

Heart Failure Prognosis & Management

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Definition

- Heart failure is a complex clinical syndrome

Can result from:

- structural or functional cardiac disorder
- impairs the ability of the ventricle to **fill** with or **eject** blood

- Inability of the heart to pump blood at an output sufficient to meet the body's demands

- Characterized by:
- signs and symptoms of intravascular and interstitial volume overload and/or
- manifestations of inadequate tissue perfusion

Common Causes

- Coronary artery disease
- Hypertension
- Dilated cardiomyopathy
- Valvular heart disease
- Cor-Pulmonale

Heart failure prevalence is expected to continue to increase¹

21 MILLION

ADULTS WORLDWIDE ARE LIVING WITH HEART FAILURE AND THIS NUMBER IS EXPECTED TO RISE^{1,2}



AGING POPULATION²



INCREASING PREVALENCE OF RISK FACTORS²

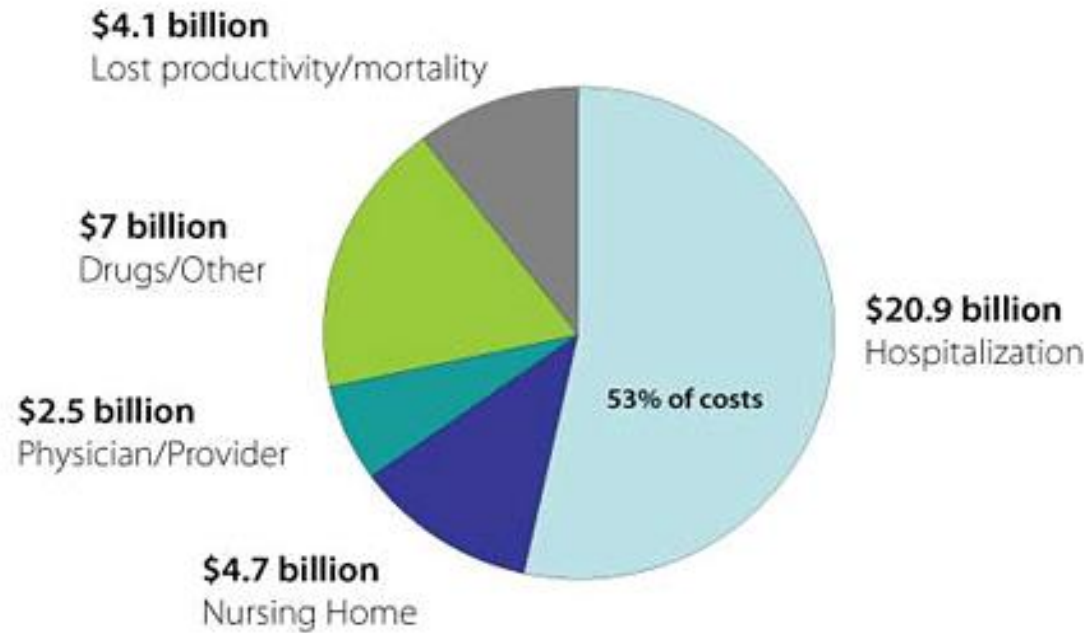


IMPROVED POST-MI SURVIVAL²

A person at age 40 has a 1 in 5 lifetime risk of developing heart failure, and more than 1 million hospitalisations due to heart failure are reported annually in Europe.^{1,4}

MI = myocardial infarction

1. Mozaffarian D, Benjamin EJ, Go AS, et al; for American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. *Circulation*. 2015;131(4):e29-e322. 2. Mosterd A, Hoes AW. Clinical epidemiology of heart failure. *Heart*. 2007;93(9):1137-1146. 3. Velagaleti RS, Vasan R. Epidemiology of heart failure. In: Mann DL, ed. *Heart Failure: A Companion to Braunwald's Heart Disease*. 2nd ed. St Louis: Saunders; 2011. 4. Ponikowski P, Anker SD, AlHabib KF, et al. Heart failure: preventing disease and death worldwide. *ESC Heart Failure*. 2014;1(1):4-25.



