: none"> Acts on distal tubules to ↓ K secretion |
| Uses | <ul style="list-style-type: none"> recent evidence suggests that it may improve survival in CHF patients due to the effect on renin-angiotensin-aldosterone system with subsequent effect on myocardial remodeling and fibrosis | <ul style="list-style-type: none"> Reduces mortality in patients with acute myocardial infarction and heart failure. | - |
| Adverse effects | <ul style="list-style-type: none"> Gynecomastia (If pt develop this, switch to eplerenone), Hyperkalemia² and chest pain. (Monitor renal function) You have to make sure to follow the patient potassium, because it is K⁺ sparing agent and most patient present with renal dysfunction | Hyperkalemia | - |

Diuretics in Davidson:

Diuretics promote urinary sodium and water excretion, leading to a reduction in blood plasma volume (p. 354), which in turn reduces preload and improves pulmonary and systemic venous congestion. They may also reduce afterload and ventricular volume, leading to a fall in ventricular wall tension and increased cardiac efficiency. Although a fall in preload (ventricular filling pressure) normally reduces cardiac output, patients with heart failure are beyond the apex of the Starling curve, so there may be a substantial and beneficial fall in filling pressure with either no change or an improvement in cardiac output (see Figs 16.24 and 16.28). Nevertheless, the dose of diuretics needs to be titrated carefully so as to avoid **excessive volume depletion**, which can cause a **fall in cardiac output with hypotension**, lethargy and **renal failure**. This is especially likely in patients with a marked diastolic component to their heart failure.

Oedema may persist, despite oral loop diuretic therapy, in some patients with severe chronic heart failure, particularly if there is renal impairment. Under these circumstances an intravenous infusion of furosemide (5–10 mg/hr) may initiate a diuresis. Combining a loop diuretic with a thiazide diuretic such as bendroflumethiazide (5 mg daily) may also prove effective but care must be taken to avoid an excessive diuresis.

Mineralocorticoid receptor antagonists, such as spironolactone and eplerenone, are potassium-sparing diuretics that are of particular benefit in patients with heart failure with severe left ventricular systolic dysfunction. They have been shown to improve long-term clinical outcome in individuals with severe heart failure or heart failure following acute MI but may cause hyperkalemia, particularly when used with an ACE inhibitor.

1- In chronic HF activation of the (RAAS) leads to increased levels of angiotensin II and plasma aldosterone, and promote development of arterial vasoconstriction and remodeling, sodium retention, oxidative process, and cardiac fibrosis. OUR GOAL IS TO PREVENT THE PATIENT FROM REACHING THIS STAGE

Spironolactone has two mechanisms of action that can help with this issue :

- aldosterone inhibitor -> so it increases the excretion of Na
- RAAS effect : fluid reduction (diuretic)

Both actions help to prevent the cardiac remodeling and fibrosis.

2- Hyperkalemia can lead to arrhythmia (if arrhythmia is developed lower dose or stop medication and monitor by ECG)

Management cont'

2- β -Blockers

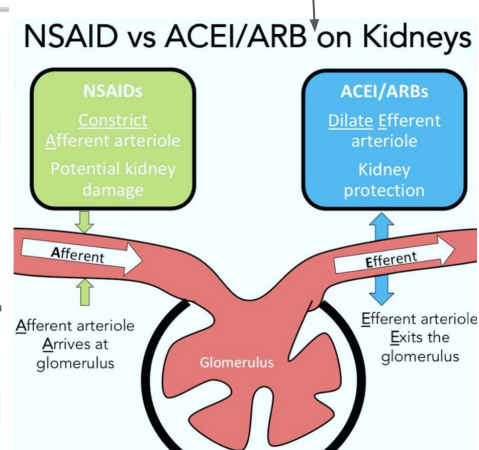
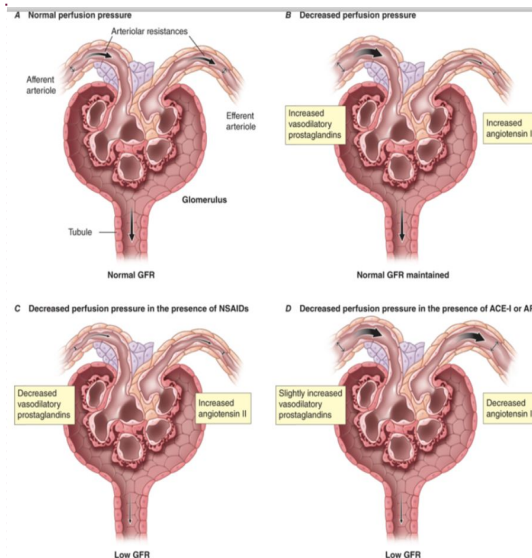
| Drug name | Bisoprolol | Carvedilol | Metoprolol succinate |
|--------------------------|---|------------|----------------------|
| General info | <ul style="list-style-type: none"> Has been traditionally contraindicated in pts with CHF Now they are the main stay in treatment on CHF & may be the only medication that shows substantial improvement in LV function | | |
| Uses | <ul style="list-style-type: none"> The benefit of beta blockers likely stems from: <ul style="list-style-type: none"> Anti-Ischemic effect, Decreasing HR (Decrease O₂ consumption) Antiarrhythmic effect In addition to improved LV function multiple studies show improved survival¹ ★ "Start low, go slow"²: Bisoprolol 1.25mg od, Carvedilol 3.124mg od Not rescue therapy. Consider cardioselective agents in mild to moderate reversible airways disease. | | |
| Contraindications | <ul style="list-style-type: none"> Severe <u>decompensated</u> CHF (AHF, Pulmonary edema) Peripheral Vascular Disease (PVD) Shock | | |

3-Inhibitors of renin-angiotensin- aldosterone system. (Important for mcq)

Reduction in cardiac output and the consequent fall in effective circulatory volume and arterial illing lead to activation of the renin-angiotensin-aldosterone system, results in increased peripheral and renal arteriolar resistance and **water and sodium retention**. These factors lead to extracellular volume expansion and increased venous pressure, **causing oedema formation**.

Renin-angiotensin-aldosterone system is activation early in the course of heart failure and plays an important role in the progression of the syndrome :

- Angiotensin receptors blockers (ARB)**
- Angiotensin converting enzyme inhibitors (ACEI)**
- Spironolactone**



A-Angiotensin II type 1 receptor blockers (ARBs)

| Drug name | losartan | irbesartan | valsartan |
|-------------|---|------------|-----------|
| Uses | <ul style="list-style-type: none"> Second-line therapy in certain conditions when ACE I are contraindicated (angioneurotic edema, cough) Has <u>comparable effect to ACEI</u>. Has mortality benefit. ARBs are normally used as an alternative to ACE inhibitors, but the two can be combined in patients with resistant or recurrent heart failure. | | |
| ADRs | <ul style="list-style-type: none"> Renal dysfunction, hyperkalemia | | |

1- Beta-blockers are more effective at reducing mortality than ACE inhibitors, with a relative risk reduction of 33% versus 20%, respectively. BB inhibit the sympathetic system -> cause vasodilation-> improve CO -> Improve LV function = improve mortality. It will improve the survival by relieving the symptoms in a **compensated pt**.

2- Because of the acute negative inotropic effects, **starting beta-blocker therapy during ADHF is not recommended**. However, when patients are euvoletic, it is safe to start a low dose prior to discharge, and patients who are started on beta-blockers prior to discharge have better outcomes.

Management of Chronic HF cont.

B-Angiotensin-converting enzyme inhibitors (ACEI)

| Drug name | Perindopril | Lisinopril | Quinapril |
|---------------------------------|---|------------|-----------|
| M.O.A | <ul style="list-style-type: none"> Block the R-A-A system by inhibiting the conversion of angiotensin I to angiotensin II → vasodilation and ↓ Na and water retention → (decrease Afterload and preload) ↓ Bradykinin degradation → ↑ its level → ↑ PG secretion & nitric oxide → <u>Vasodilation</u> They also ultimately inhibit cardiac remodelling | | |
| Uses | <ul style="list-style-type: none"> ★ They improve symptoms, limit the development of progressive heart failure and prolong survival, and should be given to all patients with heart failure. ACE Inhibitors were found to <u>improve survival by 30-35% in CHF patients</u> : <ul style="list-style-type: none"> Delay onset & progression of HF in pts with asymptomatic LV dysfunction If we perform an echo on an asymptomatic HF patient and we suddenly discovered that she has an EF= 40 directly give an ACEI. why? Bc it delays the remodeling, improves the progression of the disease and mortality. ↓ cardiac remodeling | | |
| Side effects (IMPORTANT) | <ul style="list-style-type: none"> Angioedema (from bradykinin vasodilation) Some patients are more susceptible than others. ★ Cough (If patient develops cough switch to ARBs)(from bradykinin vasodilation) Renal insufficiency we have to balance the medication & monitor, Hepatic dysfunction Rash, Hyperkalemia¹ The major side-effect is first-dose hypotension. <ul style="list-style-type: none"> ACEI treatment should be introduced gradually with a low initial dose and gradual titration every 2 days to full dose with regular blood pressure monitoring and a check on serum potassium and renal function 1-2 weeks after starting therapy; creatinine levels normally rise by about 10–15% during ACEI therapy. If patient developed hyperkalemia or renal impairment or is pregnant → switch from ACEI to Hydralazine with isosorbide dinitrate. | | |
| Contraindication | <ul style="list-style-type: none"> Renal failure Bilateral renal artery stenosis (RAS) Aortic stenosis | | |

