Heart Failure

Etiology And Diagnosis

Dr Hanan ALBackr

Definition:

Heart failure (HF) is a complex clinical syndrome that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood.

Definition of Heart Failure

Heart failure can be defined as an abnormality of cardiac structure or function leading to failure of the heart to deliver oxygen at a rate commensurate with the requirements of the metabolizing tissues, despite normal filling pressures (or only at the expense of increased filling pressures).[1]

TERMINOLOGY used to describe HF[2]

Related to EF*:	HFrEF (reduced ejection fraction: EF<40%)
	HFmEF (mildly impaired EF: EF 40-49%
	HFpEF (preserved ejection fraction: EF ≥50%)*
Related to time-course:	New onset, transient, chronic
Related to progression:	Acute, stable, worsening
Related to location:	Left heart, right heart, combined

* There is no consensus concerning the cut-off for preserved EF[2]

1. McMurray et al. Eur Heart J 2012;33:1787–847
2. Dickstein K et al. Eur Heart J 2008;29:2388–442

The burden of heart failure

NUMBER of PATIENTS
21 MILLION adults worldwide are living with heart failure
This number is expected to rise.[1,2]

ECONOMIC BURDEN
In 2012, the overall worldwide cost of heart failure was nearly **$108 BILLION.**[6]

MORTALITY
50% of heart failure patients die within 5 years from diagnosis.[5]

REHOSPITALISATION
Heart failure is the **NUMBER 1** cause of hospitalisation for patients aged >65 years.[4]

COMORBIDITIES: The vast majority of HF patients has 3 or more comorbidities [3]

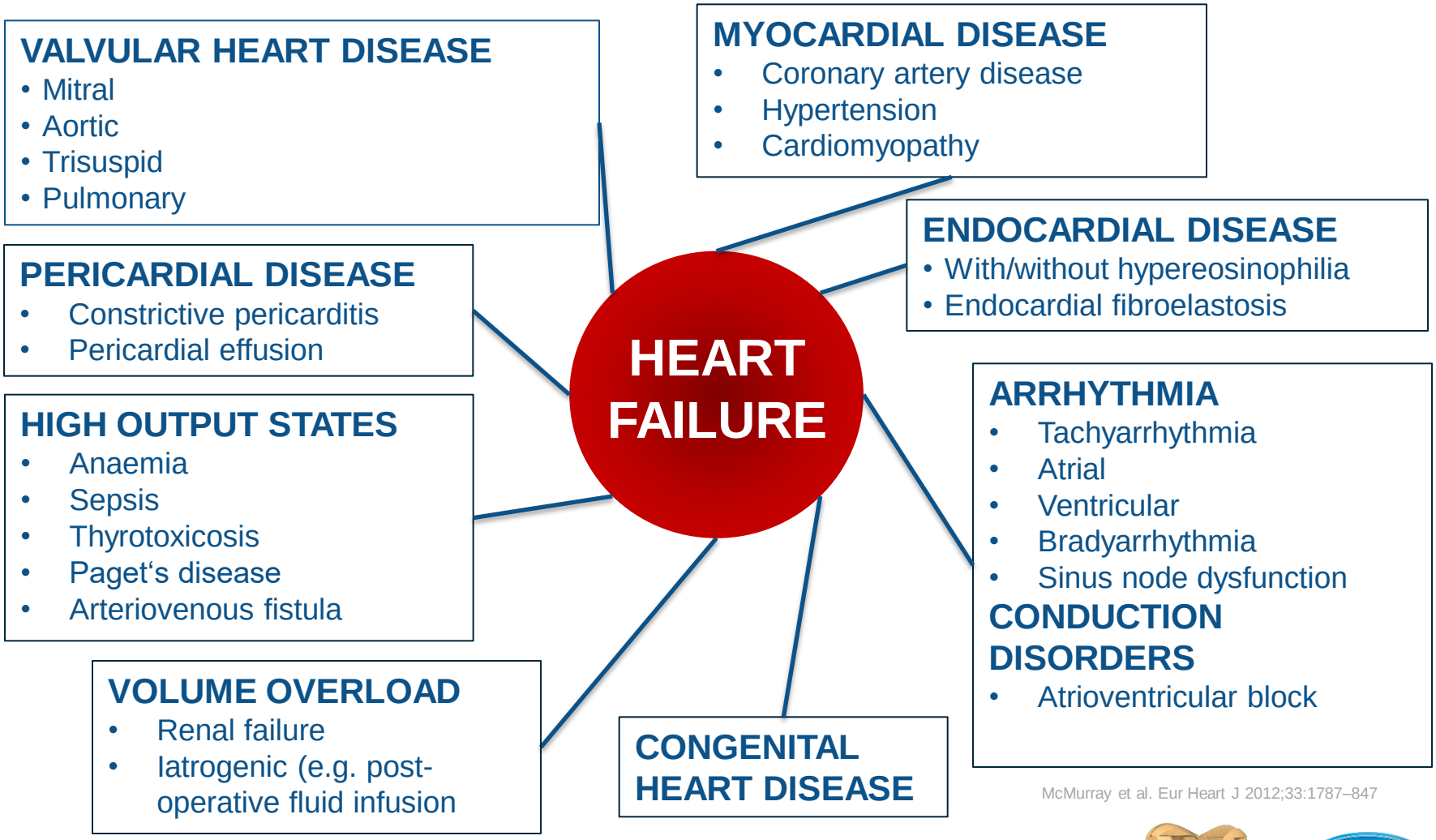
1. Mozaffarian D et al. Circulation. 2015;131(4):e29-e322.
2. Mosterd A et al. Heart. 2007;93(9):1137-1146.
3. http://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Chronic-Conditions/Downloads/2012Chartbook.pdf
4. Cowie MR et al. Oxford PharmaGenesis; 2014. http://www.oxfordhealthpolicyforum.org/AHFreport. Accessed February 18, 2015.
5. Fauci AS et al. Harrison's Principles of Internal Medicine. 17th ed. New York: McGraw-Hill; 2008.
6. Cook C et al. *Int J Cardiol*. 2014;171(3):368-376.

