Updated Management of Heart Failure

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Points to be discussed:

- What is heart failure?
- Epidemiology of HF.
- Stages and different types of heart failure
- Causes of HF
- Clinical presentation
- Investigation work up for HF
- Management of HF
- Updated management and trials
- HF in special conditions
- Summary

What is heart failure?

- Simply, "**When cardiac output is inadequate for body's requirements**."

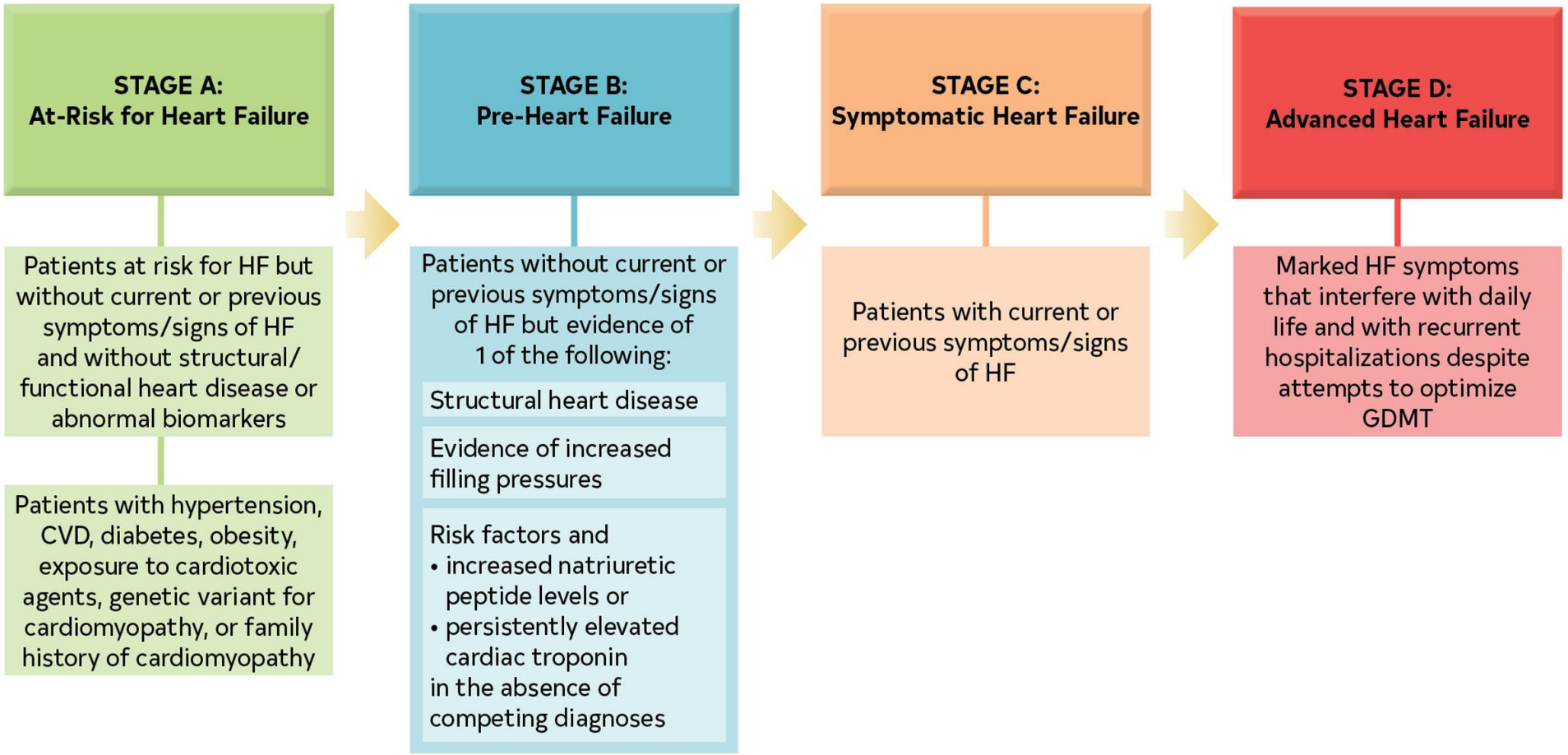
(*Jordan KM, Cameron JS, Snaith M et al,.oxford journals 2010*)

- HF is a complex clinical syndrome with symptoms and signs that result from any structural or functional **impairment of ventricular filling or ejection of blood.** *(AHA 2022)*

Epidemiology of HF:

- According to WHO 2024 estimate, global prevalence of heart failure is 64 million people
- Significant cause of CVD related morbidity and mortality
- Increase in the incidence in low to middle income countries (recent trends)
- In 2019, the global age-standardized prevalence and years lived with disability rates for heart failure were 711.90 (95% uncertainty interval [UI], 591.15–858.29) and 63.92 (95% UI, 41.49–91.95) per 100 000 population, respectively.