Estimated 2010 total heart failure costs: \$39.2 billion

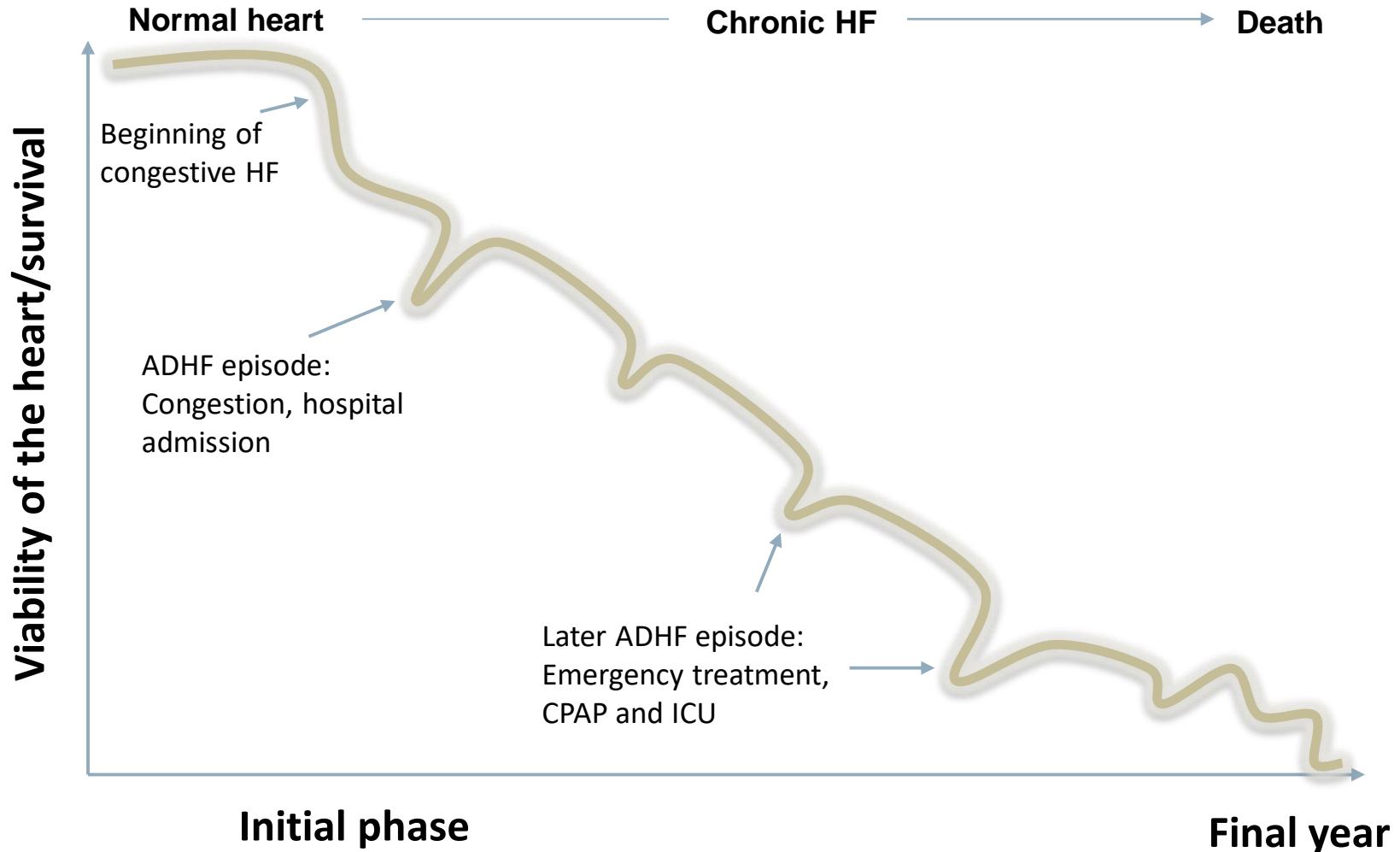
~50% OF PATIENTS DIE WITHIN
5 YEARS OF DIAGNOSIS

