# Heart failure

Is a progressive clinical syndrome associated with impairment of the ability of the ventricle to fill with (diastolic ) or eject blood (systolic).

- Coronary artery disease and HTN are the leading cause of HF.

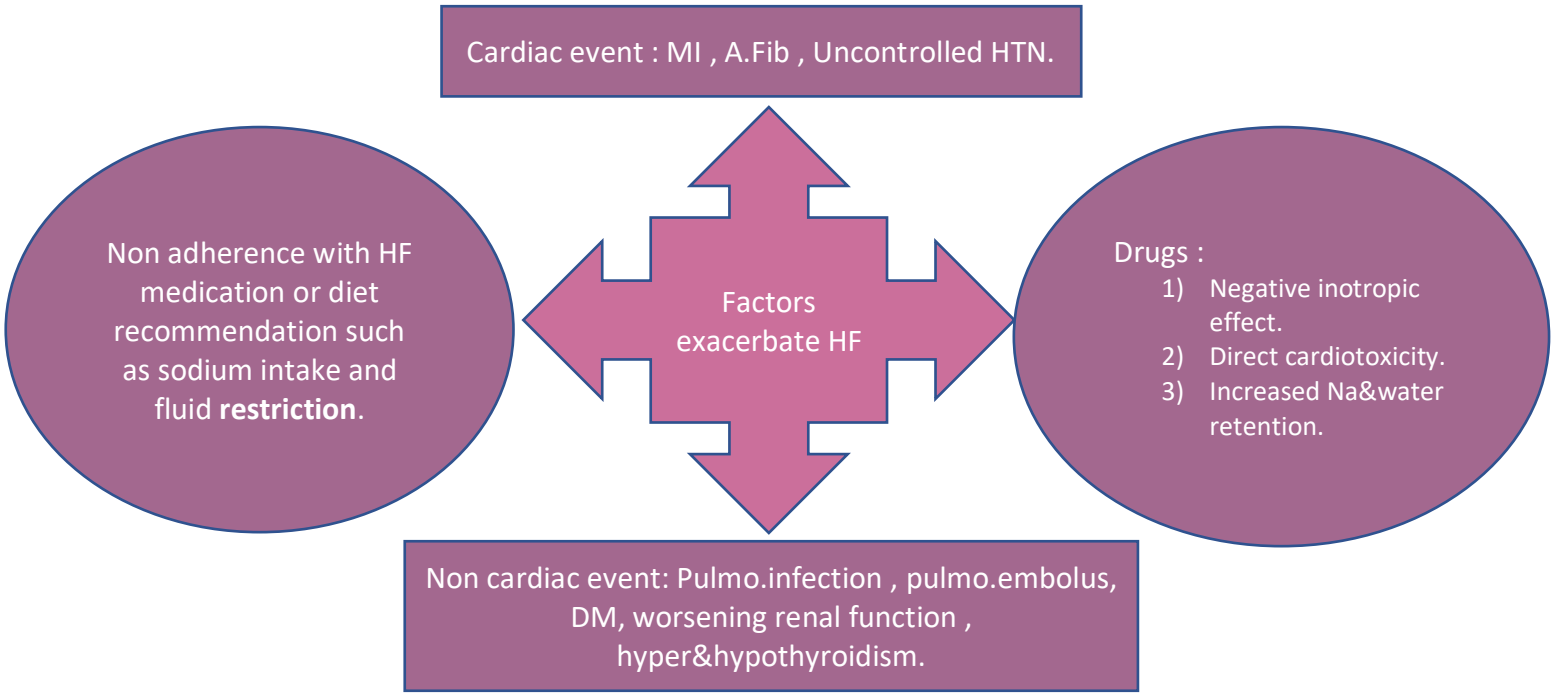
## HF with reduced ejection fraction (HFrEF)

- There is decrease in cardiac output , result in activation of compensatory response to maintain adequate CO
- Compensation done by : activation of SNS and RAAS result in vasoconstriction , Na and water retention , ventricular hypertrophy and remodeling.
- Causes of systolic dysfunction: MI , dilated cardiomyopathy , ventricular hypertrophy ,pressure overload(syst. Or pulmo. HTN , aortic or pulmo valve stenosis),volume overload (valve regurg. , shunt , high output state.