Prevalence

- Prevalence 0.4-2% overall, 3-5 % in over 65s, 10% of over 80s
- Commonest medical reason for admission
- Annual mortality of 60% over 80s
- > 10% also have AF
- Progressive condition - median survival 5 years after diagnosis

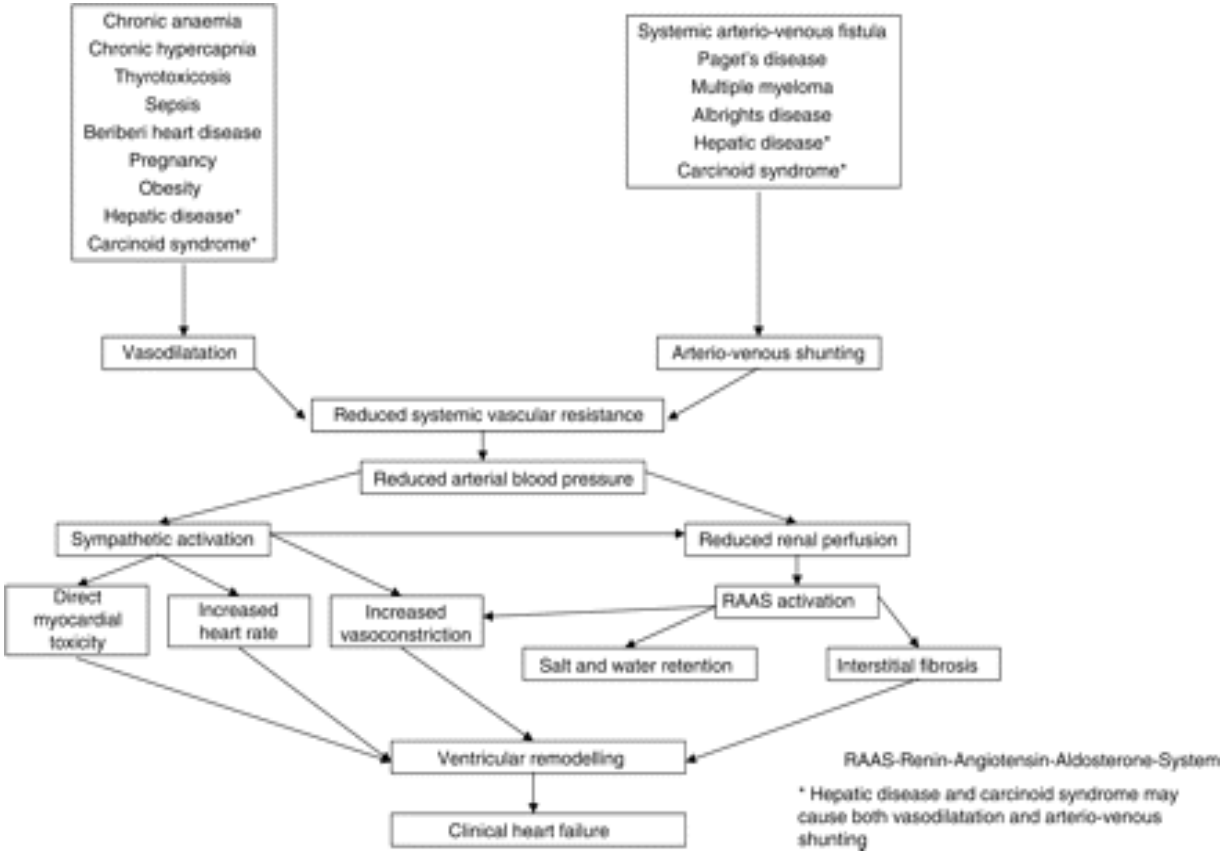
- REMEMBER LEFT VENTRICULAR FAILURE IS A TRUE LIFE THREATENING EMERGENCY

Aetiology of HF



McMurray et al. Eur Heart J 2012;33:1787–847

Figure 1. Schematic illustrating the two common routes through which various disease states lead to a reduced systemic ...



QJM, Volume 102, Issue 4, April 2009, Pages 235–241, https://doi.org/10.1093/qjmed/hcn147

Etiology

- *It is a common end point for many diseases of cardiovascular system*
- It can be caused by :

  -Inappropriate work load (volume or pressure overload)