Trials for ACEI:

- CONSENSUS 1987 – enalapril vs. placebo – 31% reduction mortality in enalapril group. Confirmed by SOLVD, AIRE, SAVE, TRACE.
- 1995 meta-analysis showed 23% reduction total mortality, 35% in combined mortality/hosp admission

1- can be beneficial in offsetting the hypokalemia associated with loop diuretic therapy. Alternatively, If the patient is on ACEI but the potassium is high and you need to keep ACEI to delay renal failure or to decrease mortality in CHF, use Paritomer, it exchanges calcium for potassium in bowel

2- Imp drugs used in HF pt that deals with RAAS (the primary compensatory response that plays a role in the disease prognosis), so if it's managed there will be no consequences :

1. ACEI
2. ARB
3. ARNI
4. Spironolactone

3-The main treatment in Hf pt that deals with RAAS is ACEI, if it's contradicted move to the other. It has two effects:

- RAAS inhibitors
- Afterload vasodilation

So it increases CO and prevents cardiac fibrosis caused by the vasoconstriction

4-Any drugs works on RAAS could lead to:

- renal insufficiency & it is a very common side effects and it should be measured in pts with renal impairment+HF, this is known as (cardio-renal syndrome)
- Hyperkalemia

5-ACEI & ARB and all the drugs that work on RAAS lead to renal impairment, so a pt with renal impairment & HF give -> vasodilator

Management of Chronic HF cont.

4- Angiotensin Receptor - Neprilysin inhibitors (ARNi)

| | |
|---------------------|--|
| Drug name | Combination of Valsartan & Sacubitril(Entresto) |
| General info | <ul style="list-style-type: none"> Recent FDA approval (2015) The only product available (valsartan/sacubitril): <ol style="list-style-type: none"> Valsartan = ARB Sacubitril = prodrug for sacubitrilat Inhibit neprilysin which breakdown the vasoactive peptides. |
| M.O.A | <ul style="list-style-type: none"> Inhibits neprilysin which is responsible for the breakdown of the endogenous diuretics ANP and BNP(Sacubitril) |
| Uses | <ul style="list-style-type: none"> Used if patient LVEF ≤ 35% and still symptomatic with ACE/ARB In this specific group of patients it improves Mortality & Morbidity |

5- Positive Inotropes

| | | |
|-----------------------------------|--|---|
| Drug name | Digitalis Glycosides (Digitoxin, Digoxin)^{1,2} | |
| M.O.A | <p>★ +ve inotropic effect by ↑ intracellular Ca & enhancing actin-myosin cross-bridge formation (binds to the Na-K ATPase → inhibits Na pump → ↑ intracellular Na → ↑ Na-Ca exchange</p> <ul style="list-style-type: none"> Has Vagotonic effect and Arrhythmogenic effect, this is why it does not work with elderly patient (because of their weak vagal tone) Not imp in treating pt with Hf bcs of its safety ,It's the last choice drug that we may use | |
| Uses | <ul style="list-style-type: none"> Indicated in patients with heart failure and atrial fibrillation. In patients with severe(refractory(to ACEIs/ARBs, ARNi,BB,..) HFrEF) heart failure (NYHA class III-IV), digoxin reduces the likelihood of hospitalisation for heart failure, it also reduces symptoms, but it has no effect on long-term survival. The role of digitalis has declined somewhat because of safety concern (Narrow therapeutic to toxic ratio) | |
| Digoxin toxicity | Cardiac manifestations (Digitalis can cause any kind of Arrhythmia) | Non cardiac manifestations |
| | <ul style="list-style-type: none"> Sinus bradycardia and arrest A/V block (usually 2nd degree) Atrial tachycardia with A/V Block Development of junctional rhythm in patients with AF PVC's, VT/V fib (bi-directional VT) | <ul style="list-style-type: none"> Anorexia Nausea, vomiting Headache Xanthopsia sotoma (yellow vision) Disorientation |
| Digoxin toxicity treatment | <ol style="list-style-type: none"> Hold the medications Observation. In case of A/V block or severe bradycardia → atropine followed by temporary PM if needed. In life threatening arrhythmia → digoxin-specific fab antibodies. Lidocaine and phenytoin could be used – try to avoid D/C cardioversion in non life threatening arrhythmia. | |

- Positive inotropes(In icu settings,last thing to be offered) are drugs that improve myocardial contractility (β adrenergic agonists, dopaminergic agents, phosphodiesterase inhibitors) e.g. Dopamine, Dobutamine, Milrinone, Amrinone (only used IV)→Several studies showed **↑ mortality with oral inotropic agents.**
- So the only use for them now is in **acute** settings as cardiogenic **shock**.

1- **It's ONLY given I.V. NOT Orally** it also has a very narrow therapeutic index and does not decrease mortality. Only improves morbidity
 2- Use with caution in renal impairment or conduction disease, and with amiodarone

Management of Chronic HF cont.

| 6-Vasodilators ¹ | | |
|-----------------------------|--|--|
| Drug name | Hydralazine | Nitrate |
| M.O.A | <ul style="list-style-type: none"> Reduction of afterload by arteriolar vasodilation → reduce LVEDP, O2 consumption, improve myocardial perfusion, stroke volume and cardiac output. | <ul style="list-style-type: none"> Reduction of preload by venous dilation → ↓ the venous return → ↓ the load on both ventricles. |
| Uses | <ul style="list-style-type: none"> Valuable in chronic heart failure, when ACE inhibitors or ARBs are contraindicated. Usually the maximum benefit is achieved by using agents with both action. HDZ/ISDN combination is recommended for African Americans with NYHA class III-IV HFrEF receiving optimal therapy with ACE inhibitors and beta blockers. HDZ/ISDN can be <u>useful</u> to reduce morbidity or mortality in patients with current or prior symptomatic HFrEF <u>who cannot be given an ACE inhibitor or ARB because of drug intolerance, hypotension, or renal insufficiency</u>, unless contraindicated. | |
| Side effects | <ul style="list-style-type: none"> Their use is limited by pharmacological tolerance and hypotension. | |