Stages of heart failure: (ACC/AHA)



Trajectory of stage C HF: (NYHA staging)

New Onset/De Novo HF:

- Newly diagnosed HF
- No previous history of HF

Resolution of Symptoms:

- Resolution of symptoms/ signs of HF

Stage C with previous symptoms of HF with persistent LV dysfunction	HF in remission with resolution of previous structural and/or functional heart disease*

Persistent HF:

- Persistent HF with ongoing symptoms/signs and/or limited functional capacity

Worsening HF:

- Worsening symptoms/ signs/functional capacity

NYHA classification of HF based on symptoms:

NYHA Class	Level of Clinical Impairment
I 	No limitation of physical activity. Ordinary physical activity does not cause undue breathlessness, fatigue, or palpitations.
II 	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
III 	Marked limitation of physical activity. Comfortable at rest, but less than ordinary physical activity results in undue breathlessness, fatigue, or palpitations.
IV 	Unable to carry on any physical activity without discomfort. Symptoms at rest can be present. If any physical activity is undertaken, discomfort is increased.

Older classification:

- Based on the involvement, and presentation:
- **A) Right heart failure:**
- Resulting from reduction in the right ventricular output and increase in right atrial and systemic venous pressure
- Common causes: Chronic lung disease, pulmonary embolism, and pulmonary valve stenosis
- Clinical features: Peripheral edema, ascites, raised JVP, tender hepatomegaly, nausea, anorexia, facial engorgement, epistaxis etc.

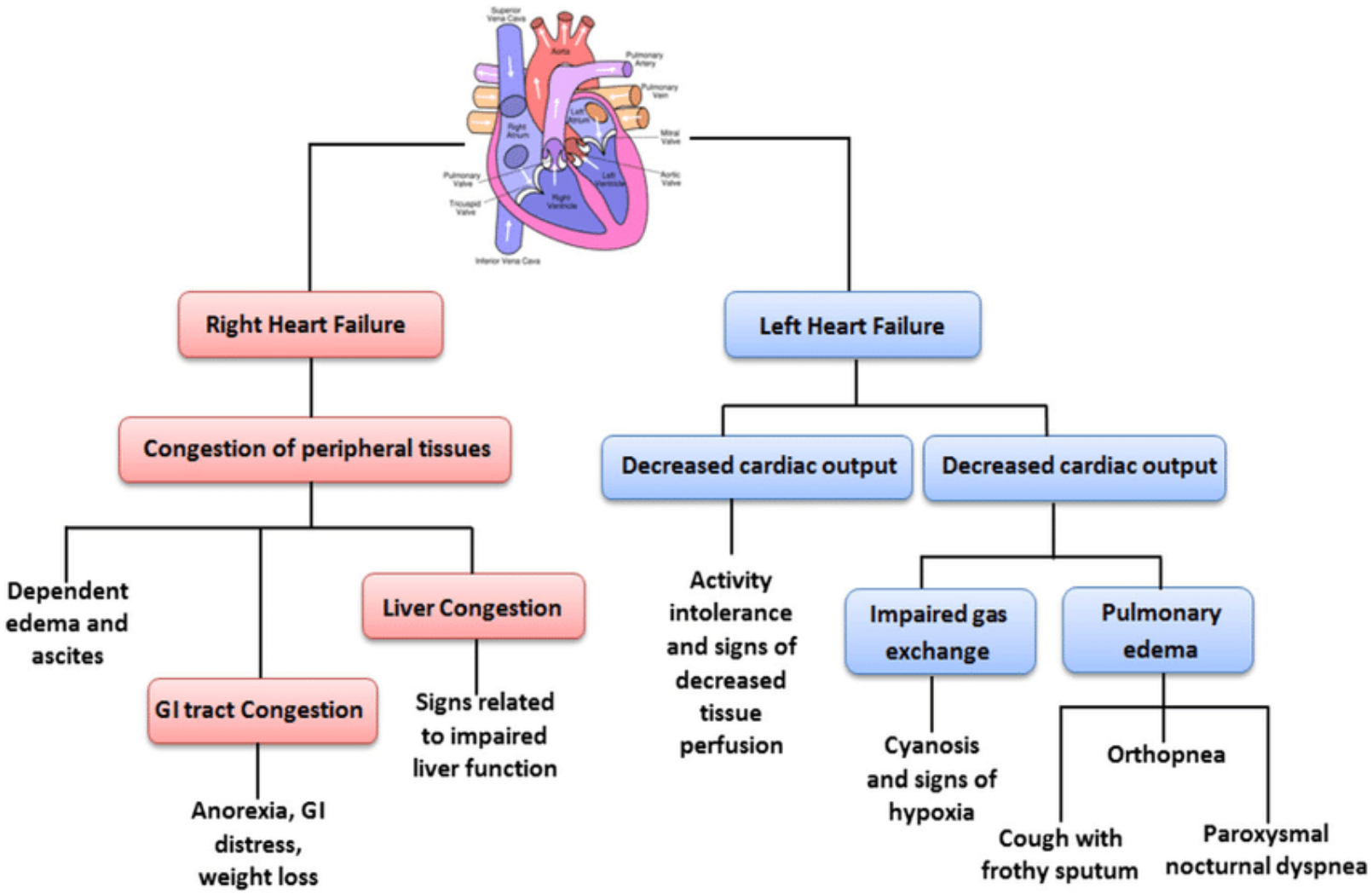
Older classification:

- **B) Left heart failure:**
- More common. Resulting from reduction in the left ventricular output and increase in the left atrial pressure and pulmonary venous pressure resulting in pulmonary congestion.