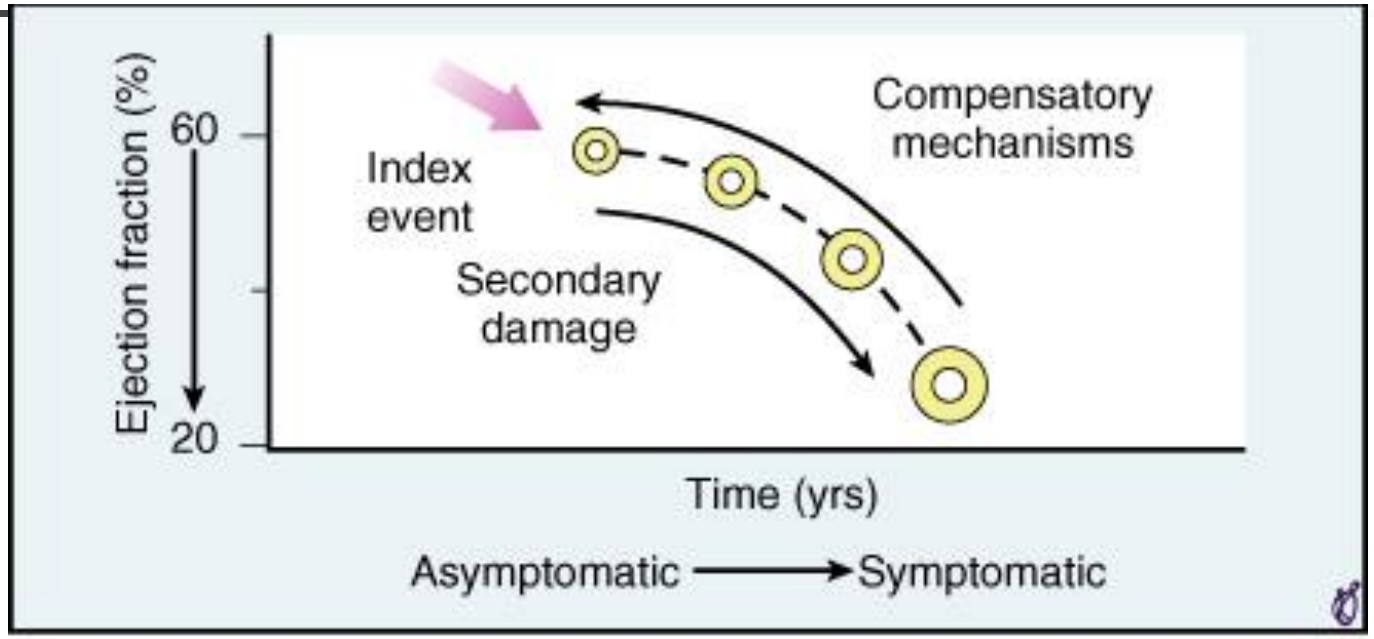
  -Restricted filling

  -Myocyte loss

Causes of left ventricular failure

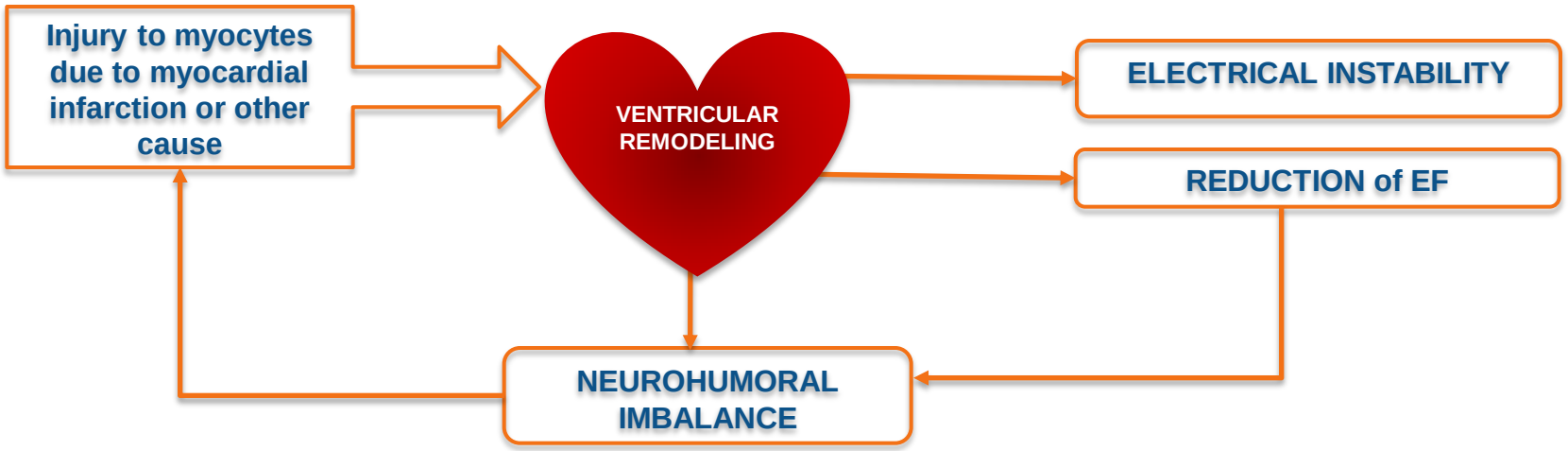
- ***Volume over load***: Regurgitate valve
  High output status
- ***Pressure overload:*** Systemic hypertension
  Outflow obstruction
- ***Loss of muscles:*** Post MI, Chronic ischemia
  Connective tissue diseases
  Infection, Poisons
  (alcohol,cobalt,Doxorubicin)
- ***Restricted Filling:*** Pericardial diseases, Restrictive cardiomyopathy, tachyarrhythmia

Background



- Heart failure pathophysiology
  - Index event
  - Compensatory mechanisms
  - Maladaptive mechanisms

Pathophysiology of HF



An imbalance occurs in three key neurohumoral systems:

- The renin–angiotensin–aldosterone system
- The sympathetic nervous system
- The natriuretic peptide system

The systemic responses in the renin–angiotensin–aldosterone and sympathetic nervous systems cause further myocardial injury, and have detrimental effects on the blood vessels, and various organs, thereby creating a pathophysiological ‘vicious cycle’. The natriuretic peptide system has a protective function, which can counterbalance these detrimental effects.

