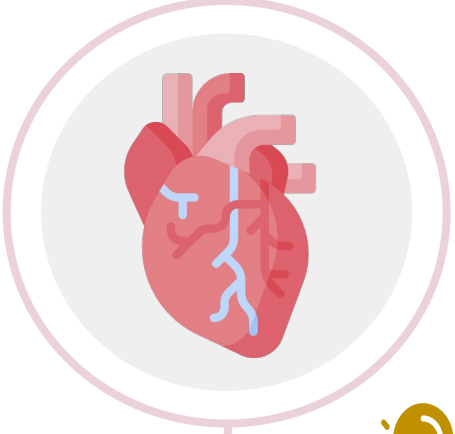
Heart failure (2) (Management & Prognosis)



Online MedEds High-Yield Brilliant Summary!

Objectives :

- ★ Know different classifications of heart failure.
- ★ Know the causes and precipitation factors for heart failure decompensation.
- ★ Describe the Pathophysiology, therapies that improve survival, and prognosis.

Editing file

Color index

- Original text
- Females slides
- Males slides
- Doctor's notes 438
- Doctor's notes 439
- Text book
- Important
- Golden notes
- Extra

Management

◀ Introduction to HF management

- **Correction of reversible causes** (1st step in T_x) 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)

Management tools

Lifestyle modification

- Diet[1]
- Fluid intake
- Exercise shows mortality benefit
- Smoke cessation
- Weight reduction

Pharmacological

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

Surgical

- Device therapy
- Assisting devices
- Transplant

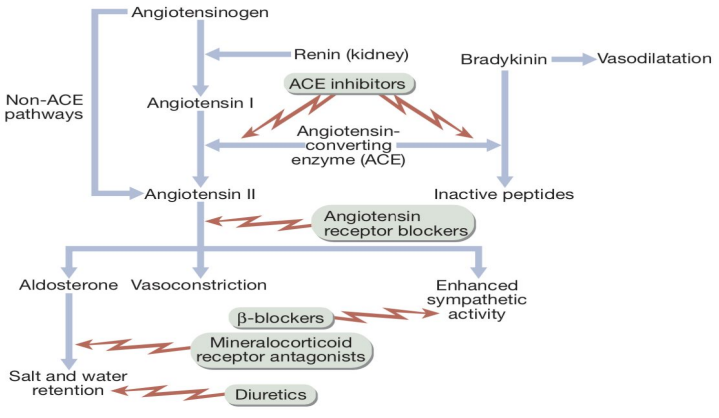
◀ Management of Chronic HF

General measures

- **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 and fluid restriction (1.5-2L/day, about 8 cups)
- **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 treatment

1. **ACEI/ARB**
2. **β-Blockers**
3. **Diuretic**
4. **Digoxin**
4. **Vasodilators**
5. **SGLT-2 inhibitors**



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'

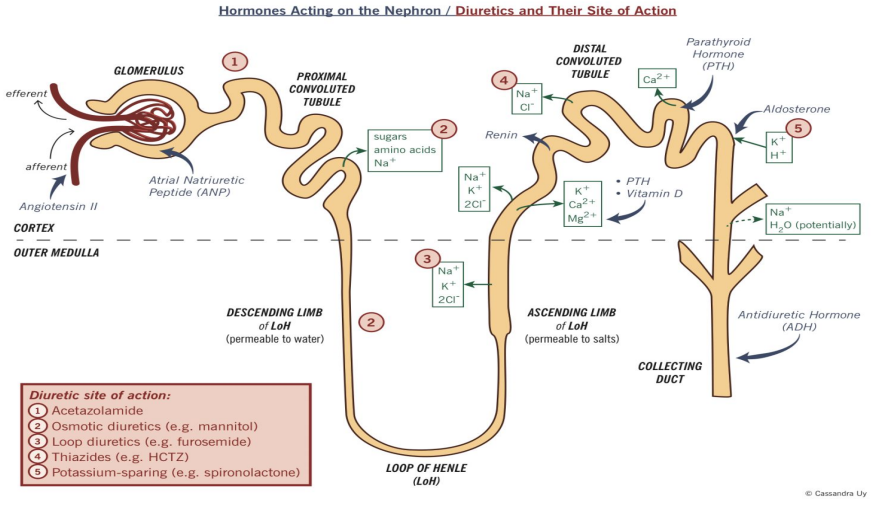
◀ Management of Chronic HF cont.