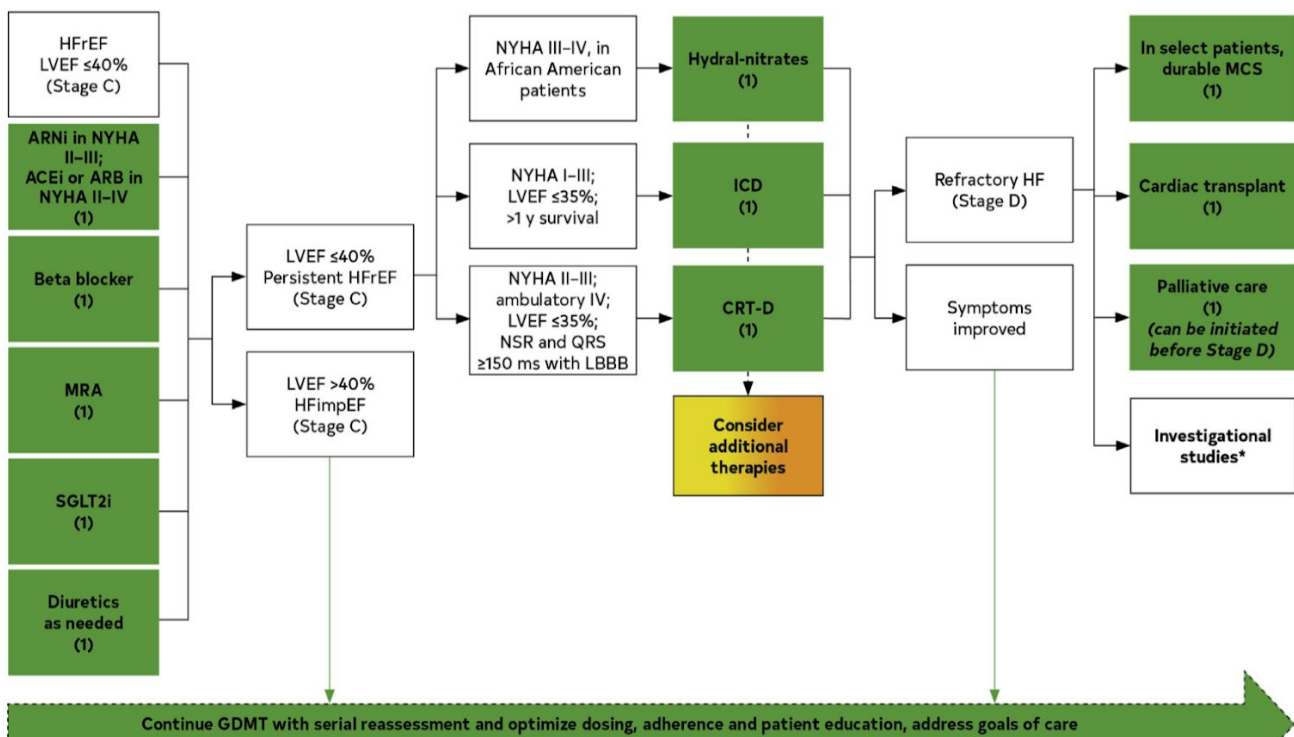
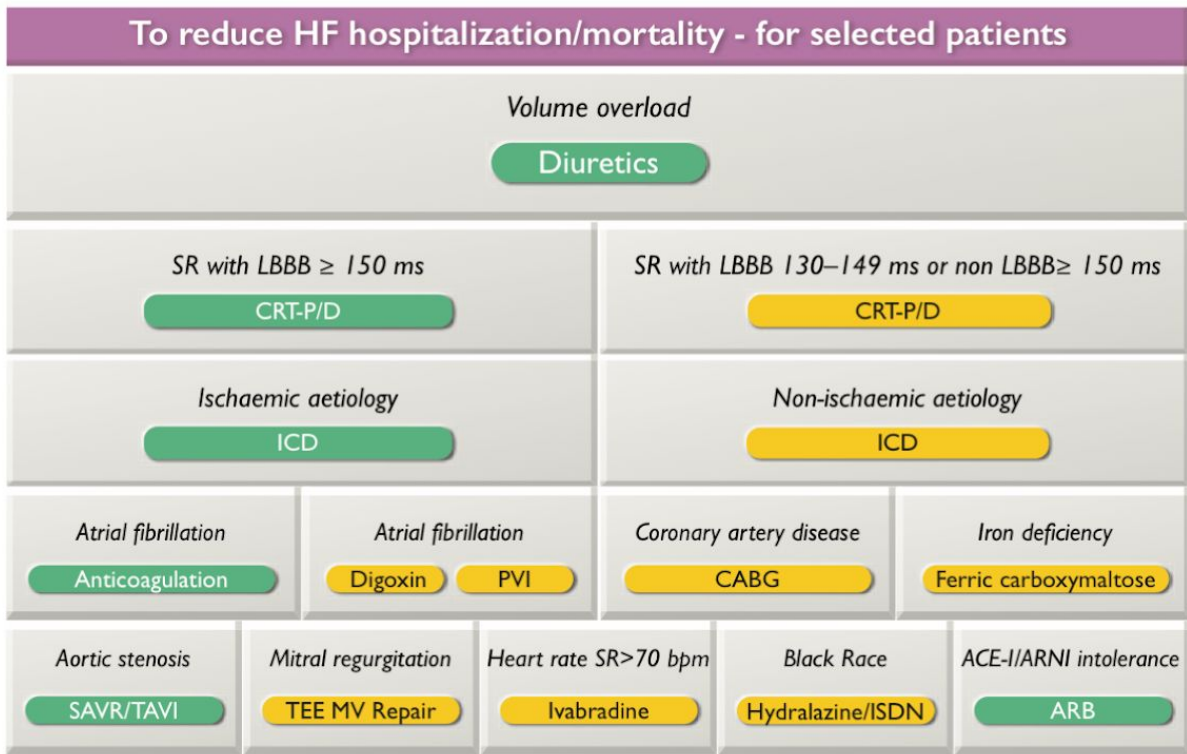
| 7- SGLT-2 inhibitors | |
|----------------------|---|
| Drug name | Dabagliflozin, Empagliflozin |
| M.O.A | <ul style="list-style-type: none"> Work on the proximal convoluted tubule, by inhibiting reabsorption of the glucose. Reduce the blood glucose, systolic and diastolic blood pressure and work as diuretic. |
| Uses | <ul style="list-style-type: none"> Recent studies showed mortality benefit in patients with heart failure. |
| ADRs | <ul style="list-style-type: none"> UTIs, DKA and osteoporosis (long term) |

| hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blockers | |
|--|--|
| Drug name | Ivabradine ² |
| M.O.A | <ul style="list-style-type: none"> Acts on the I_f inward current in the SA node (phase 4), resulting in <u>reduction of heart rate</u>. |
| Uses | <ul style="list-style-type: none"> Only use it if HR is not controlled by BB and remains ≥ 70 bpm and the patient has sinus rhythm. (It is ineffective in patients with atrial fibrillation.) In this group of patients it improve M&M. |

1-Last choice of treating HF along with the digoxin

2- Ivabradine ; Inhibit the Na inflow during the SA nodel action potential phase 4.

Management of Chronic HF cont.



Management cont'

Management of Chronic HF cont.

Anticoagulants

Drug name

Warfarin/NOAC

Uses

- Atrial fibrillation
 - H/o embolic episodes
 - Left ventricular apical thrombus
- (If patient does not suffer from one of these; we do not give Anticoagulant)

Antiarrhythmics(Amiodarone)

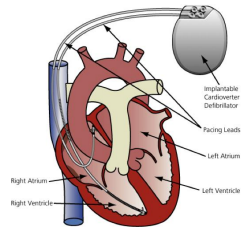
Uses

- Patients with h/o sustained VT or SCD → ICD implant
- Patients with non-sustained ventricular tachycardia
 - Correction of electrolytes and acid base imbalance.
- Most common cause of Sudden Cardiac Death (SCD) in HF patients is ventricular tachyarrhythmia.**

Devices

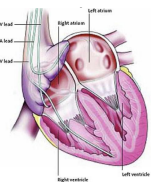
Implantable Cardioverter Defibrillator (ICD)¹

- 1-3 leads + pulse generator
- Sudden onset criteria
- Stability criteria
- Treatment zones
- Pacing
- Cardioversion
- Defibrillation
- Combined CRT-D available



Biventricular pacemaker²

- Used only in patient with Wide QRS complexes & CHF with dilated cardiomyopathy and an EF < 35%
- Resynchronise ventricles by simultaneous
- NICE guidance published 2007



Other assisting devices:

- Temporary ventricular assist devices.
- Implantable ventricular assist devices.

Cardiac Transplant:³

- It has become more widely used since the advances in immunosuppressive treatment.
- Used as the last choice, when all other treatments fail.
- Survival rate: 1 year:80% -90% 2-5 years 70%

These tables show that we should titrate the dose of diuretics carefully (Give low dose initially) to avoid excessive volume depletion, which can cause a fall in cardiac output with hypotension (Cardiogenic shock), lethargy and renal failure.



Doses are not important, you only need to memorize the names with their class.

Table 7.2 Evidence-based doses of disease-modifying drugs in key randomized trials in heart failure with reduced ejection fraction (or after myocardial infarction)

| | Starting dose (mg) | Target dose (mg) |
|---|--------------------|------------------------|
| ACE-I | | |
| Captopril ^a | 6.25 b.i.d. | 50 b.i.d. |
| Enalapril ^a | 5 b.i.d. | 10-20 b.i.d. |
| Lisinopril ^a | 10 b.i.d. | 20-50 b.i.d. |
| Ramipril ^a | 2.5 b.i.d. | 10 b.i.d. |
| Tenidapril ^a | 0.5 b.i.d. | 4 b.i.d. |
| Beta-blockers | | |
| Bisoprolol ^a | 1.25 b.i.d. | 10 b.i.d. |
| Carvedilol ^a | 3.125 b.i.d. | 25 b.i.d. ^b |
| Metoprolol succinate (CRN) ^a | 12.5-25 b.i.d. | 200 b.i.d. |
| Tibololol ^a | 1.25 b.i.d. | 10 b.i.d. |
| ARBs | | |
| Candesartan ^a | 4-8 b.i.d. | 32 b.i.d. |
| Valsartan ^a | 40 b.i.d. | 160 b.i.d. |
| Losartan ^a | 50 b.i.d. | 150 b.i.d. |
| MRA | | |
| Eplerenone ^a | 25 b.i.d. | 50 b.i.d. |
| Spironolactone ^a | 25 b.i.d. | 50 b.i.d. |
| ARNI | | |
| Lisocabaprilan ^a | 4951 b.i.d. | 97103 b.i.d. |
| Hydralazine | | |
| Hydralazine ^a | 5 b.i.d. | 75 b.i.d. |

ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor neprilysin inhibitor; b.i.d. = twice daily; MRA = mineralocorticoid receptor antagonist; i.d. = once daily; CRN = controlled-release; U.S. = up to the three times a day; ^aIndicates an ACE-I when the starting target is derived from post-myocardial infarction trials; ^bIndicates drug when a higher dose has been shown to reduce mortality; normally contraindicated with a lower dose of the same drug, but there is no substantial evidence of diuretic-contraindicated trial and the appropriate dose is uncertain; ^cIndicates a treatment not shown to reduce cardiovascular or all-cause mortality in patients with heart failure (or shown to be noninferior to treatment that does); ^dMaximum dose of 50 mg twice daily can be administered to patients weighing 60 kg.