- Causes: MI, Hypertension, cardiomyopathy, valvulopathy etc.

- Clinical feature: Dyspnea, fatigue, palpitation, exercise intolerance, PND, orthopnea, cough, hemoptysis, cyanosis etc.

RHF and LHF:


Right Heart Failure
Congestion of peripheral tissues
Dependent edema and ascites
Liver Congestion
Signs related to impaired liver function
GI tract Congestion
Anorexia, GI distress, weight loss
Left Heart Failure
Decreased cardiac output
Activity intolerance and signs of decreased tissue perfusion
Decreased cardiac output
Impaired gas exchange
Cyanosis and signs of hypoxia
Pulmonary edema
Orthopnea
Cough with frothy sputum
Paroxysmal nocturnal dyspnea

Biventricular failure:

- Also known as congestive cardiac failure
- Involves both sides of the heart
- Depends on the underlying cause, i.e. DCM, extensive MI and so forth
- LVF can subsequently cause RHF as chronic elevation of the left atrial pressure leads to pulmonary hypertension.

HF based on EF:

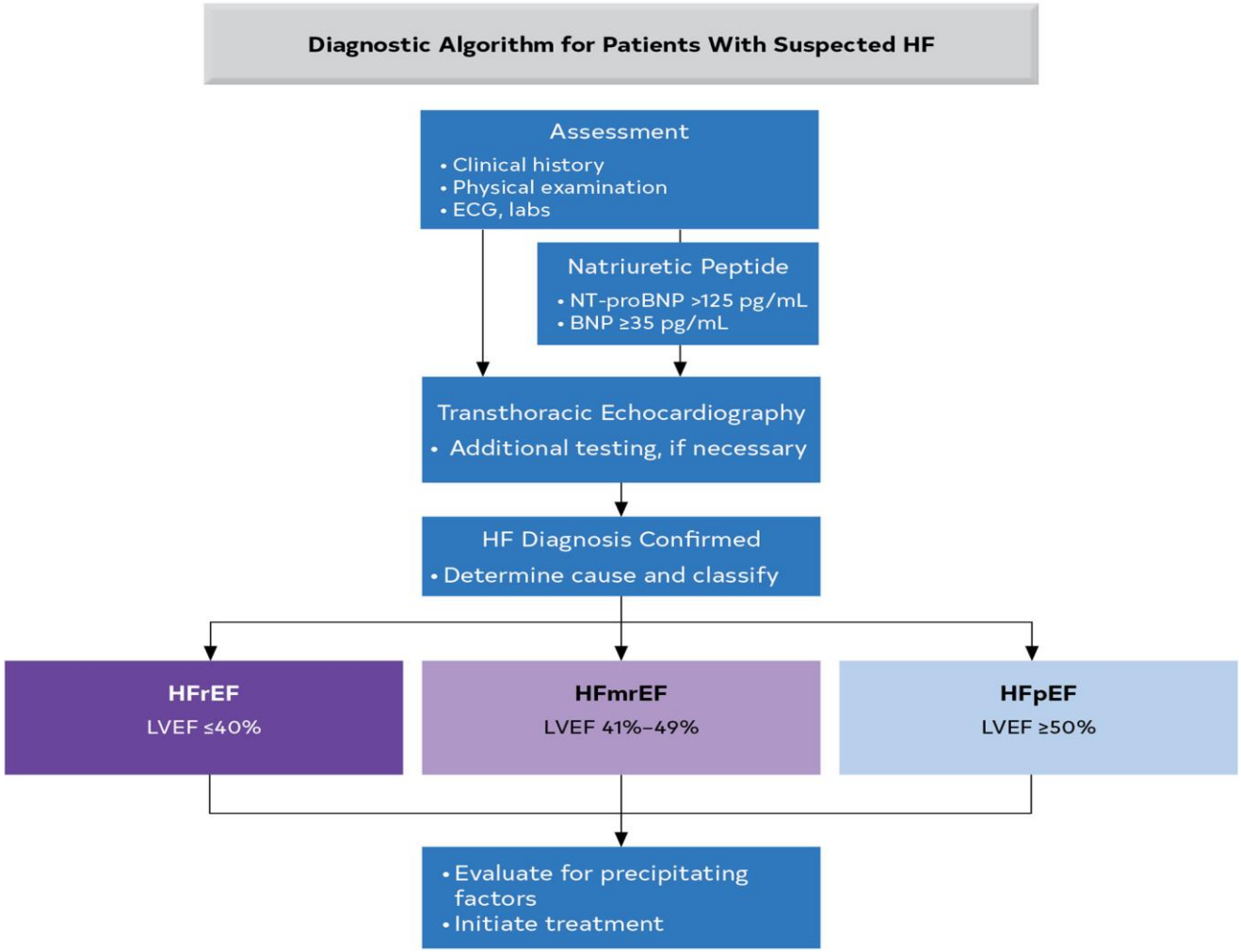
- Ejection fraction based heart failure classification is the latest and globally used classification.
- There are mainly 4 types:

Types	LVEF
1) HFrEF	LVEF ≤40%
2) HFimpEF	Previously EF≤40% but serial assessment now shows LVEF>40%
3) HFmrEF	LVEF 41%-49% (evidence of provokable or spontaneous increased LV filling pressure)
4) HFpEF	LVEF≥50% (evidence of provokable or spontaneous increased LV filling pressure)

HFpEF:

	Clinical Variables	Values	Points
H2	**H**eavy	BMI> 35 kg/m2	2
	Hypertensive	2 or more antihypertensive agents	1
F	Atrial **F**ibrillation	Paroxysmal or persistent	3
P	**P**ulmonary hypertension	Doppler echo estimated pulmonary artery systolic pressure > 35 mmHg	1
E	**E**lder	Age> 60 years	1
F	**F**illing pressure	Doppler echocardiographic E/ ’E> 9	1

Investigation:



Investigation:

Baseline tests:

- CBC with ESR, serum iron profile
- Serum urea and electrolytes
- TSH, FT4 level
- SGPT
- Glucose, fasting lipid profile
- Serum creatinine
- Urine R/E
- 12 lead ECG

Investigation:

Specific tests:

- NT-proBNP level
- Inactive breakdown product of ProBNP
- Normal value: <125 pg/ml

Imaging:

- CXR P/A view
- Echocardiography (2D, M-mode, color doppler)

Investigation:

- **Others:**
- Coronary angiogram (underlying CAD)
- Right heart catheterization (Pulmonary hypertension)
- Holter monitoring and electrophysiological studies/ EPS (cardiac dysrhythmia, intervention purposes etc.)
- Cardiac MRI (Familial cardiomyopathies, i.e ARVC)
- Endomyocardial biopsy (Cardiac amyloidosis)

Management:

Acute heart failure: A medical emergency

- Sit the patient upright
- **High-flow oxygen** if low saturation
- IV access and monitor ECG, treat any arrythmia (i.e. atrial fibrillation)
- **Diamorphine** used with caution
- **Furosemide** IV 40-80 mg
- **GTN** spray 2 puff S/L or 2 0.3 mg oral tablets (if SBP<90 mmHg, avoid)
- If SBP≥100 mmHg, IV nitrate infusion

Management:

- If patient is worsening:
- Further dose of **furosemide** IV 40-80 mg
- Consider **CPAP** 5-10 mmHg via tight fitting mask
- Further dose of **IV nitrite** (but try to maintain SBP>90 mmHg)
- If SBP< 90 mmHg, inotropes such as **dobutamine** (2.5-10 mcg/kg/min)
- **Intra-aortic balloon pump** (if facility available)
- Still deteriorating? refer to **ICU** and treat as cardiogenic shock

Management:

- **Chronic heart failure:**
- **General measures:**
- Form an MDT (multi-disciplinary team)
- Education and counselling
- Diet: Avoid added salt, high-salt foods, weight reduction for obese
- Alcohol and smoking avoided/ abstinence
- Regular moderate aerobic exercises
- Influenza and pneumococcal vaccination

Management:

- **Pharmacological:**
- **Diuretics:**
- Mineralocorticoid antagonists (MRAs), such as spironolactone and eplerenone, have already been shown to reduce total and cardiovascular mortality in heart failure with reduced ejection fraction (HFrEF) when administered on top of ACE-I, ARB and beta blockers (EMPHASIS-HF trial 2011)