1. McMurray JJ. N Engl J Med 2010;362:228–238
2. Shah AM. Lancet 2011;378:704–712

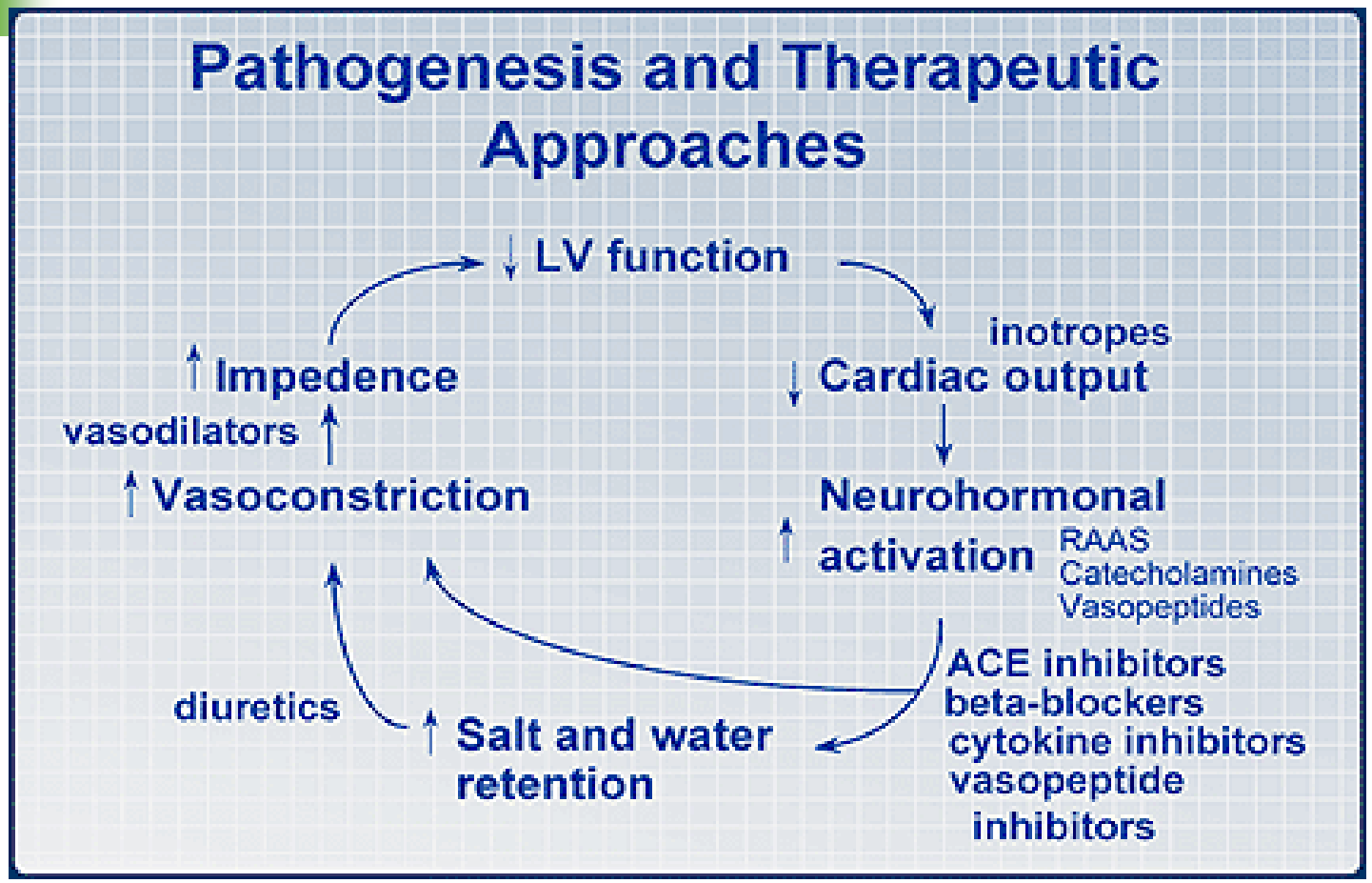
Pathophysiology

- Hemodynamic changes
- Neurohormonal changes
- Cellular changes

Hemodynamic changes

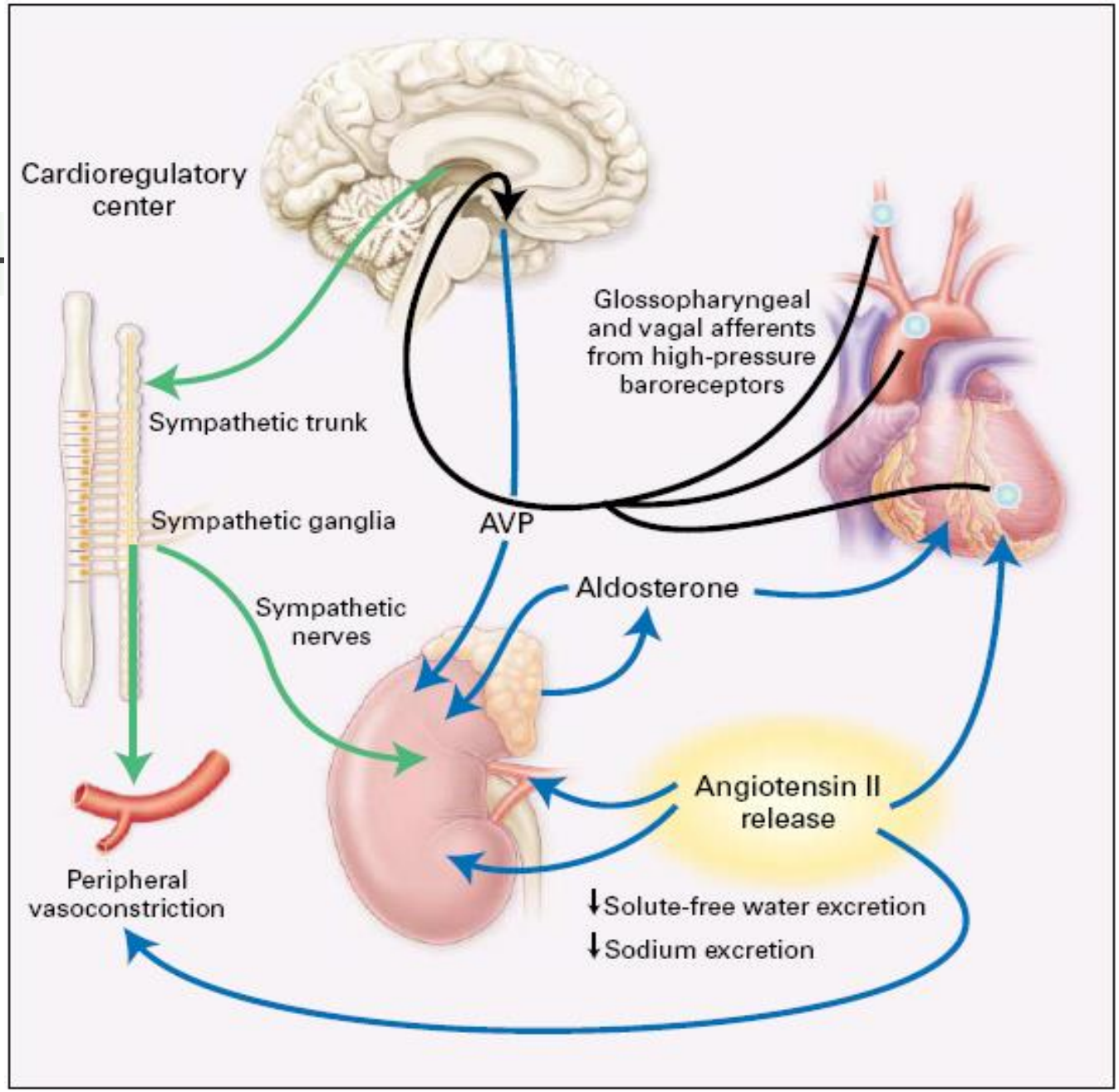
- *From hemodynamic stand point HF can be secondary to systolic dysfunction or diastolic dysfunction*

Pathogenesis and Therapeutic Approaches



Neurohormonal changes

N/H changes	Favorable effect	Unfavor. effect
↑ **Sympathetic activity**	↑ HR ,↑ contractility, vasoconst. → ↑ V return, ↑ filling	Arteriolar constriction → After load →↑ workload →↑ O_2 consumption
↑ **Renin-Angiotensin – Aldosterone**	Salt & water retention→↑ VR	Vasoconstriction → ↑ after load
↑ **Vasopressin**	Same effect	Same effect
↑ **interleukins &TNFα**	May have roles in myocyte hypertrophy	Apoptosis
↑**Endothelin**	Vasoconstriction→↑ VR	↑ After load


Cardioregulatory center
Glossopharyngeal and vagal afferents from high-pressure baroreceptors
Sympathetic trunk
Sympathetic ganglia
AVP
Aldosterone
Sympathetic nerves
Angiotensin II release
Peripheral vasoconstriction
↓Solute-free water excretion
↓Sodium excretion

Symptoms and signs of HF

The diagnosis of HF can be difficult, especially in the early stages

Symptoms	Signs
Typical	*More specific*
Breathlessness	Elevated jugular venous pressure
Orthopnoea	Hepatojugular reflux
Paroxysmal nocturnal dyspnoea	Third heart sound (gallop rhythm)
Reduced exercise tolerance	Laterally displaced apical impulse
Fatigue, tiredness, increased time to recover after exercise	Cardiac murmur
Ankle swelling	