## HF with preserved ejection fraction(HFpEF)

- Is primarily due to diastolic dysfunction of the heart (disturbances in relaxation )
- Causes : MI , ventricular hypertrophy , increase in ventricular stiffness , infiltrative myocardiopathy ( amyloidosis , sarcoidosis , fibrosis ) , mitral or tricuspid valve stenosis , pericardial disease ( pericarditis , tamponade )

- Means : changes in both myocardial calls and extracellular matrix resulting in changes in ventricular SHAPE (from ellipse to sphere) , SIZE ,STRUCTURE, FUNCTION.
- Changes in size and shape will further depress the mechanical performance of the heart and sustain progression of remodeling.
- Angiotensin 2 , NE , endothelin , aldosterone , vasopressin and inflammatory cytokines play an imp.role in initiating signal transduction cascade responsible for remodeling and are toxic to other organs, so HF is a systemic and cardiac disease.




***EXAMPLE ON DRUGS :**

- **Negative inotropic effect :**

1) Antiarrhythmics (disopyramide , flecainide,propafenone)
2)Beta blockers (propranolol , metoprolol , carvedilol)
3)CCB (verapmil , diltiazem)

-**Cardiotoxicity:**

Doxorubicin , epirubicin , daunomycin , ethanol , cyclophosphamide , trastuzumab , bevacizumab , ifosfamide , lapatinib , sunitinib , imatinib , amphetamine , cocaine.

**-Sodium and water retention:**

NSAID , cox2 inhibitor , rosiglitazone , pioglitazone , steroid , androgen&estrogen , high dose salicylate , high Na conraining drug (ticarcillin disodium).

## Therapy of CHRONIC HF

**GOALS OF Tx : Improve quality of life , relieve symptoms , prevent or minimize hospitalization , slow progression of the disease , prolong survival .**

**General measures in Tx : Accurate diagnosis , identification and Tx of risk factors , elimination the precipitating factors , appropriate pharmacologic and nonpharmacologic therapy , close monitoring and follow-up.**

***Note : Tx of HFrEF is based on numerous large , randomized , double-blind , multicenter clinical trials , while HFpEF based on studies in relatively small groups of patients and on clinical experience.**

**Things you do before giving medication : determine the cause , treat the underlying disease , revascularization or anti-ischemic in pt with CHD , stop drugs that aggravate HF , restriction of physical activity in pt with acute congestive symptoms but after stabilization you have to advice the pt to do physical exercise , restriction of Na and water intake .**

**patient with hyponatremia <130 or with persistent volume retention despite high diuretic doses and Na restriction should limit fluid intake to 2 L/DAY.**
**Be careful with na and water restriction in pt with HFpEF because there is risk of hypotension , low output state and renal insufficiency .**

Tx OF **HFpEF**: control HR&BP, alleviate causes of MI, reduce volume, maintain sinus rhythm.

**Symptoms targeted tx :**

- Decrease pulmo. Venous pressure to reduce left ventricular volume by : diuretics , nitrate , salt restriction.
- Reduce o2 demand to reduce HR&BP by : b blocker , ccb (verapamil,diltiazem),ACEI , ARB.
- Maintain atrial contraction to restore sinus rhythm by : cardioversion of A.Fib
- Improve exercise tolerance by using positive inotropic agent.

**Disease targeted tx :**

- Prevent or treat MI by : b blocker , nitrate , verapamil and diltiazem.
- Prevent or regress ventricular hypertrophy by antihypertensive drugs.

**Mechanism targeted tx :**

- Modify myocardial and extramyocardial mechanism by diuretics , ACEI, ARB , spironolactone.
- Modify intracellular and extracellular mechanism by diuretics , ACEI , ARB.

## Some NOTES about HFpEF medications:

**Diuretics :**
***Loop or thiazide can be used.**
***Do not reduce preload excessively , this will reduce stroke volume and CO.**
***Aldosterone antagonist can be used if there is no risk of hyperkalemia or other contraindication.**

**ACE inhibitor :**
***used in all pt with atherosclerotic cardiovascular disease or DM.**
***ARB is alternative if patient develops cough or angioedema.**