3 diuretics that we can use with HF pt
- Thiazides
- Loop diuretic
- K sparing diuretic spironolactone

Diuretics (for fluid overload)		
Group	**Loop diuretics** **Furosemide "Lasix"*** (20-320 mg QD) **Bumetanide "Bumex"** (1-8mg) **Torsemide** (20-200mg)	**Thiazide diuretic** **(Hydrochlorothiazides*, Chlorthalidone, Metolazone* most commonly used with furosemide)**
General	• **Most effective in controlling symptoms** (Dyspnea & Peripheral edema), but have **not been shown to reduce mortality** or improve prognosis.	
M.O.A	• **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	• Block Na reabsorption in loop of henle and distal convoluted tubules • **↓Na+- Cl** cotransporter in early distal convoluted tubule
Dr: might come in exam **Uses**	• **Most potent diuretics** used in moderate/severe HF.	• Used for mild HF • Ineffective with GFR < 30 --/min.
ADR	• Pre-renal azotemia[1] • Hypokalemia[2] • Skin rash • **Ototoxicity**[4] (single dose dependent, not accumulative) in long term use • urate retention,causing gout. • hypercalciuria leading to increased risk of calcium-based renal stones • hypomagnesaemia • decreased glucose tolerance hyperglycemia	• Pre-renal azotemia[1] • Skin rashes • Neutropenia • Thrombocytopenia • Hyperglycemia • ↑ Uric Acid[3] • Hepatic dysfunction • Hyponatremia low sodium bcs of high excretion • Hypercalcemia

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



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 cont'

◀ Management of Chronic HF cont.

K+ sparing agents			
Group	**Spironolactone (Aldosterone inhibitor)**	**Eplerenone**	**Triamterene, amiloride**
General	• Relatively weak diuretics with a potassium-sparing action		
M.O.A[1]	• Acts at the collecting duct by competitive inhibition of cytoplasmic aldosterone receptors →↑ Excretion of Na+,Cl & ↓Excretion of K+,H+,NH4	• Binds to the mineralocorticoid receptor and blocks the binding of aldosterone	• Acts on distal tubules to ↓ K secretion
Uses	• 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	• **Reduces mortality** in patients with **acute** myocardial infarction and heart failure.	-
Adverse effects	• **Gynecomastia** (If pt develop this, switch to eplerenone), **Hyperkalemia[2]** 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'

β-Blockers			
Drug name	**Bisoprolol**	**Carvedilol**	**Metoprolol**
Uses	• 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 ★ In addition to improved LV function multiple studies **show improved survival**[1] • **"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. • The benefit of beta blockers likely stems from: ○ Anti-Ischemic effect , Decreasing HR (Decrease O2 consumption) Antiarrhythmic effect		
Contraindications	• Severe decompensated CHF (AHF, Pulmonary edema) • Peripheral Vascular Disease (PVD)		

BB trials:

- US Carvedilol studies 1996
  - 65% decrease mortality in carvedilol group
  - 27% reduction in hospitalisations, reduction in progression of CCF
- CIBIS-II – Bisoprolol vs. placebo
  - 34% reduction mortality (42% reduction in sudden death and 32% hospitalisations)
- MERIT-HF - metoprolol
- COPERNICUS
  - NYHA class IV, EF < 25%
  - 35% reduction in mortality with carvedilol
- CAPRICORN - 23% reduction in mortality post MI

◄ Inhibitors of renin-angiotensin- aldosterone system.

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

Angiotensin II type 1 receptor blockers (ARBs)			
Drug name	**losartan**	**irbesartan**	**valsartan**
Uses	• **Second-line therapy** in certain conditions when ACE I are contraindicated **(angioneurotic edema, cough)** • Has comparable effect to ACEI. 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	• 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 euvolemic, 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 cont'

◄ Management of Chronic HF cont.

Angiotensin-converting enzyme inhibitors (ACEI)			
Drug name	**Perindopril**	**Lisinopril**	**Quinapril**
M.O.A	• 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 → Vasodilation • They also ultimately inhibit cardiac remodelling		
Uses	★ 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 improve survival by 30-35% in CHF patients : ○ 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	• Angioedema • Renal insufficiency we have to balance the medication & monitor, Hepatic dysfunction • Rash, Hyperkalemia[1] ★ **Cough** (If patient develops cough switch to ARBs) • **The major side-effect is first-dose hypotension.** ○ 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	• 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

مو نعطيهم راس انهبتر لانه يزيد الطين بلّه

Management cont'

◄ Management of Chronic HF cont.