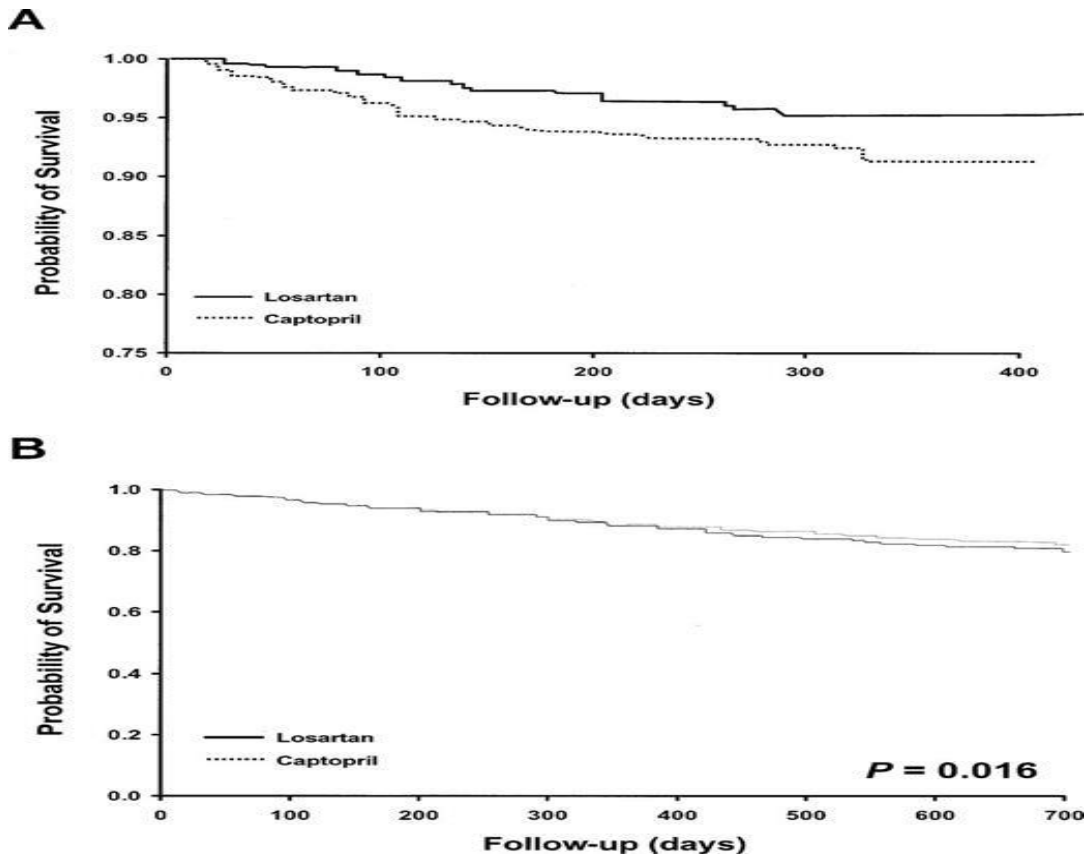
Management:

ACEi and ARB:

- ELITE (Evaluation of Losartan in the elderly) study conducted in the early 2000
- 3152 patients in the 2nd phase with NYHA class II to IV heart failure
- Followed-up for a median of 1.5 years
- No survival advantage of losartan treatment was found

Management:

- **All-cause mortality curves from the ELITE (A) and ELITE II (B) studies.**



Management:

- **Vasodilators:**
- Used when ACEi/ ARB/ ARNI are contraindicated
- Venodilator: Nitrates (reduces preload)
- Arterial dilator: Hydralazine (reduces afterload)
- Separately no prognostic value

Management:

- **Beta-blockers:**
- Reduces sympathetic overdrive, risk of arrythmia, and sudden death
- Standard dose avoided, can provoke acute-on-chronic heart failure
- Low initial dose with small incremental rise preferred
- Reduces mortality (relative risk reduction 33% all-cause HF related mortality)

Management:

- **Ivabradine:**
- Acts on “funny channel” on the SA node
- Started with 2.5-5 mg twice daily to a maximum dose of 7.5mg daily
- Suitable for patients who can’t tolerate beta-blockers
- Patient must be in sinus rhythm and HR>77/min
- Can not be given if patients have concurrent atrial fibrillation
- Has prognostic benefit just like beta-blockers