~1^{IN}4 HEART FAILURE PATIENTS
DIE WITHIN 1 YEAR OF DIAGNOSIS

~25%

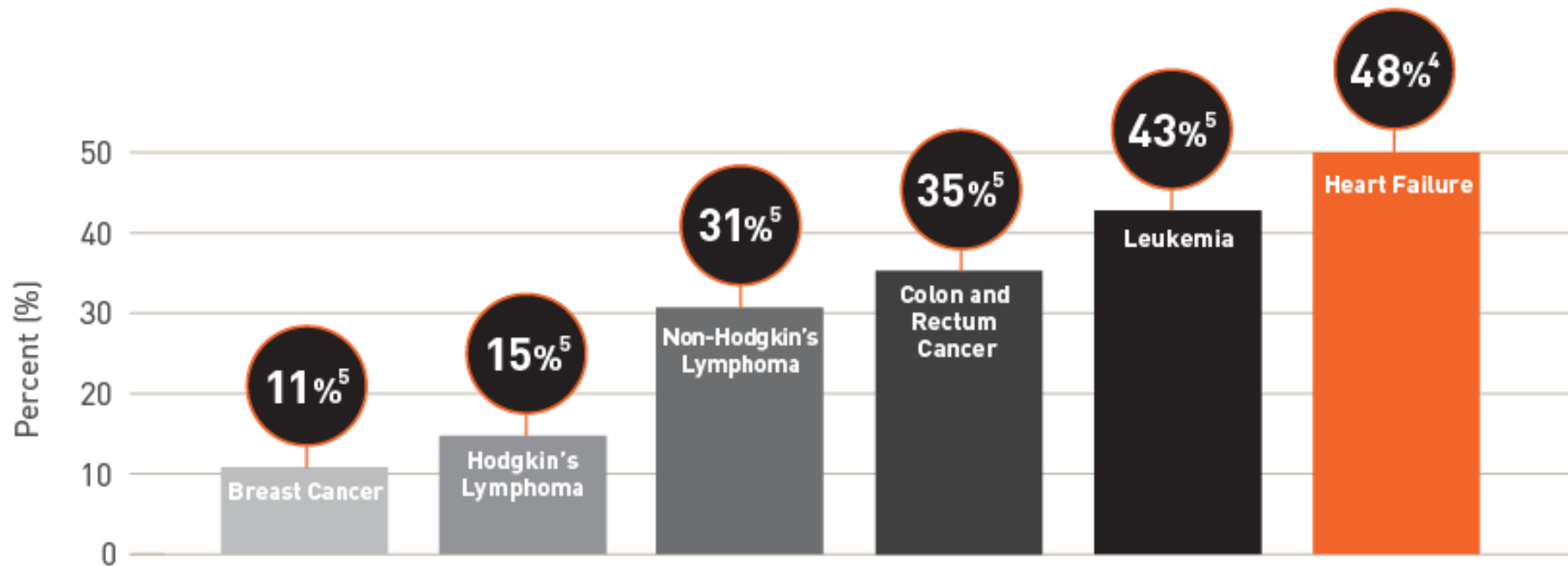
**OF HEART FAILURE PATIENTS
ARE READMITTED WITHIN
1 MONTH OF DISCHARGE⁵**

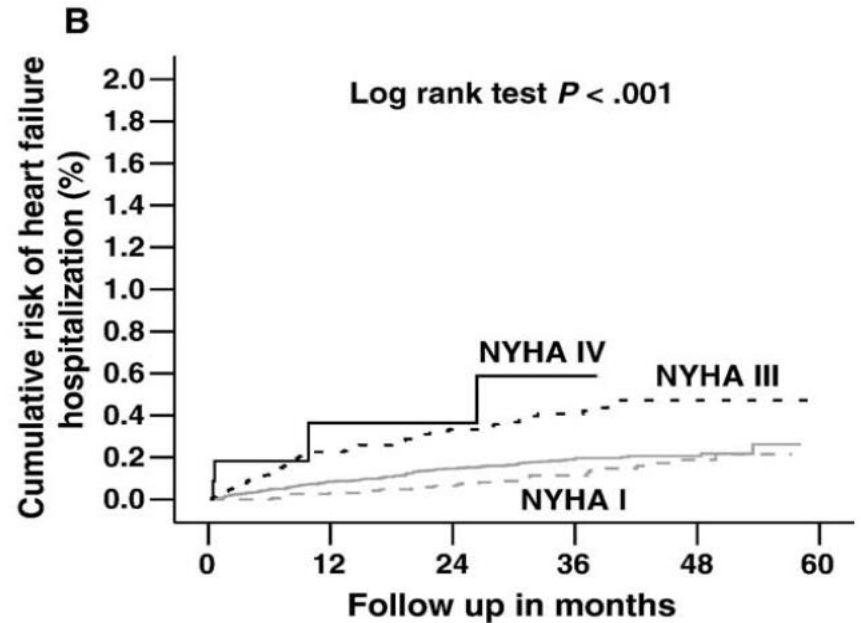
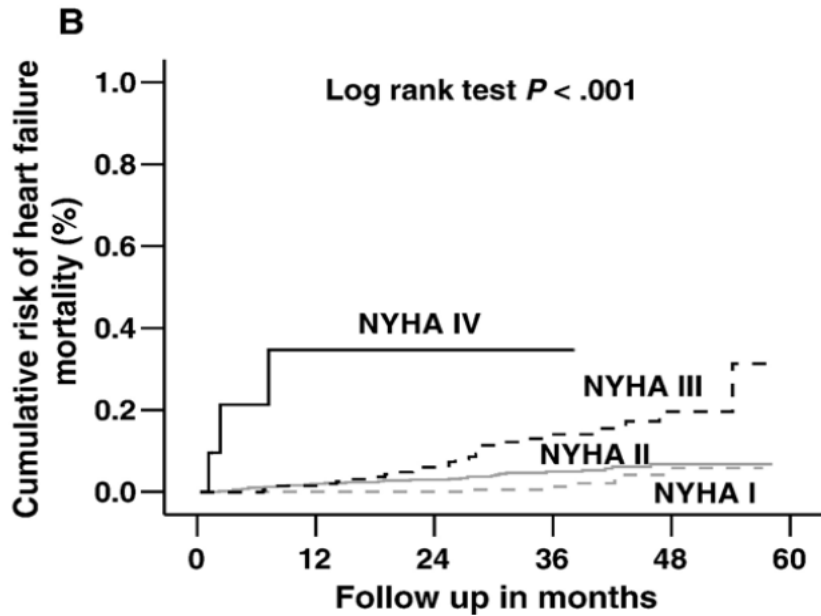
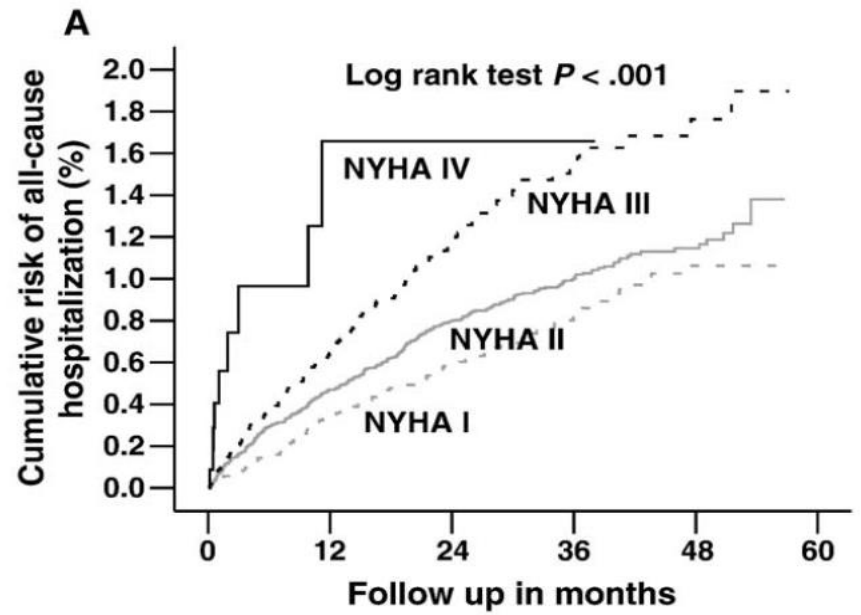
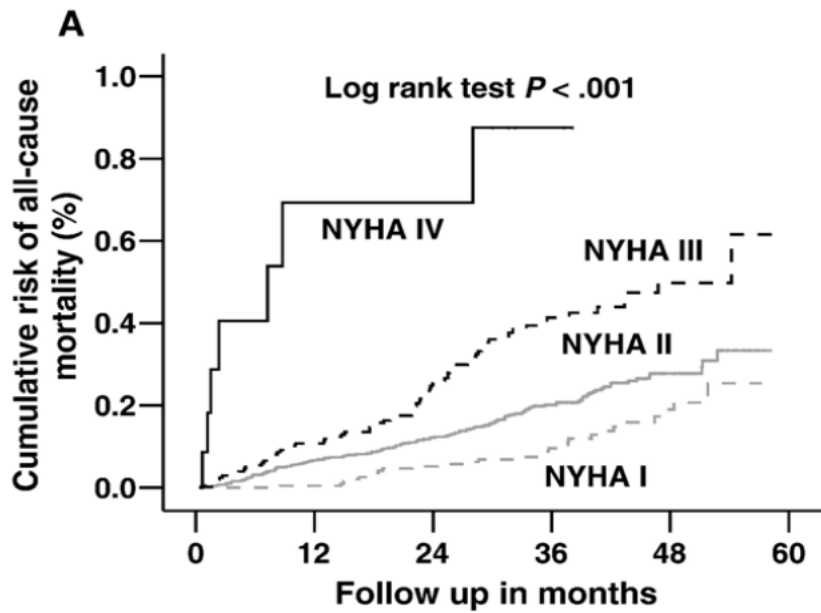
Heart failure progressive clinical course