Angiotensin Receptor - Neprilysin inhibitors (ARNi)	
Drug name	**Combination of Valsartan & Sacubitril**

General info	• Recent FDA approval (2015)
	• The only product available (valsartan/sacubitril)
	  ○ Valsartan = ARB
	  ○ Sacubitril = prodrug for sacubitrilat Inhibit neprilysin which breakdown the vasoactive peptides.

M.O.A	• Inhibits neprilysin which is responsible for the **breakdown of** the endogenous diuretics **ANP** and **BNP**.
Uses	• Used if patient LVEF ≤ 35% and still symptomatic with ACE/ARB • In this specific group of patients it **improves M&M.**

Positive Inotropes		
Drug name	**Digitalis Glycosides (Digitoxin, Digoxin)[1,2]**	
M.O.A	★ +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 • 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	• Indicated in patients with heart failure and atrial fibrillation. • In patients with severe 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**
	• 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)	• Anorexia • Nausea, vomiting • Headache • Xanthopsia sotoma (yellow vision) • Disorientation
Digoxin toxicity treatment	**1)** Hold the medications **2)** Observation. **3)** In case of A/V block or severe bradycardia ⟶ atropine followed by temporary PM if needed. **4)** In life threatening arrhythmia ⟶ digoxin-specific fab antibodies. **5)** Lidocaine and phenytoin could be used – try to avoid D/C cardioversion in non life threatening arrhythmia.	

- Positive inotropes 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 cont'

◀ Management of Chronic HF cont.

Vasodilators[1]		
Drug name	**Hydralazine**	**Nitrate**
M.O.A	• **Reduction of afterload** by arteriolar vasodilation → reduce LVEDP, O2 consumption,improve myocardial perfusion, stroke volume and COP	• **Reduction of preload** By venous dilation → ↓ the venous return → ↓ the load on both ventricles.
Uses	• 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 combincation is recommended for African • Americans with NYHA class III–IV HFrEF receiving optimal therapy with ACE inhibitors and beta blockers. • HDZ/ISDN can be useful to reduce morbidity or mortality in • patients with current or prior symptomatic HFrEF who cannot be given an ACE inhibitor or ARB because of drug intolerance, hypotension, or renal insufficiency, unless contraindicated. • **Has mortality benefit.** • Their use is limited by pharmacological tolerance and hypotension.	

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	
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.**

hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blockers	
Drug name	**Ivabradine**
M.O.A	• Acts on the I_f inward current in the SA node (phase 4), resulting in reduction of heart rate.
Uses	• 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

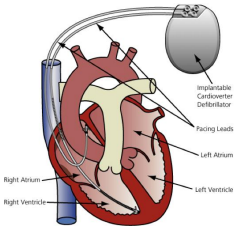
◄ Management of Chronic HF cont.

SGLT-2 inhibitors	
Drug name	**Dabagliflozin, Empagliflozin**
M.O.A	• 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	• Recent studies showed mortality benefit in patients with heart failure.
ADRs	• UTIs, DKA and osteoporosis (long term)

Devices

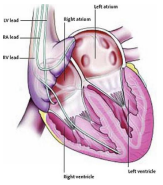
Implantable Cardioverter Defibrillator (ICD)[1]

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



Biventricular pacemaker[2]

- Used only in patient with Wide QRS complexes & CHF with dilated cardiomyopathy and an EF < 35%
- Resynchronise ventricles by simultaneous pacing
- 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.
- Survival rate:
  - 1 year 80% - 90%
  - 5 years 70%

Theses tables show that we should titre 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.

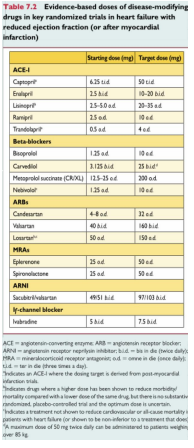


Table 7.2 Evidence-based doses of disease-modifying drugs in key randomized trials in heart failure with reduced ejection fraction (or after myocardial infarction)