Table 7.3 Doses of diuretics commonly used in patients with heart failure

| Diuretics | Initial dose (mg) | Usual daily dose (mg) | | |
|--|-------------------|-----------------------|------------|------------|
| Loop diuretics^a | | | | |
| Furosemide | 20-40 | 40-240 | | |
| Bumetanide | 0.5-1.0 | 1-5 | | |
| Torsemide | 5-10 | 10-20 | | |
| Thiazides^a | | | | |
| Bendroflumethiazide | 2.5 | 2.5-10 | | |
| Hydrochlorothiazide | 25 | 12.5-100 | | |
| Metolazone | 2.5 | 2.5-10 | | |
| Indapamide ^b | 2.5 | 2.5-5 | | |
| Potassium-sparing diuretics^a | | | | |
| | +ACE-I/ARB | -ACE-I/ARB | +ACE-I/ARB | -ACE-I/ARB |
| Spironolactone/epplerenone | 12.5-25 | 50 | 50 | 100-200 |
| Amlodipine | 2.5 | 5 | 5-10 | 10-20 |
| Tramterene | 25 | 50 | 100 | 200 |

ACE-I = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; ^aOral or intravenous dose might need to be adjusted according to volume status; weight; excessive doses may cause renal impairment and ototoxicity; ^bDo not use thiazide if estimated glomerular filtration rate < 30 mL/min/1.73 m², except when prescribed synergistically with loop diuretics; ^cIndapamide is a non-thiazide thiazolidine; ^dA mineralocorticoid antagonist (MRA) i.e. spironolactone/epplerenone is always preferred. Amlodipine and tramterene should not be combined with an MRA.

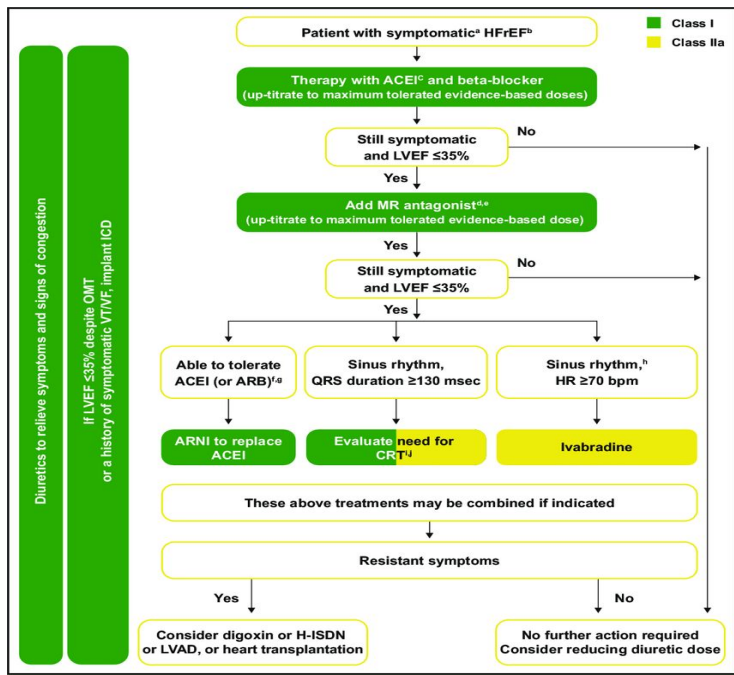
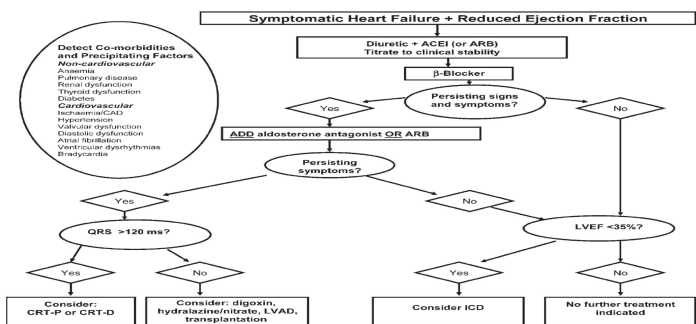
1- Used for those with ischemic cardiomyopathy and EF below 30%. Has mortality benefit.
 2- Indicated in those with dilated cardiomyopathy and an EF under 35% and a wide QRS >140ms who have persistent symptoms. Has mortality benefit.
 3- When maximal therapy (ACEI, BB, spironolactone, diuretics, digoxin) and possibly the biventricular pacemaker fail to control symptoms of CHF, then the only alternative is to seek cardiac transplant.

Management cont'

◀ **There are now 6 medications and 2 devices that reduce all cause mortality in patients with HF:**

| Management | | | | | | |
|--------------------|----------|--------------|------------------|------------|------|-------|
| Medication | ACEi/ARB | Beta blocker | MRA ¹ | Ivabradine | ARNI | SGLT2 |
| NNT mortality 5 yr | 18 | 18 | 15 | 9 | 14 | 16 |
| DEVICES | ICD | | | CRT | | |
| NNT mortality 5 yr | 14 | | | 14 | | |

◀ Management of Chronic HF cont.



| Drugs used in (according to MTB) | |
|---|--|
| Systolic dysfunction | Diastolic dysfunction |
| <ul style="list-style-type: none"> ACEi or ARB BB Spironolactone Diuretics Digoxin | <ul style="list-style-type: none"> Spironolactone Diuretics Uncertain: ACEi, ARBs NOT used: BB, Digoxin |

General recommendations

1. An ACE inhibitor should be given to all patients with heart failure unless there are contraindications. In patients intolerant of ACE inhibitors, ARBs are an alternative (level of evidence, A).
2. In symptomatic patients with heart failure, beta-blockers are recommended to reduce mortality rates (level of evidence, A).
3. Aldosterone antagonists are recommended to reduce mortality rates in certain patients with heart failure. These include patients with current or recent history of dyspnea at rest, and patients with recent myocardial infarction who have systolic dysfunction with either clinically significant signs of heart failure or with concomitant diabetes mellitus (level of evidence, B).
4. For persistently symptomatic black patients with heart failure, direct-acting vasodilators reduce overall mortality rates when added to background therapy with ACE inhibitors, beta-blockers, and diuretics (if needed). Direct-acting vasodilators are also an alternative for patients with heart failure who are intolerant of ACE inhibitors (level of evidence, B).
5. For patients with heart failure and volume overload, diuretics are recommended (level of evidence, B).

Management cont.

◀ Contraindicated drugs EXTRA

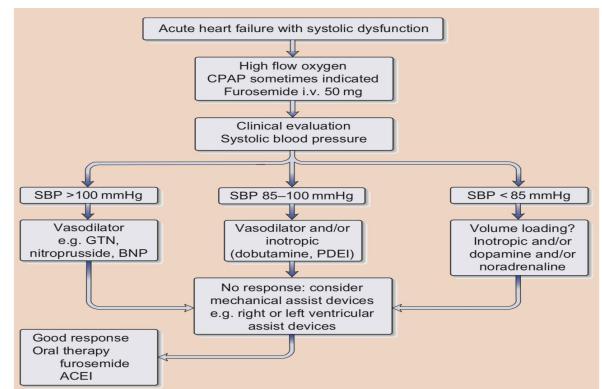
Treatments (or combinations of treatments) that may cause harm in patients with symptomatic (NYHA class II-IV) systolic heart failure:

- 1) **Thiazolidinediones (glitazones)** should not be used as they cause worsening HF and increase the risk of HF hospitalization.
- 2) **Most CCBs (with the exception of amlodipine and felodipine)** should not be used as they have a negative inotropic effect and can cause worsening HF.
- 3) **NSAIDs and COX-2 inhibitors** should be avoided if possible as they may cause sodium and water retention, worsening renal function and worsening HF.
- 4) The addition of an **ARB (or renin inhibitor) to the combination of an ACEI AND a mineralocorticoid antagonist** is NOT recommended because of the risk of renal dysfunction and hyperkalemia

◀ Management of Acute HF EXTRA

- Acute heart failure with pulmonary oedema is a medical emergency that should be treated urgently.

| 16.15 Management of acute pulmonary oedema | |
|--|--|
| Action | Effect |
| Sit the patient up | Reduces preload |
| Give high-flow oxygen | Corrects hypoxia |
| Ensure continuous positive airway pressure (CPAP) of 5–10 mmHg by tight-fitting mask | Reduces preload and pulmonary capillary hydraulic gradient |
| Administer nitrates: IV glyceryl trinitrate (10–200 µg/min) Buccal glyceryl trinitrate 2–5 mg | Reduces preload and afterload |
| Administer a loop diuretic: Furosemide (50–100 mg IV) | Combats fluid overload |
| *The dose of nitrate should be titrated upwards every 10 mins until there is an improvement or systolic blood pressure is <110 mmHg. | |