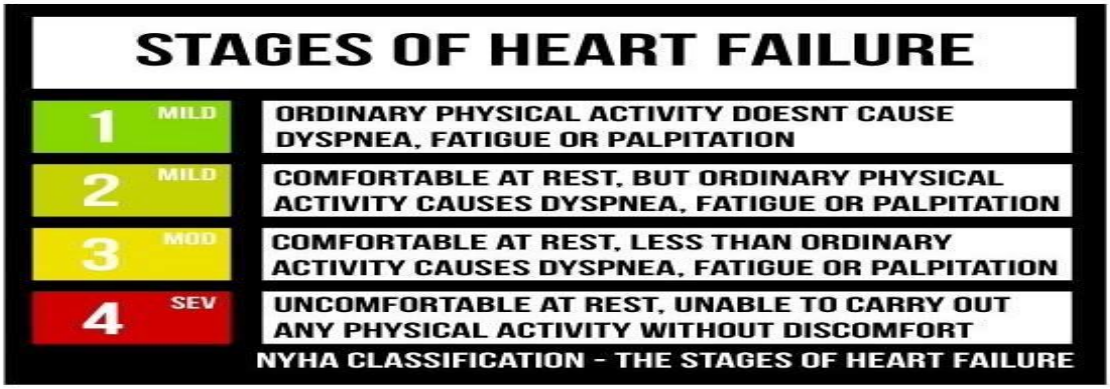
**B-blocker :**
***should be considered if pt has one or more :**

1) **MI**
2) **HTN**
3) **A.Fib**

**CCB :**
***verapamil or diltiazem.**

***used in pt with A.Fib who is not responded to b-blocker.**

***nondihydropyridine or dihydropyridine can be used for angina & HTN.**




Tx OF HFrEF (stage A,B,C,D)

**Stage A :**

- Treat the risk factors (HTN,DM,SMOKING ,dyslipidemia) *risk factors act synergistically to develop HFREF&HFPEF
- ACE I OR ARB & STATINS are imp to prevent HF in pt with cardiovascular risk factors.

**Stage B** :

- They have structural heart disease without HF symptoms , so the aim of tx is minimize remodeling process.
- No Hx of MI : ACE I OR ARB & B-blocker.
- WITH HX of MI : ACE I OR ARB & evidence based b blocker & statin .

**Stage C :**

- Patient with structural disease and symptoms .
- ACE I OR ARB & evidence based b blocker ; to slow HF progression , reduce morbidity&mortality , improve symptoms.
- LOOP diuretics , aldosterone antag. , hydralazine-isosorbide dinitrate.
- Digoxin in selected pt (ivabradine , sacubitril/valsartan).
- ICD , CRT , Biventricular pacemaker can be used.

**Stage D :**

- Is advanced,refractory or end stage HF.
- Special therapy : mechanical circulatory support , continuous IV prositive inotrope , cardiac transplantation &Tx in stage A-C.
- Restriction of Na and fluid , high doeses of diuretics(loop&thiazide) , ultrafiltration to remove excess fluid. NOTE : those pt may be less tolerant to ACEi (hypotension,worsen renal insufficiency) , b-blocker (worsen HF) , so starting with low doses , slow upward titration and close monitoring are imp.

| Medications | | **HFpEF** | **HFrEF** |
|---|---|---|---|
| B-BLOCKER | Decrease HR , prolong diastole , modify hemodynamic response to exercise. | | Improve the inotropic state and modify LV remodeling. |
| DIURETICS | Doses are much smaller than → | | |
| CCB | Improve exercise capacity , treat HTN&CAD , they lower HR. | | Should be avoided |

## Some NOTES about HFrEF medication :

### Diuretics

-Benefits : reduce symptoms associated with fluid retention / improve exercise tolerance & quality of life / reduce hospitalization / reduce pulmo&peripheral edema through reduction of preload .
- They do not prolong survival .
-Risks : over-diuresis lead to hypotension and renal injury specially in pt with ACE I OR B-BLOCKER.
-Hypotension more common in HFpEF ; small change in volume causes large change in filling pressure and cardiac output.
-Thiazide or thiazide like diuretics (metolazone,indapamide) can be used with loop diuretics in pt with mild fluid retention.
-Loop are imp to restore and maintain euvolemia , they induce prostaglandin-mediated increase in renal blood flow, so coadministration of NSAID with diminish diuretic efficacy.
-Unlike thiazide , loop can be used even in impaired renal function.

### ACE I

-They attenuate ventricular remodeling , myocardial fibrosis , apoptosis , cardiac hypertrophy , NE release , vasoconstriction , Na & water retention , lower glomerular capillary pressure.
-Bradykinin is increased due to the release of histamine & prostaglandin.
-Captopril , ramipril , trandolapril are used in post – MI pt.
-Monitoring is imp ; there is risk of worsening renal function and/or hyperkalemia.
-They improve survival 20-30%.