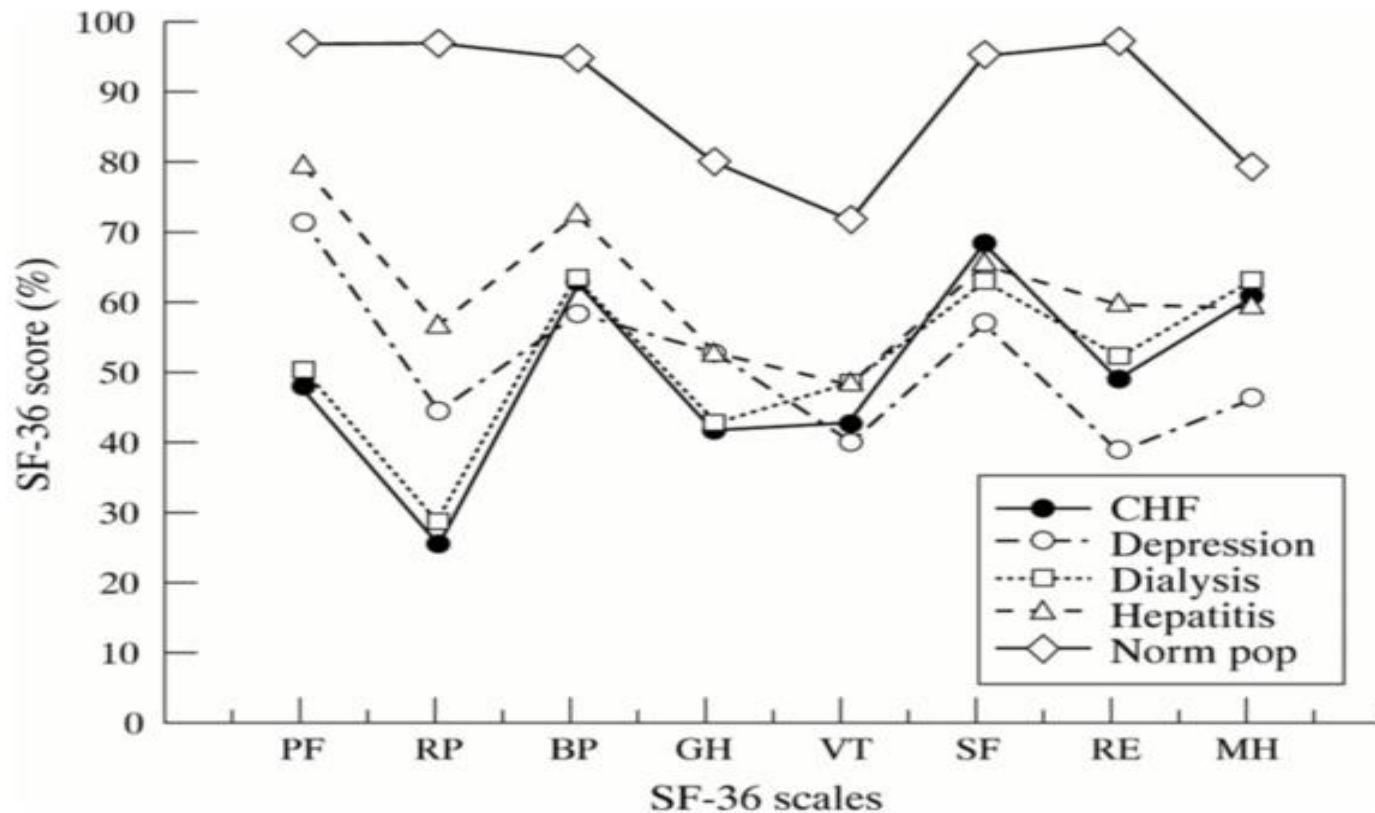
Heart failure is deadlier than many cancers