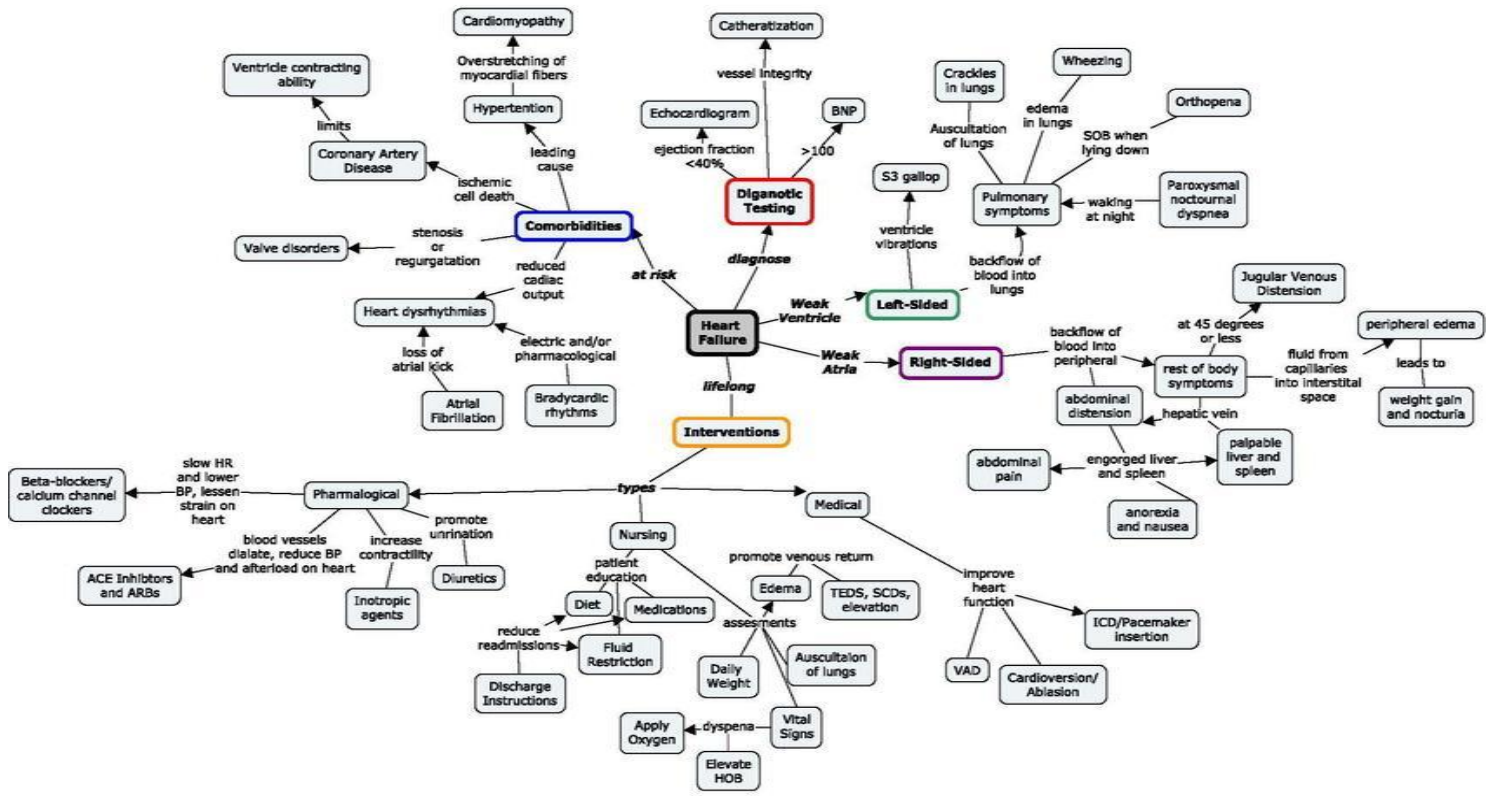
Note: If these measures **prove ineffective use dobutamine.**

◀ Prognosis:

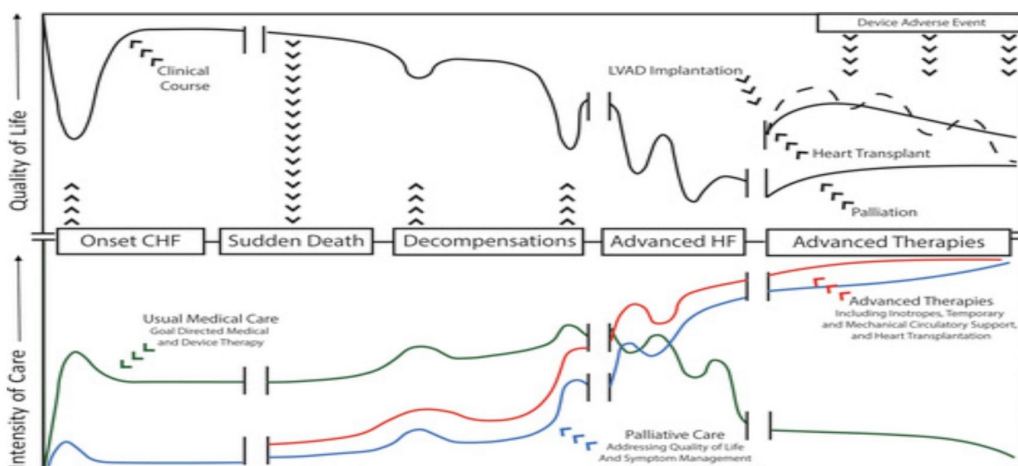
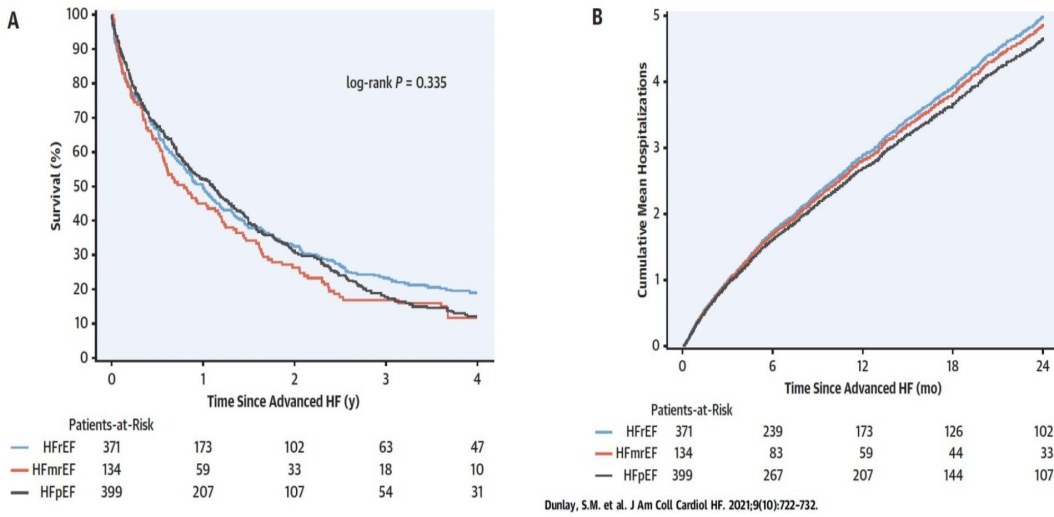
- Annual mortality rate depends on patients symptoms and LV function.
- 5% in patients with mild symptoms and mild ↓ in LV function.
- 30% to 50% in patient with advances LV dysfunction and severe symptoms.
- **40% – 50% of death is due to SCD.**

◀ What factors indicate poor prognosis in HF?

| | |
|------------------------------|---|
| Clinical | <ul style="list-style-type: none"> • High NYHA class, hypotension, tachycardia at rest, JVD, S3 |
| Labs | <ul style="list-style-type: none"> • Hyponatremia, elevated BNP, renal insufficiency |
| EKG | <ul style="list-style-type: none"> • QRS >120, LBBB |
| Echo | <ul style="list-style-type: none"> • Severe reduction in EF, pulmonary hypertension, diastolic dysfunction, RV function impairment |
| Associated conditions | <ul style="list-style-type: none"> • Anemia, AF, DM |

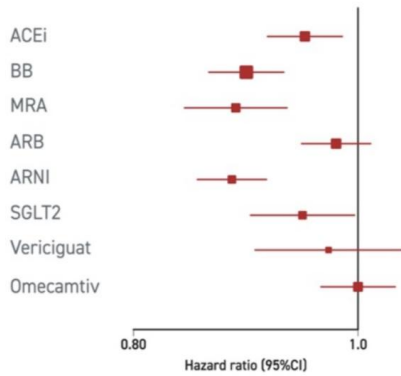


^This mind map has all you need to know about heart failure



Helpful Figures From the Slides

Relative Risk Reduction for All-cause Mortality against Placebo



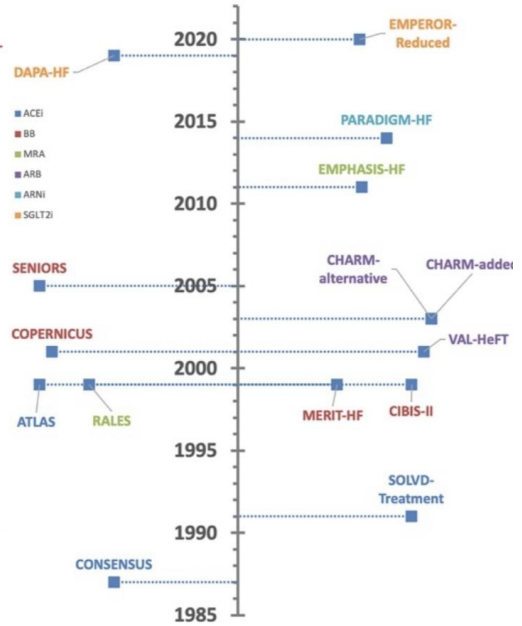
ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; ARNI: angiotensin receptor-neprilysin inhibitor; BB: beta-blocker; MRA: mineralocorticoid receptor antagonist; SGLT2: sodium glucose cotransporter-2
Adapted from Tramp J et al. JACC Heart Fail. 2022 Feb;10(2):73-84.