	Starting dose (mg)	Target dose (mg)
ACE-I		
Captopril[a]	6.25 t.i.d.	50 t.i.d.
Enalapril	2.5 b.i.d.	10–20 b.i.d.
Lisinopril[a]	2.5–5.0 o.d.	20–35 o.d.
Ramipril	2.5 o.d.	10 o.d.
Trandolapril[a]	0.5 o.d.	4 o.d.
Beta-blockers		
Bisoprolol	1.25 o.d.	10 o.d.
Carvedilol	3.125 b.i.d.	25 b.i.d.[c]
Metoprolol succinate (CR/XL)	11.5–23 o.d.	200 o.d.
Nebivolol[a]	1.25 o.d.	10 o.d.
ARBs		
Candesartan	4–8 o.d.	32 o.d.
Valsartan	40 b.i.d.	160 b.i.d.
Losartan[a,c]	50 o.d.	150 o.d.
MRAs		
Eplerenone	25 o.d.	50 o.d.
Spironolactone	25 o.d.	50 o.d.
ARNI		
Sacubitril/valsartan	49/51 b.i.d.	97/103 b.i.d.
If-channel blocker		
Ivabradine	5 b.i.d.	7.5 b.i.d.

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor neprilysin inhibitor; b.i.d. = bis in die (twice daily); MRA = mineralocorticoid receptor antagonist; o.d. = omne in die (once daily); t.i.d. = ter in die (three times a day).
[a]Indicates an ACE-I where the dosing target is derived from post-myocardial infarction trials.
[b]Indicates drugs where a higher dose has been shown to reduce morbidity/mortality compared with a lower dose of the same drug, but there is no substantial randomized, placebo-controlled trial and the optimum dose is uncertain.
[c]Indicates a treatment not shown to reduce cardiovascular or all-cause mortality in patients with heart failure (or shown to be non-inferior to a treatment that does).
[d]A maximum dose of 50 mg twice daily can be administered to patients weighing over 85 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		
Torasemide	5–10	10–20		
Thiazides[b]				
Bendroflumethiazide	2.5	2.5–10		
Hydrochlorothiazide	25	12.5–100		
Metolazone	2.5	2.5–10		
Indapamide[c]	2.5	2.5–5		
Potassium-sparing diuretics[d]				
	+ACE-I/ ARB	-ACE-I/ ARB	+ACE-I/ ARB	-ACE-I/ ARB
Spironolactone/ eplerenone	12.5–25	50	50	100–200
Amiloride	2.5	5	5–10	10–20
Triamterene	25	50	100	200

ACE-I = angiotensin-converting enzyme inhibitor, ARB = angiotensin receptor blocker.
[a]Oral or intravenous; dose might need to be adjusted according to volume status/weight; excessive doses may cause renal impairment and ototoxicity.
[b]Do not use thiazides if estimated glomerular filtration rate <30 mL/min/1.73 m^2, except when prescribed synergistically with loop diuretics.
[c]Indapamide is a non-thiazide sulfonamide.
[d]A mineralocorticoid antagonist (MRA) i.e. spironolactone/eplerenone is always preferred. Amiloride and triamterene should not be combined with an MRA.

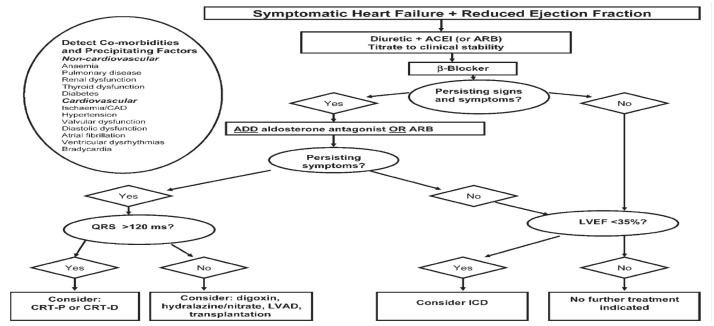
1- Used for those with ischemic cardiomyopathy and EF below 30%. Has mortality benefit.
2- Indicated in those with dilated cardiomyopathy and an EF under 35% and a wide QRS >140ms who have persistent symptoms. Has mortality benefit.
3- When maximal therapy (ACEI, BB, spironolactone, diuretics, digoxin)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

Management cont'