FIVE-YEAR DEATH RATES

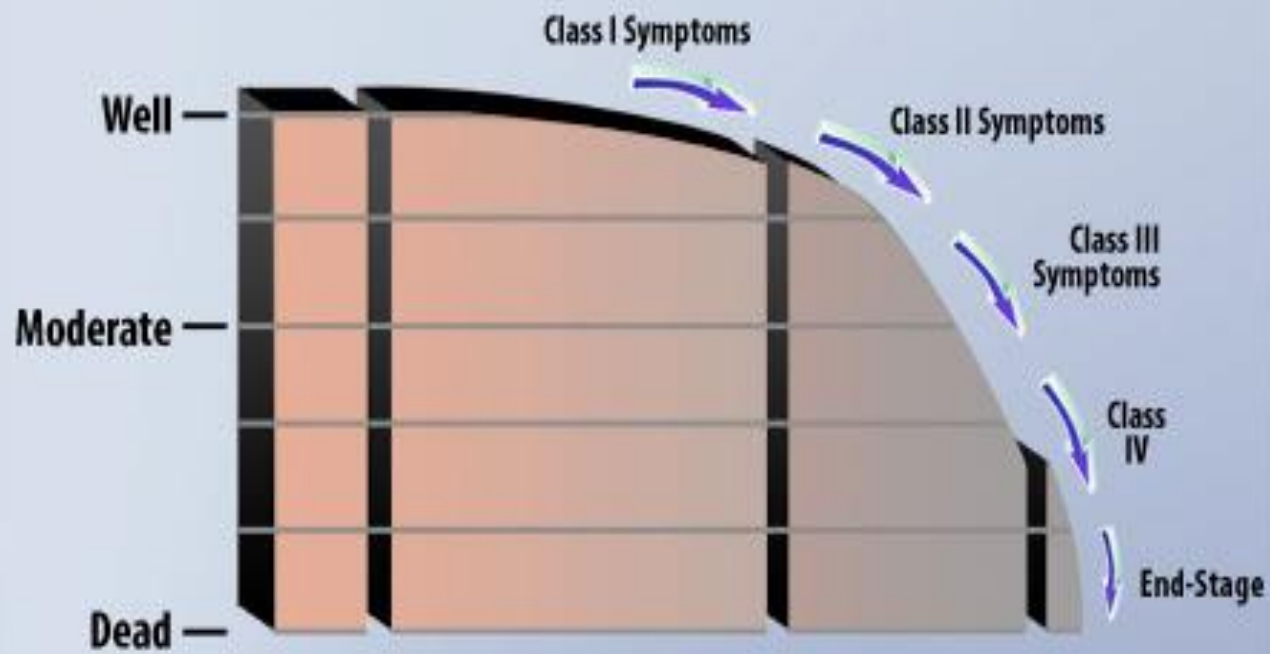




Quality of Life in Heart Failure



New York Heart Association (NYHA) Classifications



Stages, Phenotypes and Treatment of HF

At Risk for Heart Failure

Heart Failure

STAGE A

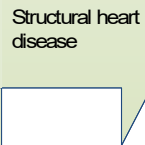
At high risk for HF but without structural heart disease or symptoms of HF

e.g., Patients with:

- HTN
 - Atherosclerotic disease
 - DM
 - Obesity
 - Metabolic syndrome
- or

Patients

- Using cardiotoxins
- With family history of cardiomyopathy



Structural heart disease

STAGE B

Structural heart disease but without signs or symptoms of HF

e.g., Patients with:

- Previous MI
- LV remodeling including LVH and low EF
- Asymptomatic valvular disease



Development of symptoms of HF

STAGE C

Structural heart disease with prior or current symptoms of HF

e.g., Patients with:

- Known structural heart disease and
- HF signs and symptoms



Refractory symptoms of HF at rest, despite GDMT

STAGE D

Refractory HF

e.g., Patients with:

- Marked HF symptoms at rest
- Recurrent hospitalizations despite GDMT

THERAPY

Goals

- Heart healthy lifestyle
- Prevent vascular, coronary disease
- Prevent LV structural abnormalities

Drugs

- ACEI or ARB in appropriate patients for vascular disease or DM
- Statins as appropriate

THERAPY

Goals

- Prevent HF symptoms
- Prevent further cardiac remodeling

Drugs

- ACEI or ARB as appropriate
- Beta blockers as appropriate

In selected patients

- ICD
- Revascularization or valvular surgery as appropriate

THERAPY

Goals

- Control symptoms
- Improve HRQOL
- Prevent hospitalization
- Prevent mortality

Strategies

- Identification of comorbidities

Treatment

- Diuresis to relieve symptoms of congestion
- Follow guideline driven indications for comorbidities, e.g., HTN, AF, CAD, DM
- Revascularization or valvular surgery as appropriate

THERAPY

Goals

- Control symptoms
- Patient education
- Prevent hospitalization
- Prevent mortality

Drugs for routine use

- Diuretics for fluid retention
- ACEI or ARB
- Beta blockers
- Aldosterone antagonists

Drugs for use in selected patients

- Hydralazine/isosorbide dinitrate
- ACEI and ARB
- Digoxin

In selected patients

- CRT
- ICD
- Revascularization or valvular surgery as appropriate

THERAPY

Goals

- Control symptoms
- Improve HRQOL
- Reduce hospital readmissions
- Establish patient's end-of-life goals

Options

- Advanced care measures
- Heart transplant
- Chronic inotropes
- Temporary or permanent MCS
- Experimental surgery or drugs
- Palliative care and hospice
- ICD deactivation

Nomenclature

- Heart failure vs.
- Cardiomyopathy
- LV dysfunction
- Pulmonary edema

Classification

- Left vs. Right
- Systolic vs. Diastolic
- High output vs. low output

ESC guidelines

| Type of HF | | HFrEF | HFmrEF | HFpEF |
|-----------------|----------|-------------------------------|---|---|
| CRITERIA | 1 | Symptoms ± Signs ^a | Symptoms ± Signs ^a | Symptoms ± Signs ^a |
| | 2 | LVEF <40% | LVEF 40–49% | LVEF ≥50% |
| | 3 | – | 1. Elevated levels of natriuretic peptides ^b ; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2). | 1. Elevated levels of natriuretic peptides ^b ; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2). |

Heart Failure Syndrome

- The initial manifestations of hemodynamic dysfunction are a reduction in stroke volume and a rise in ventricular filling pressures under conditions of increased systemic demand for blood flow
- This stimulates a variety of interdependent compensatory responses involving the cardiovascular system, neurohormonal systems, and alterations in renal physiology

Evaluation

Evidence for Congestion (Elevated Filling Pressure)

- Orthopnea
- High Jugular Venous Pressure
- Increasing S_3
- Loud P_2
- Edema
- Ascites
- Rales (Uncommon)
- Abdominojugular Reflux
- Valsalva Square Wave

Congestion at Rest?

Evidence for Low Perfusion

- Narrow Pulse Pressure
- Pulsus Alterations
- Cool Forearms and Legs
- May Be Sleepy, Obtunded
- ACE Inhibitor-Related
 - Symptomatic Hypotension
- Declining Serum Sodium Level
- Worsening Renal Function

Low Perfusion at Rest?

| | No | Yes |
|-----|-------------------|-------------------|
| No | Warm and Dry A | Warm and Wet B |
| Yes | Cold and Dry L | Cold and Wet C |

NYHA Classification

| | |
|-----------|--|
| Class I | No limitations of activities; no symptoms with ordinary activities |
| Class II | Slight or mild limitation of activity; comfortable with rest or mild exertion |
| Class III | Marked limitation of activity; comfortable only at rest |
| Class IV | Any physical activity brings on discomfort, and symptoms occur at rest |

Investigations to consider in all patients

Transthoracic echocardiography is recommended to evaluate cardiac structure and function, including diastolic function (Section 4.1.2), and to measure LVEF to make the diagnosis of HF, assist in planning and monitoring of treatment, and to obtain prognostic information.

A 12-lead ECG is recommended to determine heart rhythm, heart rate, QRS morphology, and QRS duration, and to detect other relevant abnormalities (*Table 5*). This information also assists in planning treatment and is of prognostic importance. A completely normal ECG makes systolic HF unlikely.