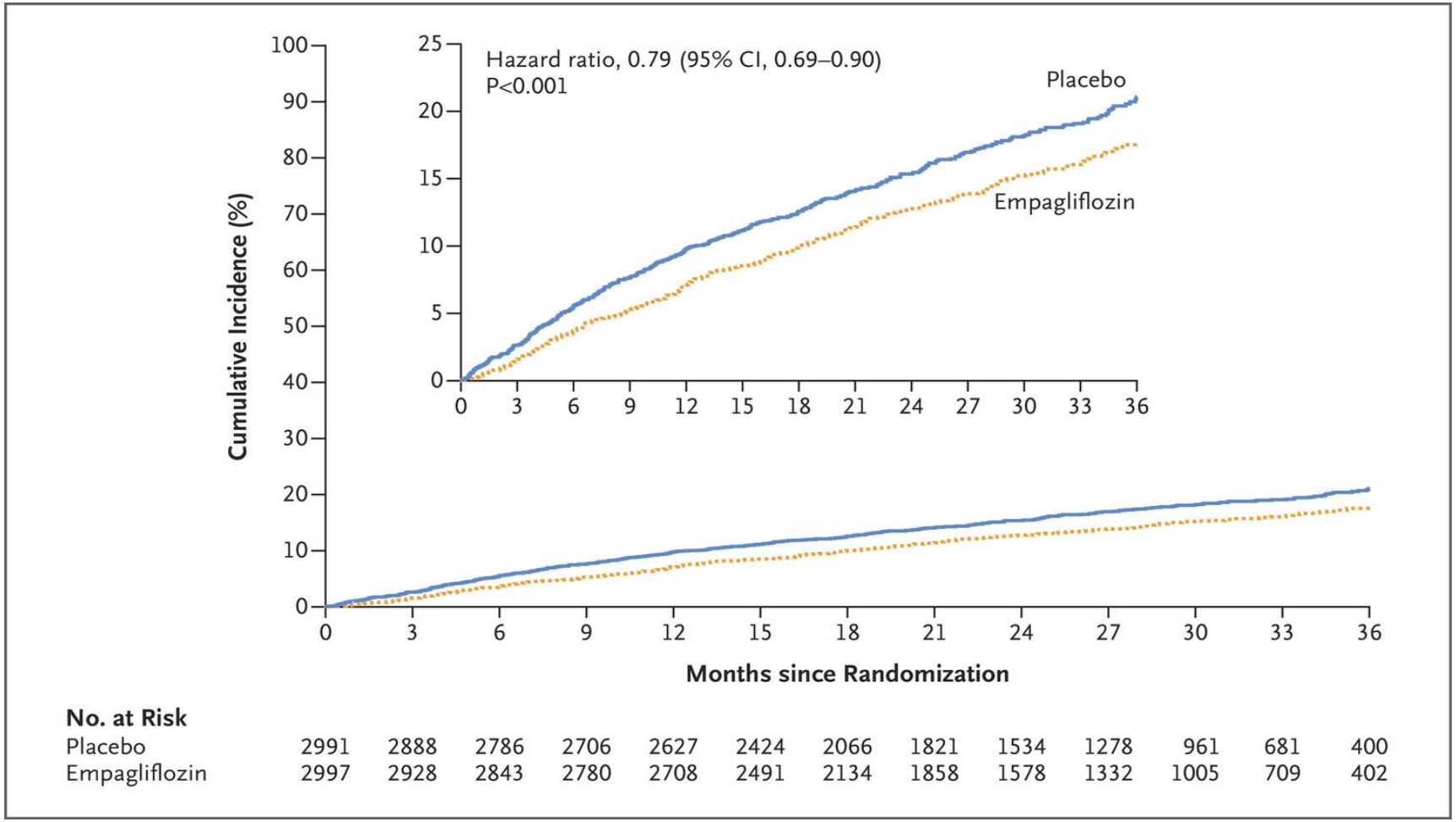
Management:

- **Digoxin:**
- Given to patients with heart failure and atrial fibrillation (to provide rate control)
- Caution needed for elderly people, renal impairment, and potassium, magnesium and calcium abnormalities should be corrected (if any)
- Has no effect on long-term survival

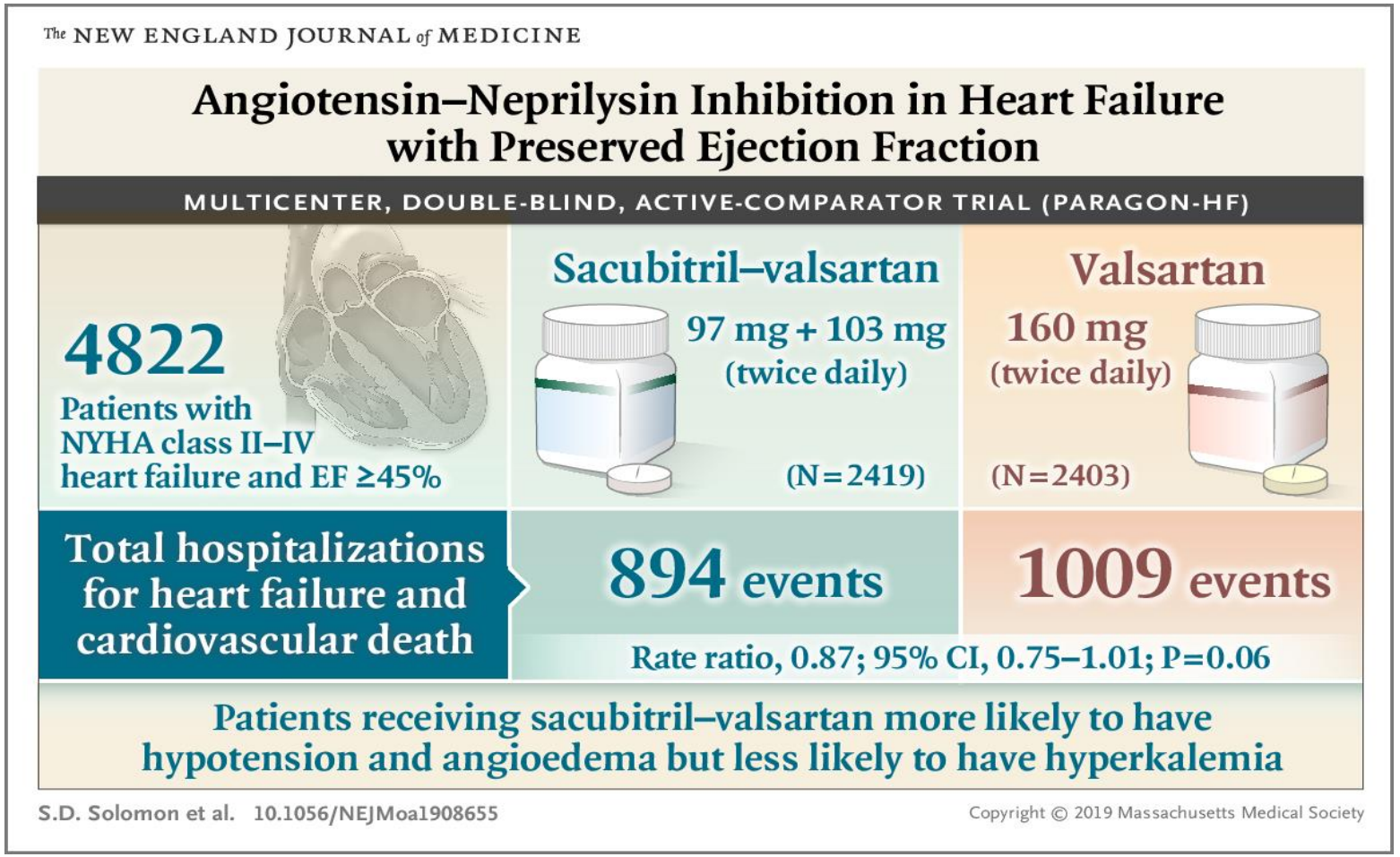
Management:

- **SGLT2i:**
- EMPEROR trial, a double-blinded RCT
- 5988 participants, NYHA stage II-IV
- Median 26.2 months
- Reduced the combined risk of cardiovascular death or hospitalization
- Regardless of diabetes status
- Almost 20% relative risk reduction

Management:


Hazard ratio, 0.79 (95% CI, 0.69–0.90)
P<0.001
Placebo
Empagliflozin
Cumulative Incidence (%)
Months since Randomization
No. at Risk
Placebo 2991 2888 2786 2706 2627 2424 2066 1821 1534 1278 961 681 400
Empagliflozin 2997 2928 2843 2780 2708 2491 2134 1858 1578 1332 1005 709 402

Management:


The NEW ENGLAND JOURNAL of MEDICINE
Angiotensin–Neprilysin Inhibition in Heart Failure with Preserved Ejection Fraction
MULTICENTER, DOUBLE-BLIND, ACTIVE-COMPARATOR TRIAL (PARAGON-HF)
4822
Patients with NYHA class II–IV heart failure and EF ≥45%
Sacubitril–valsartan
97 mg + 103 mg (twice daily)
(N=2419)
Valsartan
160 mg (twice daily)
(N=2403)
Total hospitalizations for heart failure and cardiovascular death
894 events
1009 events
Rate ratio, 0.87; 95% CI, 0.75–1.01; P=0.06
Patients receiving sacubitril–valsartan more likely to have hypotension and angioedema but less likely to have hyperkalemia
S.D. Solomon et al. 10.1056/NEJMoa1908655
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Management:

- **Neprilysin inhibitors:**
- Also known as “ARNI” (ARB+ Neprilysin Inhibitor)
- Neprilysin, a neural endopeptidase responsible for breakdown of ANP and BNP, vasoactive peptides (bradykinin, substance P)
- Example: Sacubitril 24 mg + Valsartan 26 mg
- Additional symptomatic and mortality benefit over ARB alone in **HFrEF**
- In HFrEF, ARNI is superior to ACEi/ ARB (21% all-cause mortality risk reduction in PARAGON-HF phase 1 trial)

Management:

- **Neprilysin inhibitors:**
- PARAGON-HF trial (Phase 2)
- Sacubitril–valsartan *did not* result in a significantly lower rate of total hospitalizations for heart failure and death from cardiovascular causes among patients with **HFpEF**

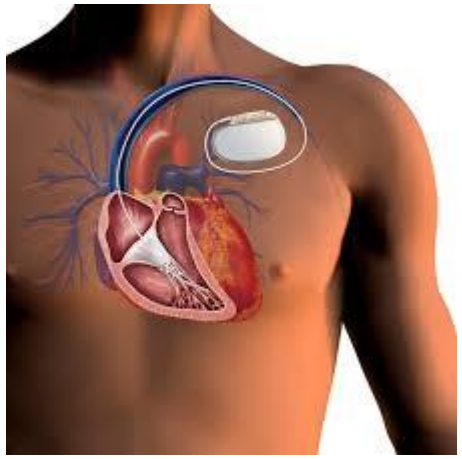
Management:

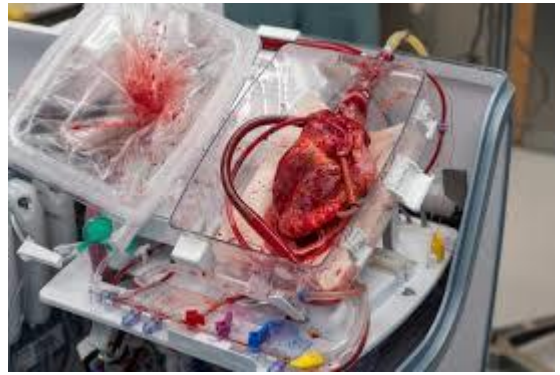
Drugs that have prognostic benefit	No prognostic benefit
Beta-blockers	Calcium channel blockers
ACEi/ ARB/ ARNI	Digoxin
MRA/ Spironolactone	Loop diuretics/ Thiazide diuretics
SGLT2i	Hydralazine
Ivabradine	GTN/ Nitrates
Hydralazine+ Isosorbide nitrate combination	Amiodarone