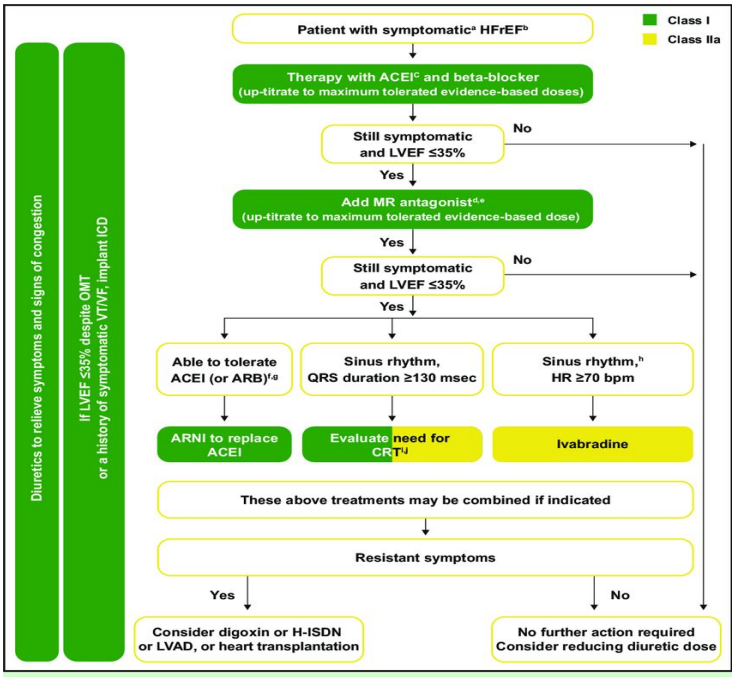
◀ There are now 6 medications and 2 devices that reduce all cause mortality in patients with HF:

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**
• ACEI or ARB • BB • Spironolactone • Diuretics • Digoxin	• 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).

1- k+ sparing diuretics

Management cont.

◀ Contraindicated drugs

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

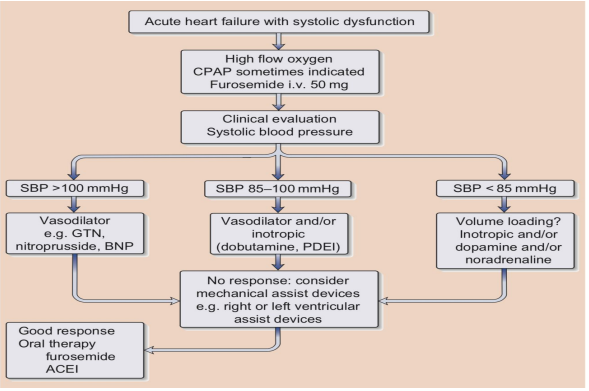
◀ Management of Acute HF

- 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	• High NYHA class, hypotension, tachycardia at rest, JVD, S3
Labs	• Hyponatremia, elevated BNP, renal insufficiency
EKG	• QRS >120, LBBB
Echo	• Severe reduction in EF, pulmonary hypertension, diastolic dysfunction, RV function impairment
Associated conditions	• Anemia, AF, DM

EXTRA

Treatment of HF

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

Treatment of cardiovascular risk factors	• 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	• Every patient with HFrEF	• Examples **1.Enalapril 2.Ramipril 3.Lisinopril** • Monitoring: BP, renal function, and potassium 1–2 weeks after initiation or dose change
ARBs	• Patients who cannot tolerate ACEIs (e.g., because of a dry cough)	• Examples **1.Candesartan 2.Losartan 3.Valsartan** • Monitoring: BP, renal function, and potassium 1–2 weeks after initiation or dose change
Beta Blockers	• Add once the patient is stable on ACEIs. • Avoid in patients with decompensated cardiac failure until they are stabilized.	• Examples **1.Bisoprolol 2.Carvedilol 3.Metoprolol** • Monitoring: ○ 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	• All HFrEF patients with NYHA class II–IV symptoms and an LVEF of < 35% • Consider adding for patients with HFpEF	• Examples **1.Spironolactone 2.Eplerenone** • Monitoring: regularly for hyperkalemia
Loop & Thiazide diuretics	• All patients with fluid retention • Begin treatment with loop diuretics to treat volume overload. • Thiazides may be added for a synergistic effect.	• 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: ○ Titrate the dose according to weight and volume status ○ Regularly check electrolytes.
Isosorbide dinitrate	• Patients who cannot tolerate ACEIs or ARBs • Certain African American patients with HFrEF	• Examples 1.**Fixed-dose combination** 2.**Separate dosing of ISDN and hydralazine** • Monitoring: volume depletion and hypotension
ARNIs	• HFrEF and persistent or worsening symptoms despite adequate treatment regimen with first-line drugs ○ 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	• Examples: sacubitril/valsartan • Initiation: ○ Stop ACEIs (elevated risk of angioedema otherwise). ○ Administer ARNI no earlier than 36 hours after the last dose of ACEI. • Monitoring: ○ Monitor for hypotension, dizziness, or cough. ○ Regular laboratory studies for hyperkalemia

Stage D (Additions): Refractory HF

Additional measures	• 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”).