Medical change

Heart Failure Reviews (2023) 28:1221–1234

Dr. Ismail R Raslan 2023

Historical GDMT trials



How to best prescribe?

HFrEF: LVEF ≤ 40% AND SYMPTOMS

Step 1: Initiate Standard Therapies

ARNI or ACEi/ARB then substitute ARNI

BETA BLOCKER

MRA

SGLT2 INHIBITOR

Step 2: Assess Clinical Factors for Additional Interventions

HR >70 bpm and sinus rhythm
• Consider ivabradine*

Recent HF hospitalization
• Consider vericiguat**

Black patients on optimal GDMT, or patients unable to tolerate ARNI/ACEi/ARB
• Consider combination hydralazine-nitrate

Suboptimal rate control for AF, or persistent symptoms despite optimized GDMT
• Consider digoxin

Initiate standard therapies as soon as possible and titrate every 2-4 weeks to target or maximally tolerated dose over 3-6 months

Step 3: Reassess LVEF, Symptoms, Clinical Risk

NYHA III/IV, Advanced HF or High-Risk Markers

CONSIDER

- Referral for advanced HF therapy (mechanical circulatory support/transplant)
- Referral for supportive/palliative care

LVEF ≤ 35% and NYHA I-IV (ambulatory)

Refer to CCS CRT/ICD recommendations

LVEF > 35%, NYHA I, and Low Risk

Continue present management, reassess as needed

TREAT COMORBIDITIES PER CCS HF RECOMMENDATIONS (INCL. AF, FUNCTIONAL MR, IRON DEF, CKD, DM)
DIURETICS TO RELIEVE CONGESTION (TITRATED TO MINIMUM EFFECTIVE DOSE TO MAINTAIN EUVOLEMIA)

ADVANCE CARE PLANNING AND DOCUMENTATION OF GOALS OF CARE
NON-PHARMACOLOGIC THERAPIES (EDUCATION, SELF-CARE, EXERCISE)

Stage A: At risk for HF but without structural heart disease or symptoms of HF

| | |
|--|---|
| Treatment of cardiovascular risk factors | <ul style="list-style-type: none"> Heart failure medications are not routinely recommended. Treat associated risk factors, e.g., hypertension, dyslipidemia, and diabetes mellitus. |
|--|---|

Stage B: Structural heart disease but without signs or symptoms of HF

| Class | Indication | Administration |
|---------------|---|--|
| ACEIs | <ul style="list-style-type: none"> Every patient with HFrEF | <ul style="list-style-type: none"> Examples 1.Enalapril 2.Ramipril 3.Lisinopril Monitoring: BP, renal function, and potassium 1–2 weeks after initiation or dose change |
| ARBs | <ul style="list-style-type: none"> Patients who cannot tolerate ACEIs (e.g., because of a dry cough) | <ul style="list-style-type: none"> Examples 1.Candesartan 2.Losartan 3.Valsartan Monitoring: BP, renal function, and potassium 1–2 weeks after initiation or dose change |
| Beta Blockers | <ul style="list-style-type: none"> Add once the patient is stable on ACEIs. Avoid in patients with decompensated cardiac failure until they are stabilized. | <ul style="list-style-type: none"> Examples 1.Bisoprolol 2.Carvedilol 3.Metoprolol Monitoring: <ul style="list-style-type: none"> Aim to titrate slowly to the target or maximum tolerated dose; if hypotension occurs, consider reducing the dose of ACEI to accommodate beta-blocker titration. Assess for symptoms of worsening heart failure or development of bradycardia |

Stage C (Additions) : Structural heart disease with prior or current symptoms of HF

| | Indication | Administration |
|---------------------------|--|--|
| Aldosterone antagonist | <ul style="list-style-type: none"> All HFrEF patients with NYHA class II–IV symptoms and an LVEF of < 35% Consider adding for patients with HFpEF | <ul style="list-style-type: none"> Examples 1.Spirolactone 2.Eplerenone Monitoring: regularly for hyperkalemia |
| Loop & Thiazide diuretics | <ul style="list-style-type: none"> All patients with fluid retention Begin treatment with loop diuretics to treat volume overload. Thiazides may be added for a synergistic effect. | <ul style="list-style-type: none"> Examples 1. Loop 1.1 Torsemide 1.2 Furosemide 1.3 Bumetanide 2. Thiazide diuretics 2.1 Chlorthalidone 2.2 Hydrochlorothiazide 2.3 Metolazone Monitoring: <ul style="list-style-type: none"> Titrate the dose according to weight and volume status Regularly check electrolytes. |
| Isosorbide dinitrate | <ul style="list-style-type: none"> Patients who cannot tolerate ACEIs or ARBs Certain African American patients with HFrEF | <ul style="list-style-type: none"> Examples 1.Fixed-dose combination 2.Separate dosing of ISDN and hydralazine Monitoring: volume depletion and hypotension |
| ARNIs | <ul style="list-style-type: none"> HFrEF and persistent or worsening symptoms despite adequate treatment regimen with first-line drugs <ul style="list-style-type: none"> Administered as combination (valsartan-sacubitril): valsartan is an ARB, while sacubitril is a neprilysin inhibitor. Sacubitril impairs the breakdown of angiotensin II, substance P, and natriuretic peptides (e.g., BNP) → ↑ natriuresis, diuresis, and vasodilation → ↓ extracellular fluid Increased reduction in mortality compared to ACEI or ARB therapy | <ul style="list-style-type: none"> Examples: sacubitril/valsartan Initiation: <ul style="list-style-type: none"> Stop ACEIs (elevated risk of angioedema otherwise). Administer ARNI no earlier than 36 hours after the last dose of ACEI. Monitoring: <ul style="list-style-type: none"> Monitor for hypotension, dizziness, or cough. Regular laboratory studies for hyperkalemia |

Stage D (Additions): Refractory HF

| | |
|---------------------|--|
| Additional measures | <ul style="list-style-type: none"> Most patients require invasive interventions or a change in focus to palliative care. Consider continuous intravenous inotropic support as a bridge to transplant or MCS (see also “Treatment of refractory acute heart failure” in “Acute heart failure”). |
|---------------------|--|

A 70-year-old man presents to the emergency department complaining of increased shortness of breath with minimal exercise, cough, and fatigue. These symptoms began 2 weeks ago and have progressed gradually. He reports he used to feel this way “all the time” years ago but that this has not happened much since he began using his inhalers and his “water pill.” He also has a history of chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), coronary artery disease (CAD), diabetes mellitus, hypertension, and 30-pack-year of smoking. He denies swelling of the extremities, fever or chills, productive cough, chest pain, or palpitations. He cannot remember the names of his medications but says he has not missed any doses. When asked about his diet, he says he has been eating more hot soup since the weather has gotten colder. His temperature is 37.5°C (99.5°F), blood pressure is 135/90 mm Hg, heart rate is 90/min, respiratory rate is 18/min, and oxygen saturation is 94% on room air. Examination of the neck reveals mild jugular venous distention. Examination of the lungs reveals loud crackles throughout the lung fields bilaterally. Examination of the heart reveals a laterally displaced point of maximum impulse with no murmurs, rubs, or gallops. There is mild clubbing of the extremities, as well as pitting edema of the lower extremities to the knee, bilaterally. His plasma brain natriuretic peptide level on rapid bedside assay is 500 pg/mL, and an x-ray of the chest reveals perivascular haziness, interstitial edema, and an enlarged cardiac silhouette.

Q1: What conditions should be included in the differential diagnosis?

CAD, COPD, and CHF each may present with dyspnea on exertion and fatigue. It is of primary importance to distinguish between them when evaluating the presenting symptoms. Etiologies of gradually worsening shortness of breath and fatigue can include both cardiac and pulmonary diseases, including the following: Anemia, Heart failure secondary to ischemia/infarction, dysrhythmia, valvular dysfunction, infection, or volume overload, Lung infections (pneumonia, bronchitis, bronchiectasis), Mechanical impairment of ventilation, Pulmonary edema, Pulmonary embolism, Sepsis.

Q2: What's the most likely diagnosis?

CHF exacerbation leading to pulmonary edema. This patient's dyspnea, jugular venous distension, and tachypnea in the presence of crackles, pulmonary edema, elevated brain natriuretic peptide (BNP) level, and cardiomegaly suggest an acute exacerbation of CHF. An exacerbation of COPD is unlikely given that this patient does not have fever, productive cough, or wheezing. Additionally, the patient reported increasing intake of soup, a particularly salty food, which can significantly increase water retention, thereby worsening CHF.