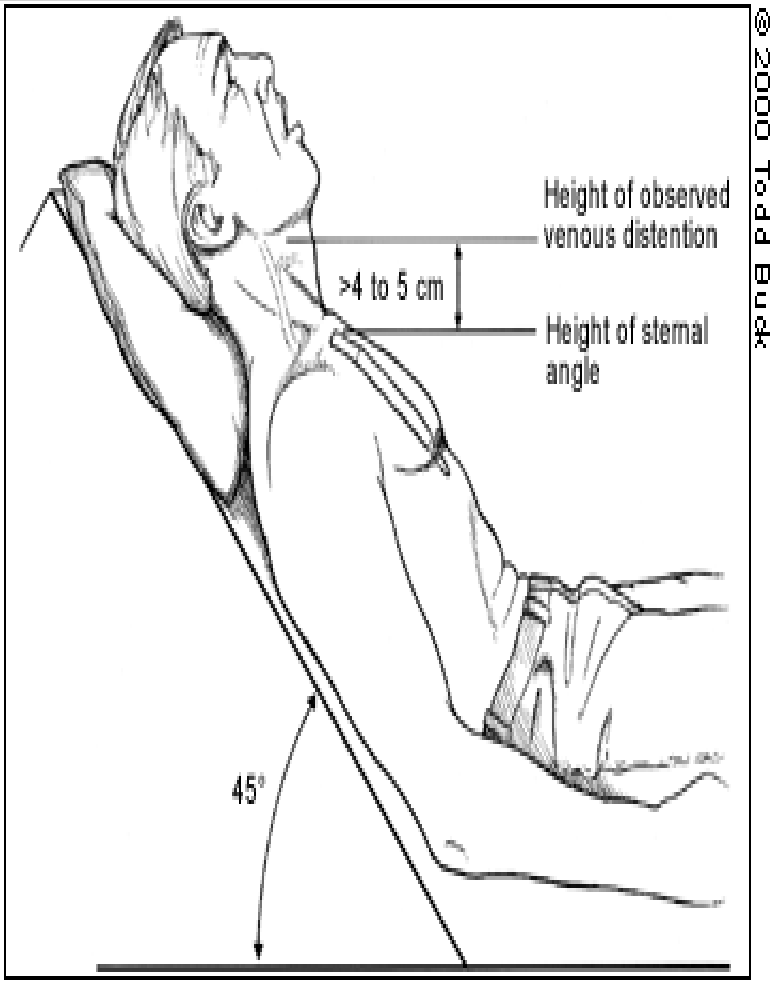
McMurray et al. Eur Heart J 2012;33:1787–847

Symptoms

- **SOB, Orthopnea, paroxysmal nocturnal dyspnea**
- **Low cardiac output symptoms**
- **Abdominal symptoms:** *Anorexia,nausea, abdominal fullness, Rt hypochondrial pain*

Physical Signs

- High diastolic BP & occasional decrease in systolic BP (decapitated BP)
- JVD
- Rales *(Inspiratory)*
- Displaced and sustained apical impulses
- Third heart sound – *low pitched sound that is heard during rapid filling of ventricle*



Physical signs (cont.)

- Mechanism of S_3 sudden deceleration of blood as elastic limits of the ventricles are reached
- Vibration of the ventricular wall by blood filling
- Common in children

Physical signs (cont.)

- **Fourth heart Sound (S_4)**

  - Usually at the end of diastole
  - Exact mechanism is not known

  Could be due to contraction of atrium against stiff ventricle

- **Pale, cold sweaty skin**

Forms of heart failure (cont.)

- **Right vs Left sided heart failure:**

Right sided heart failure :

Most common cause is left sided failure

Other causes included : Pulmonary embolisms
Other causes of pulmonary htn.
RV infarction
MS

Usually presents with: LL edema, ascites
hepatic congestion
cardiac cirrhosis (on the long run)

Classification of Heart Failure

ACC/AHA stages of HF (based on structure and damage to heart)		NYHA functional classification (based on symptoms or physical activity)	
Stage A	At high risk for HF, but without structural or functional abnormality No signs or symptoms	Class I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation or dyspnoea
Stage B	Developed structural heart disease strongly associated with development of HF, but without signs or symptoms	Class II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in HF symptoms
Stage C	Symptomatic HF associated with underlying structural heart disease	Class III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity results in HF symptoms
Stage D	Advanced structural heart disease and marked symptoms of HF at rest, despite maximal medical therapy	Class IV	Symptoms of HF present at rest. If any physical activity is undertaken, discomfort is increased

Dickstein et al. Eur Heart J 2008;29:2388–442
Hunt et al. J Am Coll Cardiol 2009;53:e1–90

Differential diagnosis

- Pericardial diseases
- Liver diseases
- Nephrotic syndrome
- Protein losing enteropathy

questions

- Definition of heart failure
- Causes of heart failure
- Pathophysiology of HF
- Staging of heart failure
- Phenotypes of HF
- S/S of HF
- Diagnosis of HFREF

Principles of diagnosis of HF

All diagnostic steps are equally important

- **Consider:** *Medical history, signs, symptoms*
- **Confirm:** *Natriuretic peptides, Echocardiography*
- **Assess clinical phenotype**: *HFrEF vs. HFpEF*
- **Assess etiology:** *Angiography, cMRI, Biopsy*
- **Risk stratification**
- **Workup for targeted therapies**

Diagnosing HF

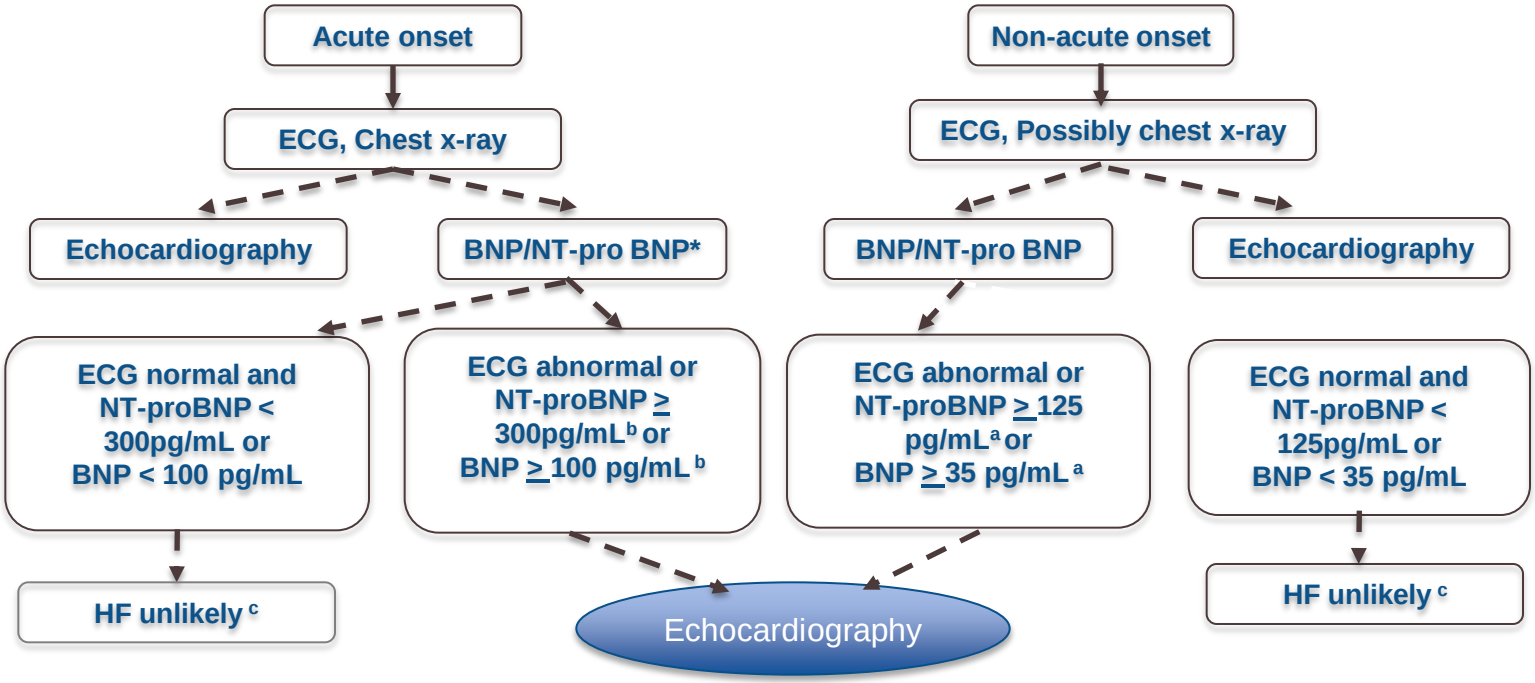
The diagnosis of HFpEF is more difficult than the diagnosis of HFrEF