Case Summary

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)

- Impaired contractility, EF is reduced.
- Causes: IHD, HTN, VHD etc

Diastolic dysfunction (HFpEF)

- Impaired ventricular filling, EF is preserved.
- Causes: HTN leading to myocardial hypertrophy.

High 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

Low Output HF

Cardiac output is inadequate to perfuse the body (i.e. EF <40%), or can only be adequate with high filling pressures.

Acute HF

- 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.

Chronic HF

- 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

- **Reduction in left ventricular output** and an **increase in left atrial and pulmonary venous pressure. T**his 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.

Right sided HF

- **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

1) **Oxygen**
2) **Loop diuretics** (Furosemide)
3) **Nitrate** (IV and Buccal Glyceryl trinitrate)
4) **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.

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

Chronic HF

HFrEF

- ACEI or ARB
- BB
- Spironolactone
- Diuretics
- Digoxin

HFpEF

- Spironolactone
- Diuretics
- Uncertain: ACEI, ARBs
- **NOT used:** BB, Digoxin

EXTRA

Helpful figures & Tips

- **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.**

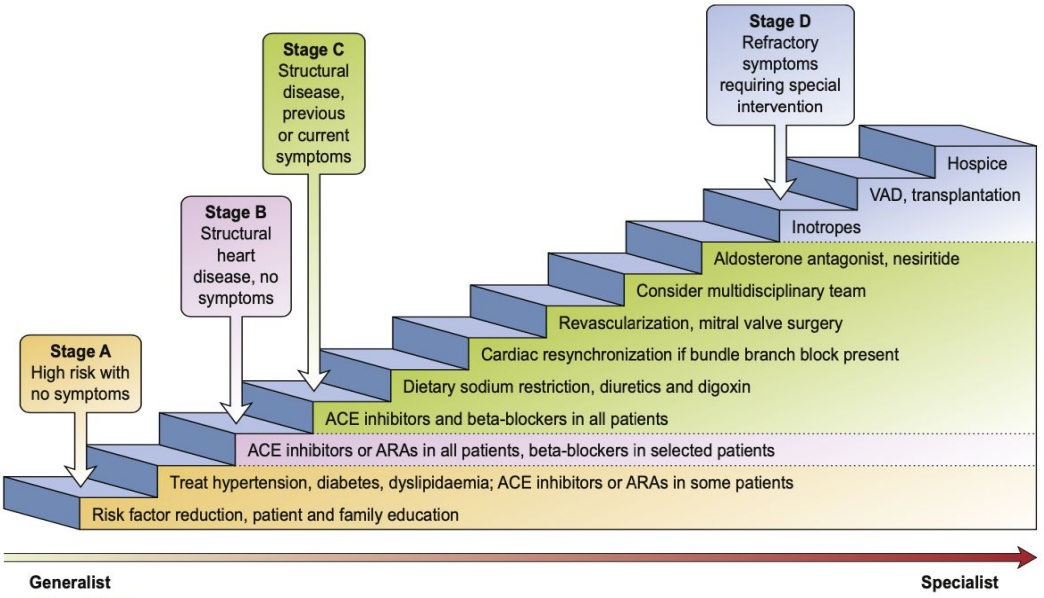


Fig. 30.57 Stages of heart failure and treatment options for systolic heart failure. ACE, angiotensin-converting enzyme; ARA, angiotensin II receptor antagonist; VAD, ventricular assisted device.

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. ×2 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		
Glyceryl 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	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 >2 μg/kg per min	Medium dose acts on β-receptors to increase myocardial contractility and cardiac output
	High dose >5 μg/kg per min	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, 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 2–6 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 ×2 daily	
Captopril	6.25 mg ×3 daily/50 mg ×3 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 ×3 daily	
Hydralazine	37.5–75 mg ×3 daily	
I_f Channel blocker		
Ivabradine	5 mg daily/7.5 mg ×2 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 128/61mmHg. 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 dis- tention, 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. here 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. he 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..

Answers: Q1:D | Q2:A | Q3:C | Q4:D | Q5:C | Q6:C

Answers Explanation File!

GOOD LUCK !

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