Q3: What are the typical laboratory and imaging findings in this condition?

In addition to an x-ray of the chest that may show pulmonary edema, patients with CHF exacerbations may have the following: Decreased hematocrit (anemia may exacerbate CHF), Increased potassium, creatinine, and blood urea nitrogen levels (renal failure may exacerbate CHF), Increased plasma BNP level, which is usually elevated in CHF exacerbations, A chest radiograph showing cardiomegaly, cephalization of pulmonary vessels, and/or pleural effusion, ECG changes showing left ventricular hypertrophy, arrhythmias, or ischemia or low-voltage or old infarcts (in fact, a normal ECG makes systolic dysfunction highly unlikely), ECG showing abnormal ventricular size (dilated, hypertrophic, or restrictive cardiomyopathy) or function (systolic or diastolic).

Q4: What's the most appropriate treatment for this patient?

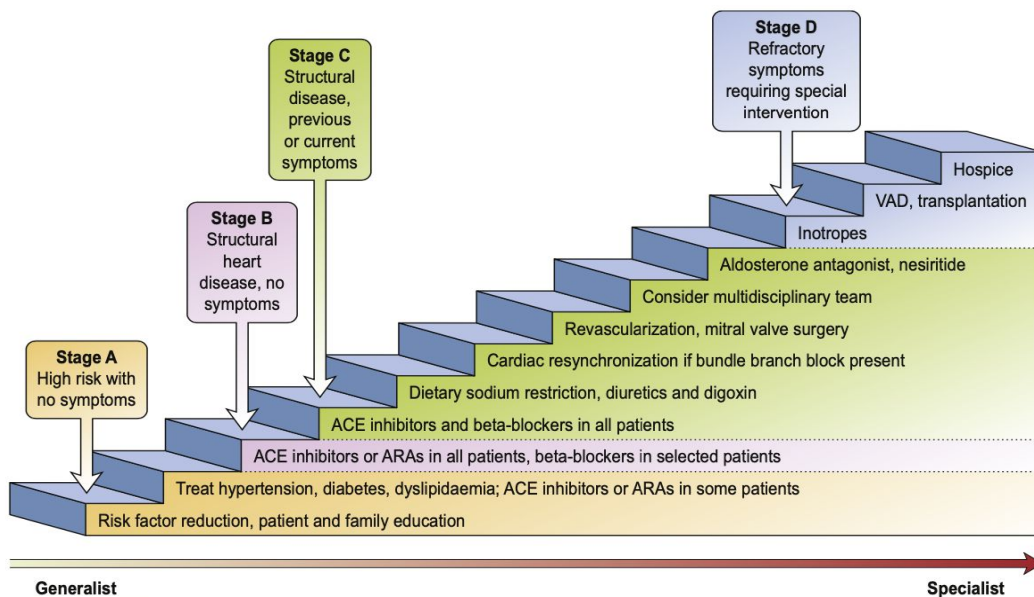
This patient appears to have stage C heart failure. His physical exam and x-ray of the chest show evidence of myocardial hypertrophy, and he is having recurrent symptoms. He should be admitted to the hospital for a trial of intravenous diuresis (which often succeeds when oral diuretics fail). An echocardiogram should be obtained to evaluate for left ventricular structural abnormalities as well as determine an ejection fraction. He should be prescribed an ACE inhibitor or an angiotensin receptor blocker (given his atherosclerosis, hypertension, and diabetes mellitus), a diuretic (given his evidence of fluid retention), and digitalis (if his ejection fraction is less than 25%, as this has been shown to reduce hospitalization). He should also receive frequent blood pressure and weight monitoring, exercise counseling, and possibly an aldosterone antagonist (depending on his ejection fraction). In addition, he should take aspirin and a statin for his CAD.

Summary



| Heart failure | | |
|---|---|---|
| Classification | Systolic dysfunction (HFrEF) | Diastolic dysfunction (HFpEF) |
| | <ul style="list-style-type: none"> Impaired contractility, EF is reduced. Causes: IHD, HTN, VHD etc | <ul style="list-style-type: none"> Impaired ventricular filling, EF is preserved. Causes: HTN leading to myocardial hypertrophy. |
| | High Output HF | Low Output HF |
| | Conditions that increase demand on CO, causing a clinical picture of heart failure due to an excessively high CO e.g. Severe anemia, thyrotoxicosis, pregnancy, A/V fistula, Beriberi and Paget's disease | Cardiac output is inadequate to perfuse the body (i.e. EF <40%), or can only be adequate with high filling pressures. |
| | Acute HF | Chronic HF |
| | <ul style="list-style-type: none"> Acute left heart failure presents with a sudden onset of dyspnoea at rest that rapidly progresses to acute respiratory distress, orthopnoea and prostration. Often there is a clear precipitating factor (e.g. large MI, aortic valve dysfunction, myocarditis, and cardiogenic shock) which may be apparent from the history. | <ul style="list-style-type: none"> Patients with chronic heart failure commonly follow a relapsing and remitting course, with periods of stability and episodes of decompensation*, leading to worsening symptoms that may necessitate hospitalisation |
| | Left sided HF | Right sided HF |
| | <ul style="list-style-type: none"> Reduction in left ventricular output and an increase in left atrial and pulmonary venous pressure. This increases pulmonary vascular resistance and causes pulmonary hypertension, which in turn impairs right ventricular function. Hallmark: Increased LVEDP Symptoms: Dyspnea, Orthopnea, PND Signs: Displaced PMI, Cardiomegaly, S3, S4 and crackles at lung bases. | <ul style="list-style-type: none"> Reduction in right ventricular output and an increase in right atrial and systemic venous pressure. The most common cause of right Hf is left HF other causes include: Pulmonary HTN and chronic lung disease (cor pulmonale) Symptoms: Peripheral edema, Nocturia, Abdominal symptoms Signs: JVD, Hepatomegaly and Ascites |
| Treatment | Acute HF | |
| | <ol style="list-style-type: none"> Oxygen Loop diuretics (Furosemide) Nitrate (IV and Buccal Glyceryl trinitrate) Morphine: Can be of value in distressed patients but must be used sparingly, as they may cause respiratory depression and exacerbation of hypoxaemia and hypercapnia. <p>Note: If these measures prove ineffective use dobutamine.</p> | |
| | Chronic HF | |
| | HFrEF | HFpEF |
| <ul style="list-style-type: none"> ACEI or ARB BB Spironolactone Diuretics Digoxin | <ul style="list-style-type: none"> Spironolactone Diuretics Uncertain: ACEI, ARBs NOT used: BB, Digoxin | |

- **ACE Inhibitors and ARBs should be given to all patients with systolic dysfunction at any stage of disease. The beneficial effects of ACEI and ARBs occur with any drug in the class.**
- **Sacubitril with valsartan is an alternative to an ACE inhibitor. Sacubitril lowers mortality and is the right answer when there is cough with an ACE inhibitor.**
- **What is the management of a patient with severe CHF who develops gynecomastia? Switch spironolactone to eplerenone.**
- **Don't walk into the exam without being 100% clear on which drugs lower mortality in CHF.**
- **Most common cause of death from HF is sudden death from ventricular arrhythmias. Ischemia provokes ventricular arrhythmias.**



Generalist

Specialist

Fig. 30.57 Stages of heart failure and treatment options for systolic heart failure. ACE, angiotensin-converting enzyme; ARA, angiotensin II receptor antagonist; VAD, ventricular assisted device.