The diagnosis of HFrEF requires three conditions to be satisfied
1. Symptoms typical of HF
2. Signs typical of HF
3. Reduced LVEF

The diagnosis of HFpEF requires four conditions to be satisfied
1. Symptoms typical of HF
2. Signs typical of HF
3. Normal or only mildly reduced LVEF and LV not dilated
4. Relevant structural heart disease (LV hypertrophy/LA enlargement) and/or diastolic dysfunction

McMurray et al. Eur Heart J 2012;33:1787–847

ESC HF diagnostic algorithm 2012

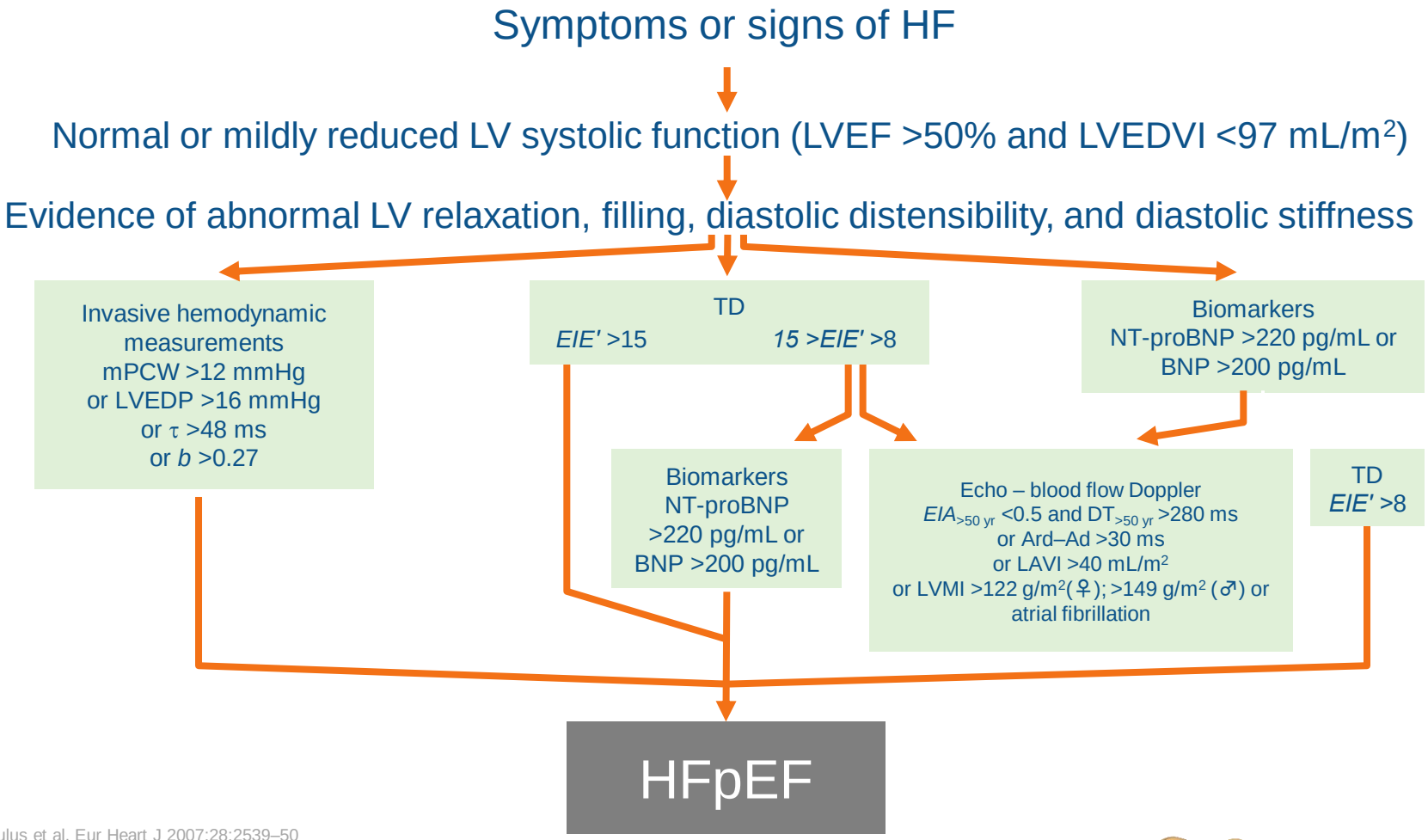


If heart failure is confirmed by echocardiography, determine aetiology and start appropriate treatment.

*In the acute setting, MR-proANP may also be used (cut-off point 120 pmol/L, i.e. <120 pmol/L = heart failure unlikely).
a.Exclusion cut-off points for natriuretic peptides are chosen to minimize the false-negative rate while reducing unnecessary referrals for echocardiography.
b.Other causes of elevated natriuretic peptide levels in the acute setting are an acute coronary syndrome, atrial or ventricular arrhythmias, pulmonary embolism, and severe chronic obstructive pulmonary disease with elevated right heart pressures, renal failure, and sepsis. Other causes of an elevated natriuretic level in the non-acute setting are:
old age (>75 years), atrial arrhythmias, left ventricular hypertrophy, chronic obstructive pulmonary disease, and chronic kidney disease.
c. Treatment may reduce natriuretic peptide concentration, and natriuretic peptide concentrations may not be markedly elevated in patients with HF-PEF.