### ARB (candesartan,losartan,valsartan)

-Attenuate ventricular remodeling .
-No release OF bradykinin , so they´re used in pt who can´t tolerate cough&edema from ACEi
-Angiotensin 2 can be formed in many tissues including heart through pathways (chymase ,cathepsin ,kallikrein.

### B-BLOCKER (carvedilol, metoprolol succinate ,bisoprolol)

-They decrease ventricular mass , improve the sphericity of V , decrease systolic& diastolic volume; all these are called Reverse Remodeling.
-Used in all **stable** patient with mild or well controlled symptoms .
-Also , used in asymptomatic pt with low EF , to decrease the progression .
-B-blocker are used after giving ACEi , because there is risk of decompensation if they are used first.
-Patient with tachycardia or K concentration preclude due to ACEi , may benefit from initiating b blocker.
-DO NOT USE B-BLOCKER IN PT WITH IV INOTROPIC SUPPORT.
-VERY IMP to give HFpEF b-blocker ; they cant tolerate tachycardia and may promote ischemia due to increase in o2 demand , but be careful not to induce excessive bradycardia because they decrease cardiac output.

### Aldosteron antagonist

-Spironolactone , eplerenone
-they have potassium sparing effect , attenuate atherogenesis , oxidative stress cause by aldosterone.
-attenuate cardiac fibrosis by inhibiting cardiac extracellular matrix and collagen deposition.
-spironolactone decrease mortality 30% , they cause gynecomastia & hyperkalemia.
-eplerenone decrease mortality 15% , it causes hyperkalemia.
- people more susceptible to develop hyperkalemia : impaired renal function / fail to decrease k supplement / DM / high k food intake / use ACEI , ARB , NSAID .
-things you do to decrease risk of hyperkalemia:
1)Avoid starting in female with Cr >2 and male >2.5 or CrCL<30 , pt with worsen renal function, serum k >5 , Hx of hyperkalemia .
2)start with low dose & stop k supplement
3)avoid NSAID,ACEI,ARB , high k food
4)monitor serum k weekly then monthly , if it exceeds 5.5 mg/dl , reduce or stop the drug.

# Drug therapy for selected patient with HFrEF

## Nitrate & Hydralazine (combination)

-IF there is contraindication for using ACEI/ARB then give NITRATE (venodilator , decrease preload) & HYDRALAZINE (vasodilator , decrease afterload).

-Hydralazine reduces oxidative stress & mortality .
-Nitrate attenuate myocardial remodeling , reduce cardiac hypertrophy ,dilation and mortality.
- combination is important , 3 times daily
-It provides limited benefit to patients with HFpEF unless they have angina , they will benefit from nitrate.

## ARB/Neprilysin inhibitor (fixed dose combination)

-Neprilysin is a zinc dependant metalloprotease that break down the natriuretic peptides ANP & BNP bradykinin , it causes vasodilation . natriuresis and diuresis **if** you inhibit it by medication called **Sacubitril**.

## Valsartan / Sacubitril (combination)

-useful in HFrEF
- Side effect : hypotension , dizziness , hyperkalemia , cough , angioedema .
-Drug interaction : don't use with ACEI , ARB , Aliskiren (direct renin inhibitor).
-CONTRAINDICATION (Hx of angioedema , pregnancy , hyperkalemia , renal artery stenosis , severe hepatic impairement , renal dysfunction , diabetic pt taking aliskiren.

## Ivabradine

-It controls the heart rate and slows the spontaneous depolarization of SA node .
- ONLY 2 indication for this drug :
1) patient with HFrEF & HR > 70 that is receiving max. tolerated Tx with B-BLOCKER
2) " " " " with contraindication to B-BLOCKER.
-Is metabolized by CYP3A4 , so avoid taking it with CYP3A4 inhibitors (itraconazole , macrolide ,hiv protease inhibitor , verapmil , diltiazem , grapefruit juice )
-AVOID taking it with CYP3A4 inducers (St.Johns wort , rifampin , phenytoin)
-Side effect : QT prolongation , bradycardia , effect on vision (transient brightness) , atrial fibrillation.

## Digoxin

-Is positive inotropic drug , improves cardiac function , no benefit on mortality or hospitalization .
-No benefit in HFpEF with normal sinus rhythm , but pt with HFpEF&A.Fib may benefit .
- is not a first line agent in HF.

Please read slides from 80-88
The doctor didn't explain them , he said just read them .
Thank you <3