Box 30.29 Pharmacological therapy in acute heart failure

| Drug | Dose | Indications/mechanism of action |
|---|---|---|
| Myocardial oxygenation | | |
| Oxygen | 35–50% inspired oxygen concentration | Ensure airway is patent and maintain arterial saturation at 95–98% |
| Non-invasive positive pressure ventilation (NIPPV), e.g. CPAP | | Use if failing to maintain arterial saturation Increases pulmonary recruitment and functional residual capacity – reduces work of breathing |
| Intubation/mechanical ventilation | | Use if patient is failing to maintain arterial saturation and is fatigued (reduced respiratory rate, increased arterial CO ₂ , confusion) |
| Opiate | | |
| Morphine | 2.5–5.0 mg i.v. (with antiemetic metoclopramide 10 mg i.v.) | Use in agitated patient Relieves dyspnoea, venous and arterial dilation |
| Antithrombin | | |
| Low-molecular-weight heparin | e.g. Enoxaparin 1 mg/kg s.c. x2 daily ACS or 40 mg s.c. daily prophylaxis | Use in patients with AHF, ACS or atrial fibrillation, or for DVT prophylaxis Caution if creatinine clearance <30 mL/min |
| Vasodilators | | |
| Glycerol trinitrate | 10–200 µg/min i.v. infusion | Reduces pulmonary congestion; at low doses causes venodilation, reducing preload; at high doses causes arterial vasodilation, reducing afterload Ensure BP >85–90 mmHg |
| Sodium nitroprusside | 0.3–5 µg/kg per min i.v. infusion | Use in severe AHF where there is predominantly high afterload, e.g. hypertensive AHF Needs arterial BP monitoring for profound hypotension |
| Diuretic | | |
| Furosemide | Bolus 40–100 mg i.v. or infusion 5–40 mg/h | Low doses produce vasodilation, reduce right atrial pressure and PCWP, and promote diuresis Need to monitor sodium, potassium and creatinine |
| Inotropes | | |
| Dopamine | Low dose <2 µg/kg per min Medium dose >2 µg/kg per min High dose >5 µg/kg per min | Low dose acts on peripheral dopamine receptors to produce vasodilation (renal, splanchnic, coronary, cerebrovascular) and may improve diuresis although evidence of significant improvements in outcomes is lacking Medium dose acts on β-receptors to increase myocardial contractility and cardiac output High dose acts on α-receptors, causing vasoconstriction and increasing total peripheral resistance (increases afterload, PAP) |
| Dobutamine | 2–20 µg/kg per min (patients on beta-blockers may need high dose) | Stimulates β ₁ and β ₂ -receptors, producing vasodilation. Increases heart rate and cardiac output, and also diuresis as haemodynamics are improved |
| Milrinone | Bolus 25–75 µg/kg over 10–20 min then 0.375–0.75 µg/kg per min | Inhibits phosphodiesterase and maintains cAMP Increases cardiac output and stroke volume, reduces PAP/PCWP/total peripheral resistance/BP |
| Levosimendan | Bolus 12–24 µg/kg over 10 min then 0.05–2 µg/kg per min | Positive inotropic drug with vasodilator effects by increasing sensitivity of contractile proteins to calcium and opening potassium channels Increases cardiac output and reduces PCWP |
| Vasopressors | | |
| Noradrenaline (norepinephrine) | 0.2–1.0 µg/kg per min | Stimulates α-receptors Increases total peripheral resistance and BP |
| Adrenaline (epinephrine) | Bolus 1 mg at resuscitation then 0.05–0.5 µg/kg per min | Stimulates α ₁ , β ₁ - and β ₂ -receptors Increases cardiac output, heart rate, total peripheral resistance and BP |
| Cardiac glycoside | | |
| Digoxin | 0.5 mg i.v. repeated after 2–8 h | Inhibits myocardial sodium/potassium ATPase, leading to increased calcium and sodium exchange Increases cardiac output and slows AV conduction Use in AF; avoid in ACS |

Box 30.25 Drugs used in heart failure

| Drug | Dose (initial/maximum) | Precautions |
|--|---|---|
| ACE inhibitors/ARAs | | |
| Ramipril | 1.25–2.5 mg daily/10 mg daily | Monitor renal function and use with caution if baseline serum creatinine >250 µmol/L or baseline blood pressure <90 mmHg |
| Enalapril | 2.5 mg daily/10 mg x2 daily | |
| Captopril | 6.25 mg x3 daily/50 mg x3 daily | |
| Candesartan | 4 mg daily/32 mg daily | |
| Lisinopril | 2.5–5 mg daily/20–40 mg daily | |
| Perindopril | 2 mg daily/8–16 mg daily | |
| Valsartan | 80 mg daily/320 mg daily | |
| Losartan | 50 mg daily/100 mg daily | |
| Beta-adrenoceptor-blocking drugs | | |
| Bisoprolol | 1.25 mg daily/10 mg daily | Use with caution in obstructive airways disease, bradyarrhythmias |
| Carvedilol | 3.125 mg x2 daily/50 mg x2 daily | Avoid in acute heart failure until patient is cardiovascularly stable |
| Metoprolol succinate (CR/XL) | 12.5–25 mg daily/200 mg daily | |
| Nebivolol | 1.25 mg daily/10 mg daily | |
| ARNIs | | |
| Angiotensin receptor neprilysin inhibitor Sacubitril/valsartan | 24/26–49/51 mg x2 daily/ 97/103 mg x daily | Monitor renal function, check for hyperkalaemia. Discontinue ACE inhibitor 3 days prior to starting, discontinue ARA the day of starting. |
| Diuretics | | |
| Furosemide | 20–40 mg daily/250–500 mg daily | Monitor renal function and check for hypokalaemia and hypomagnesaemia |
| Bumetanide | 0.5–1.0 mg daily/5–10 mg daily | |
| Bendroflumethiazide | 2.5 mg daily/10 mg daily | Rarely need more than 2.5 mg daily. Reduced efficacy when eGFR<30 mL/min/1.73 m ² |
| Metolazone | 2.5 mg daily/10 mg daily | Use in severe heart failure |
| Aldosterone antagonists | | |
| Spironolactone | 12.5–25 mg daily/50 mg daily | Monitor renal function, check for hyperkalaemia, gynaecomastia with spironolactone |
| Eplerenone | 25 mg daily/50 mg daily | |
| Cardiac glycosides | | |
| Digoxin | 0.125–0.25 mg daily (reduce dose in elderly or in renal impairment) | Use with caution in renal impairment or conduction disease, and with amiodarone |
| Vasodilators | | |
| Isosorbide dinitrate | 20–40 mg x3 daily | |
| Hydralazine | 37.5–75 mg x3 daily | |
| β Channel blocker | | |
| Ivabradine | 5 mg daily/7.5 mg x2 daily | Use with caution in sick sinus syndrome; AV block |

Lecture Quiz

Q1: A 78-year-old woman is admitted with heart failure. The underlying cause is determined to be aortic stenosis. Which sign is most likely to be present?

- A- Pleural effusion on chest x-ray
- B- Raised jugular venous pressure (JVP)
- C- Bilateral pedal oedema
- D- Bibasal crepitations

Q2: A 78-year-old woman is admitted to your ward following a 3-day history of shortness of breath and a productive cough of white frothy sputum. On auscultation of the lungs, you hear bilateral basal coarse inspiratory crackles. You suspect that the patient is in congestive cardiac failure. You request a chest x-ray. Which of the following signs is not typically seen on chest x-ray in patients with congestive cardiac failure?

- A- Lower lobe diversion
- B- Cardiomegaly
- C- Pleural effusions
- D- Alveolar edema

Q3: A 71-year-old man is being treated for congestive heart failure with a combination of drugs. He complains of nausea and anorexia, and has been puzzled by observing yellow rings around lights. His pulse rate is 53/minute and irregular and blood pressure is 128/61 mmHg. Which of the following medications is likely to be responsible for these symptoms?

- A- Lisinopril
- B- Spironolactone
- C- Digoxin
- D- Furosemide

Q4: A 71-year-old woman presents to ambulatory clinic with a chief complaint of dyspnea upon exertion. Over the past few weeks, she has had a chronic cough and shortness of breath when walking more than two city blocks. She has a long history of hypertension that has been poorly controlled in recent years. On physical examination, she has an elevated jugular venous pulse and rales are evident on lung examination. Cardiac enzymes are negative. Which modality is the most appropriate next step in distinguishing systolic from diastolic heart failure?

- A- Cardiac catheterization
- B- Clinical judgment based on physical examination
- C- CT scan of the chest
- D- Echocardiography

Q5: A 65-year-old woman with chronic systolic heart failure (left ventricular ejection fraction, 30%) comes for a routine clinic visit. She reports that she is dyspneic climbing one light of stairs and uses two pillows to sleep at night. She has intermittent lower extremity edema, especially after eating a salty meal. Her medications include lisinopril 20 mg daily, carvedilol 25 mg twice daily, spironolactone 25 mg daily, and torsemide 40 mg daily. On examination, she has a heart rate of 70 beats per minute, blood pressure of 110/70 mm Hg, no jugular venous distention, normal heart sounds, a II/VI holosystolic murmur at the apex, and trace-1+ peripheral edema. Her laboratory values are notable for sodium 140 mEq/L, potassium 4.8 mEq/L, blood urea nitrogen 20 mg/dL, and creatinine 1.2 mg/dL. What is the next most appropriate step in her management?

- A- Continue her current medications.
- B- Increase lisinopril to 30 mg daily.
- C- Stop lisinopril and start sacubitril/valsartan 49/51 mg twice daily after 36-hour washout.
- D- Increase torsemide to 60 mg daily.

Q6: A 74-year-old man with hypertension, coronary artery disease, GERD, and osteoarthritis presents for follow-up. He had an ST segment myocardial infarction 2 years prior and underwent successful stenting of a complete LAD arterial occlusion. For the past 3 weeks, he has noted worsening dyspnea on light exertion coupled with lower extremity swelling. He has had no recurrent chest pain. His medications include metoprolol, nifedipine, aspirin, and rosuvastatin. On examination, his blood pressure is 126/80 mm Hg. His heart rate is 70 beats per minute. His jugular venous pressure is 14 cm H₂O. The first and second heart sounds are normal, and a third heart sound is appreciated. There is lower extremity edema to the knee bilaterally. A stress echocardiogram reveals mild anterior wall hypokinesis at rest, and all walls augment appropriately with stress. His left ventricular ejection fraction at rest is estimated at 40%. In addition to diuresis and discontinuation of nifedipine, what is the most appropriate management?

- A- Add hydralazine and isosorbide mononitrate.
- B- Add clopidogrel.
- C- Add lisinopril.
- D- Add spironolactone.

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