McMurray et al. Eur Heart J 2012;33:1787–847

HFA/ESC diagnostic recommendations HFpEF



Paulus et al. Eur Heart J 2007;28:2539–50

Particular relevance of BNP

- diagnosis
- staging
- risk stratification
- monitor/titrate therapy
- admission/discharge decisions:
  > rule out symptomatic LV dysfunction

A normal natriuretic peptide level in an untreated patient virtually excludes significant cardiac disease
Consider different cut-off values in various clinical situations

Laboratory Findings

- Anemia
- Hyperthyroid
- Chronic renal insuffiency, electrolytes abnormality
- Pre-renal azotemia
- Hemochromatosis

Electrocardiogram

- Old MI or recent MI
- Arrhythmia
- Some forms of Cardiomyopathy are tachycardia related
- LBBB⟶*may help in management*

Chest X-ray

- Size and shape of heart
- Evidence of pulmonary venous congestion (dilated or upper lobe veins → perivascular edema)
- Pleural effusion

Echocardiogram

- Function of both ventricles
- Wall motion abnormality that may signify CAD
- Valvular abnormality
- Intra-cardiac shunts

Cardiac Catheterization

- When CAD or valvular is suspected
- If heart transplant is indicated

In conclusion, congestive heart failure is often assumed to be a disease when in fact it is a syndrome caused by multiple disorders.

TREATMENT

- Correction of reversible causes
  - Ischemia
  - Valvular heart disease
  - Thyrotoxicosis and other high output status
  - Shunts
  - Arrhythmia
    - A fib, flutter, PJRT
  - Medications
    - Ca channel blockers, some antiarrhythmics

Diet and Activity

- Salt restriction
- Fluid restriction
- Daily weight (tailor therapy)
- Gradual exertion programs

Diuretic Therapy

- The most effective symptomatic relief
- Mild symptoms
  - HCTZ
  - Chlorthalidone
  - Metolazone
  - Block Na reabsorbtion in loop of henle and distal convoluted tubules
  - Thiazides are ineffective with GFR < 30

Diuretics (cont.)

- **Side Effects**
  - Pre-renal azotemia
  - Skin rashes
  - Neutropenia
  - Thrombocytopenia
  - Hyperglycemia
  - ↑ Uric Acid
  - Hepatic dysfunction

Diuretics (cont.)

- **More severe heart failure → loop diuretics**
  - **Lasix** (20 – 320 mg QD), Furosemide
  - **Bumex** (Bumetanide 1-8mg)
  - **Torsemide** (20-200mg)

Mechanism of action: Inhibit chloride reabsortion in ascending limb of loop of Henle results in natriuresis, kaliuresis and metabolic alkalosis

Adverse reaction:

pre-renal azotemia
Hypokalemia
Skin rash
ototoxicity

K^+ Sparing Agents

- **Triamterene & amiloride** – acts on distal tubules to ↓ K secretion
- **Spironolactone** (Aldosterone inhibitor)

  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

Inhibitors of renin-angiotensin-aldosterone system

- 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
- Angiotensin receptors blockers
- Spironolactone

Angiotensin Converting Enzyme Inhibitors

- *They block the R-A-A system by inhibiting the conversion of angiotensin I to angiotensin II → vasodilation and ↓ Na retention*
- *↓ Bradykinin degradation ↑ its* level *→ ↑ PG secretion & nitric oxide*
- Ace Inhibitors were found to improve survival in CHF patients
  - Delay onset & progression of HF in pts with asymptomatic LV dysfunction
  - ↓ cardiac remodeling

Side effects of ACE inhibitors

- Angioedema
- Hypotension
- Renal insuffiency
- Rash
- cough

Angiotensin II receptor blockers

- Has comparable effect to ACE I
- Can be used in certain conditions when ACE I are contraindicated (angioneurotic edema, cough)

Digitalis Glycosides (Digoxin, Digitoxin)

- The role of digitalis has declined somewhat because of safety concern
- Recent studies have shown that digitals does not affect mortality in CHF patients but causes significant
  - Reduction in hospitalization
  - Reduction in symptoms of HF

Digitalis (cont.)
Mechanism of Action

- +ve inotropic effect by ↑ intracellular Ca & enhancing actin-myosin cross bride formation (binds to the Na-K ATPase → inhibits Na pump → ↑ intracellular Na → ↑ Na-Ca exchange
- Vagotonic effect
- Arrhythmogenic effect

Digitalis Toxicity

- Narrow therapeutic to toxic ratio

- Non cardiac manifestations

  Anorexia,

  Nausea, vomiting,

  Headache,

  Xanthopsia sotoma,

  Disorientation

Digitalis Toxicity

- **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 a fib
  - PVC's, VT/ V fib (bi-directional VT)

Digitalis Toxicity
Treatment

- 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

β Blockers

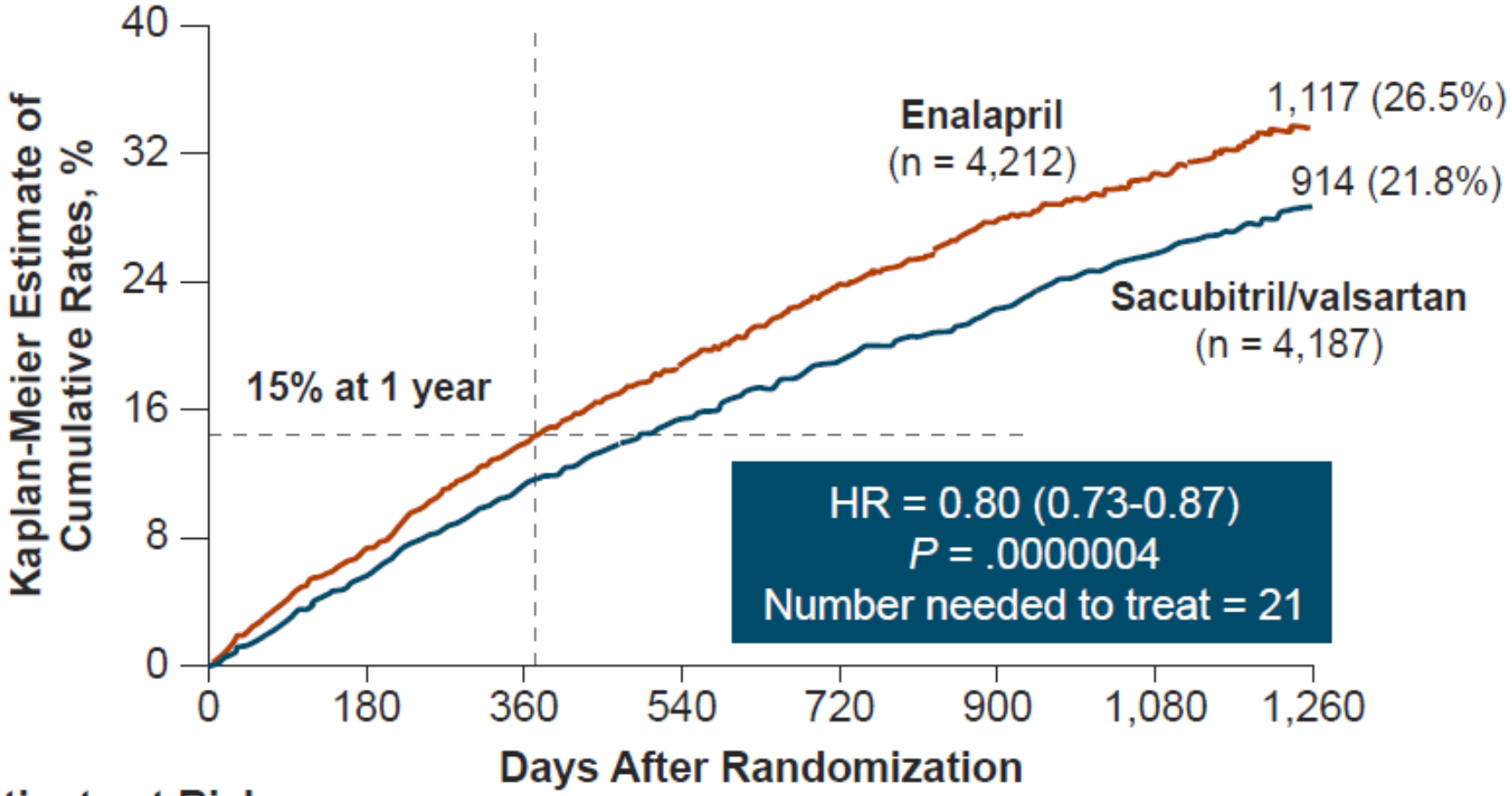
- Has been traditionally contraindicated in pts with CHF
- Now they are the main stay in treatment on CHF & may be the only medication that shows substantial improvement in LV function
- In addition to improved LV function multiple studies show improved survival
- The only contraindication is severe decompensated CHF