Measurement of blood chemistry (including sodium, potassium, calcium, urea/blood urea nitrogen, creatinine/estimated glomerular filtration rate, liver enzymes and bilirubin, ferritin/TIBC) and thyroid function is recommended to:

- (i) Evaluate patient suitability for diuretic, renin–angiotensin–aldosterone antagonist, and anticoagulant therapy (and monitor treatment)
- (ii) Detect reversible/treatable causes of HF (e.g. hypocalcaemia, thyroid dysfunction) and co-morbidities (e.g. iron deficiency)
- (iii) Obtain prognostic information.

A complete blood count is recommended to:

- (i) Detect anaemia, which may be an alternative cause of the patient's symptoms and signs and may cause worsening of HF
- (ii) Obtain prognostic information.

Measurement of natriuretic peptide (BNP, NT-proBNP, or MR-proANP) should be considered to:

- (i) Exclude alternative causes of dyspnoea (if the level is below the exclusion cut-point—see *Figure 1*—HF is very unlikely)
- (ii) Obtain prognostic information.

A chest radiograph (X-ray) should be considered to detect/exclude certain types of lung disease, e.g. cancer (does not exclude asthma/ COPD). It may also identify pulmonary congestion/oedema and is more useful in patients with suspected HF in the acute setting.

Investigations to consider in selected patients

CMR imaging is recommended to evaluate cardiac structure and function, to measure LVEF, and to characterize cardiac tissue, especially in subjects with inadequate echocardiographic images or where the echocardiographic findings are inconclusive or incomplete (but taking account of cautions/contraindications to CMR).

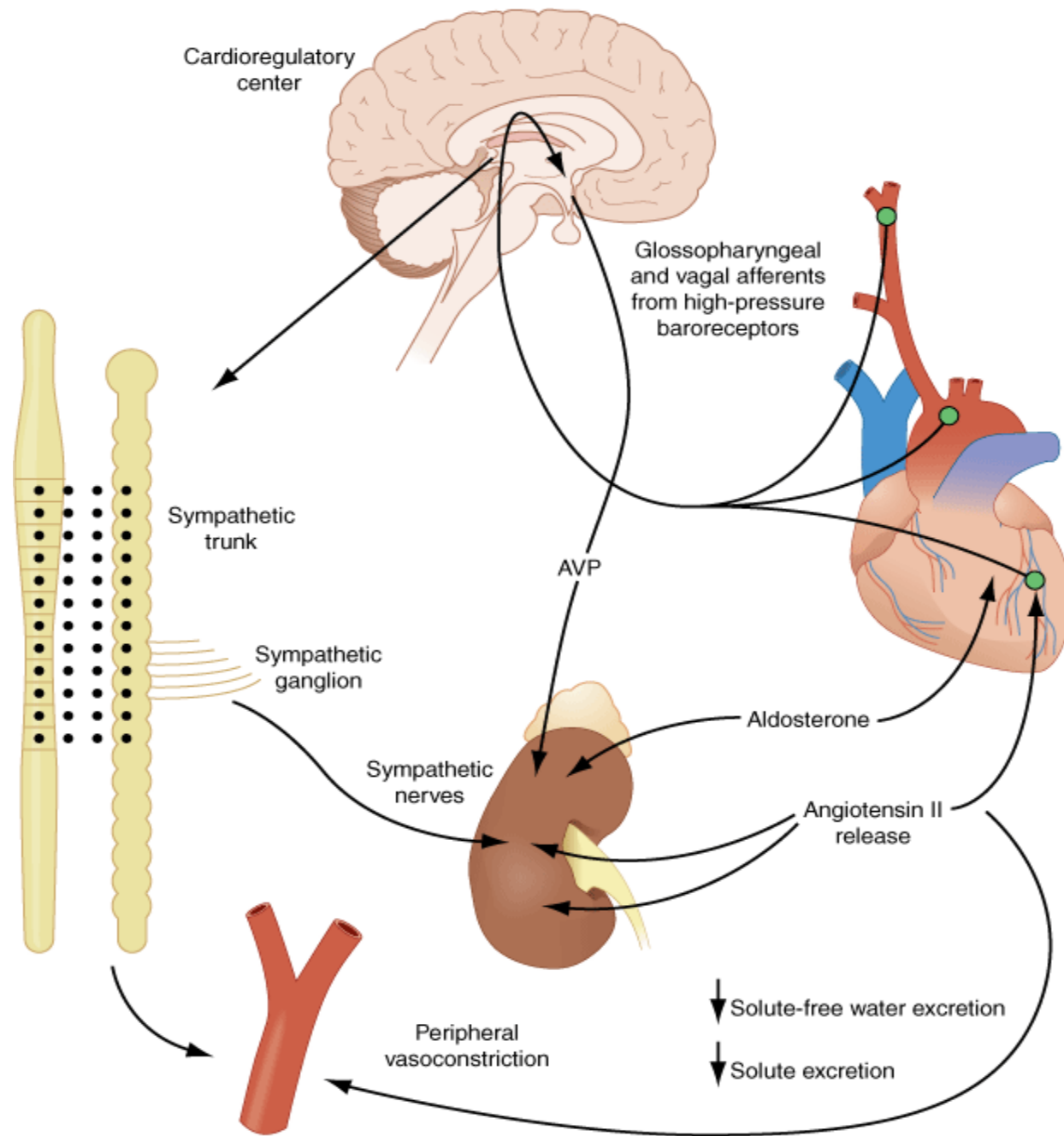
Coronary angiography is recommended in patients with angina pectoris, who are considered suitable for coronary revascularization, to evaluate the coronary anatomy.