Management (What Not To Give):

COR	LOE	Recommendations
3: No Benefit	A	1. In patients with HFrEF, dihydropyridine calcium channel-blocking drugs are not recommended treatment for HF.[1,2]
3: No Benefit	B-R	2. In patients with HFrEF, vitamins, nutritional supplements, and hormonal therapy are not recommended other than to correct specific deficiencies.[3–9]
3: Harm	A	3. In patients with HFrEF, nondihydropyridine calcium channel-blocking drugs are not recommended.[10–13]
3: Harm	A	4. In patients with HFrEF, class IC antiarrhythmic medications and dronedarone may increase the risk of mortality.[14–16]
3: Harm	A	5. In patients with HFrEF, thiazolidinediones increase the risk of worsening HF symptoms and hospitalizations.[17–21]
3: Harm	B-R	6. In patients with type 2 diabetes and high cardiovascular risk, the dipeptidyl peptidase-4 (DPP-4) inhibitors saxagliptin and alogliptin increase the risk of HF hospitalization and should be avoided in patients with HF.[22–24]
3: Harm	B-NR	7. In patients with HFrEF, NSAIDs worsen HF symptoms and should be avoided or withdrawn whenever possible.[25–28]

Management (Non-pharmacological):





Management (Non-pharmacological):

Implantable cardiac defibrillator (ICD):

- Reduce malignant ventricular arrhythmia and sudden cardiac death
- “Shock box” also delivers anti-tachycardia pacing (ATP)- improves mortality
- Primary prevention: MI>4 weeks ago, LVEF<35% and non-sustained VT and positive EPS or LVEF<30% and QRSd>120 ms.
- Familial condition with high-risk SCD: HOCM, Brugada, WPW, ARVC etc.
- Secondary prevention: cardiac arrest due to VT/VF or, hemodynamically compromising VT or VF with LVEF<35%

Management (Non-pharmacological):

Cardiac resynchronization therapy (CRT):

- Also known as Bi-ventricular pacemakers (BiV)
- Extra LV pacemaker lead via coronary sinus (CRT-D)
- When to consider:
- LVEF<35%
- NYHA II-IV on maximal GDMT
- Sinus rhythm and QRSd>150 ms (if LBBB morphology, >120 ms)

Management (Non-pharmacological):

Left ventricular assisting device (LVAD):

- Can be used as a “bridging therapy” before cardiac transplantation
- Implantable and portable forms available
- Sometimes used as “restoration” therapy in acute insults, i.e viral myocarditis
- Complications are : bleeding, infection, systemic embolism, neurological and renal sequelae.

Management (Non-pharmacological):

Cardiac transplantation:

- Most common indications: CAD, DCM
- Definitive management
- Cadaveric donor, higher centers, expensive
- Contraindicated in pulmonary vascular diseases or, primary pulmonary hypertension
- Complications: Graft-versus host disease/ rejection, infection, accelerated atherosclerosis etc.

Special situations:

Geriatric heart failure:

- Common causes are myocardial infarction, cardiomyopathy, degenerative valvular heart diseases.
- Diastolic dysfunction takes place due to hypertension
- ACEi/ARBs can be given but they experience postural hypotension and renal impairment easily
- Loop diuretics poorly tolerated in those with urinary incontinence and BPH.

Special situations:

Heart failure in pregnancy:

- Causes: Pre-existing structural heart diseases, gestational hypertension, peripartum cardiomyopathy etc.

- Drugs **not to be given** during pregnancy:
- ACE inhibitors.
- Angiotensin receptor blockers (ARBs).
- Aldosterone antagonists.
- Some anticoagulant medications, like warfarin.
- Some medications that treat pulmonary hypertension, like riociguat and bosentan.

Summary:

- **Stages of heart failure:** 4, at-risk, pre-HF, symptomatic HF and advanced HF
- **Classification of HF:** 4, HFrEF, HFimpEF, HFmrEF, HFpEF
- **Investigation:** 12-lead ECG, Echo, NT-proBNP
- **Acute HF:** Oxygen+ diuretics+ GTN
- **Chronic HF:** The fantastic 4 drugs! ACEi/ ARB/ ARNI+ MRA+ Beta-blocker+ SGLT2i
- **SGLT2i** to be given in HFpEF, pre-HF because of cardiac benefit

Summary:

- **ARNI:** In HFrEF, ARNI is superior to ACEi/ ARB, but no prognostic benefit seen in HFpEF as of yet.

- **Continuation:** Improvement in LVEF does not mean full myocardial recovery or normalization of LV function. So a patient with HFrEF now HFimpEF/ HFmrEF should receive the same GDMT when diagnosed with LVEF<40%
- **Intervention techniques:** ICD, CRT, LVAD, cardiac transplantation.

Thank you!