Nitrate/Hydralazine (ISDN/HDZ)

- 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.

PARADIGM-HF: CV Death or HF Hospitalization (Primary Endpoint)



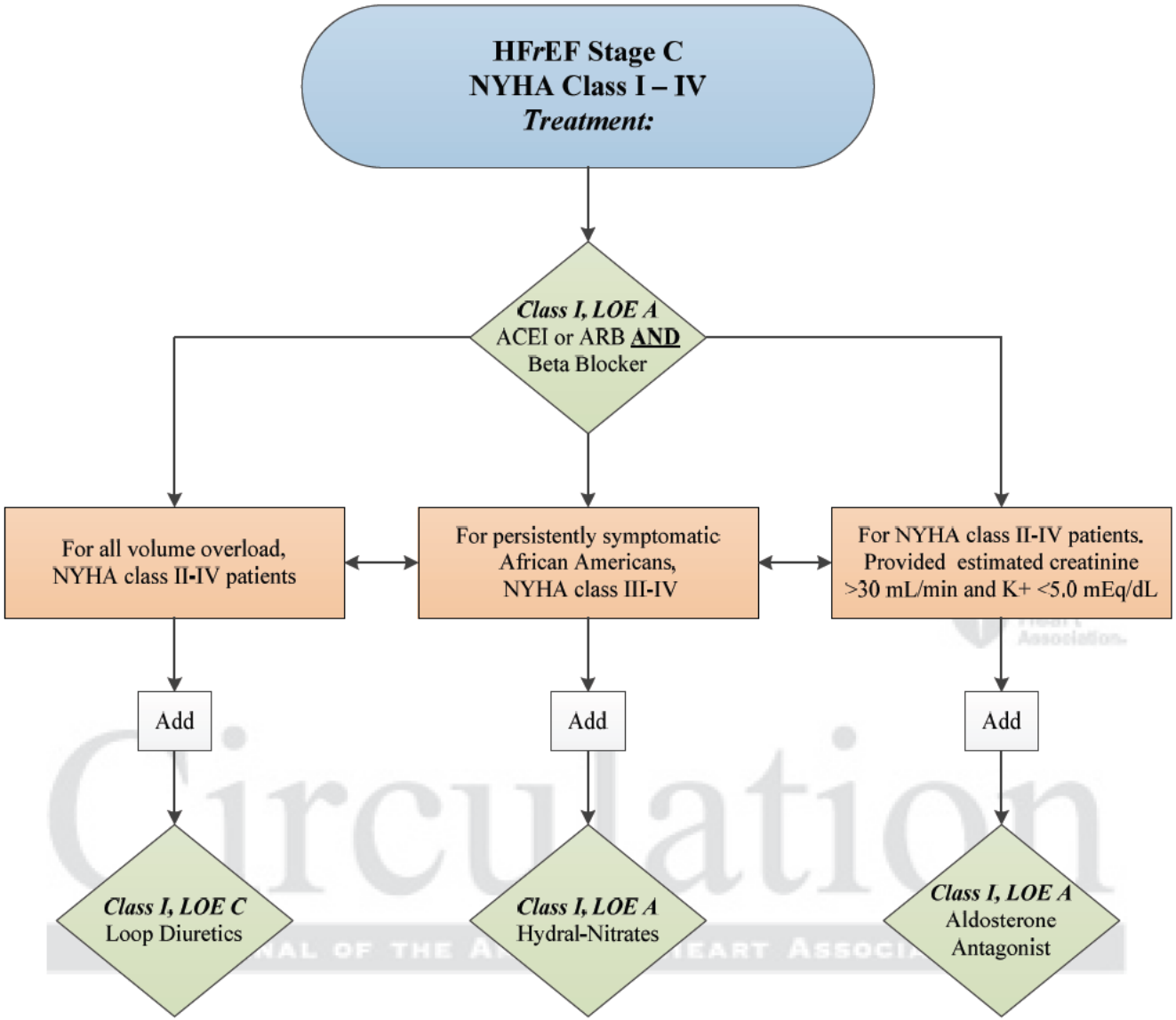
Patients at Risk

LCZ696	4,187	3,922	3,663	3,018	2,257	1,544	896	249
Enalapril	4,212	3,883	3,579	2,922	2,123	1,488	853	236

1. McMurray JJ et al. N Engl J Med. 2014;371:993-1004

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

Therapy	NNT mortality 5 yr
ACEi/ARB	18
Beta blocker	18
MRA	15
Ivabradine	9
ARNI	14
SGLT2	16
DEVICES	
ICD	14
CRT	14



ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blocker; HFrEF, heart failure with reduced ejection fraction; Hydral-Nitrates, hydralazine and isosorbide dinitrate; LOE, Level of Evidence; and NYHA, New York Heart Association.

2013 ACCF/AHA Guideline for the Management of Heart Failure

Antiarrhythmics

- Most common cause of SCD in these patients is ventricular tachyarrhythmia
- Patients with h/o sustained VT or SCD → ICD implant

New Methods

- **Implantable ventricular assist devices**
- **Biventricular pacing** (only in patient with LBBB & CHF)
- **Artificial Heart**

Cardiac Transplant

- It has become more widely used since the advances in immunosuppressive treatment

- Survival rate
  - 1 year 80% - 90%
  - 5 years 70%

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