Myocardial perfusion/ischaemia imaging (echocardiography, CMR, SPECT, or PET) should be considered in patients thought to have CAD, and who are considered suitable for coronary revascularization, to determine whether there is reversible myocardial ischaemia and viable myocardium.

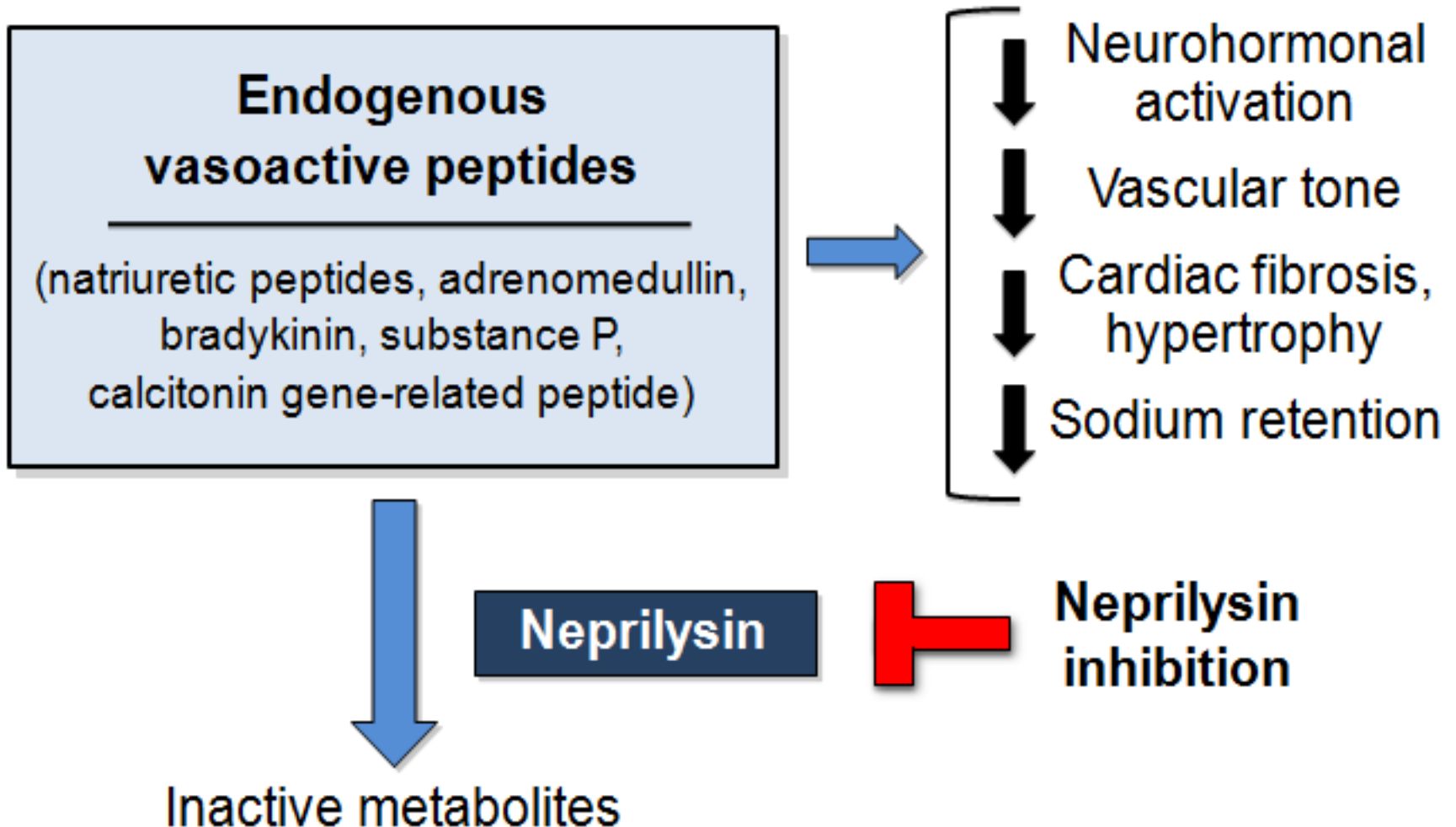
Left and right heart catheterization is recommended in patients being evaluated for heart transplantation or mechanical circulatory support, to evaluate right and left heart function and pulmonary arterial resistance.

Exercise testing should be considered:

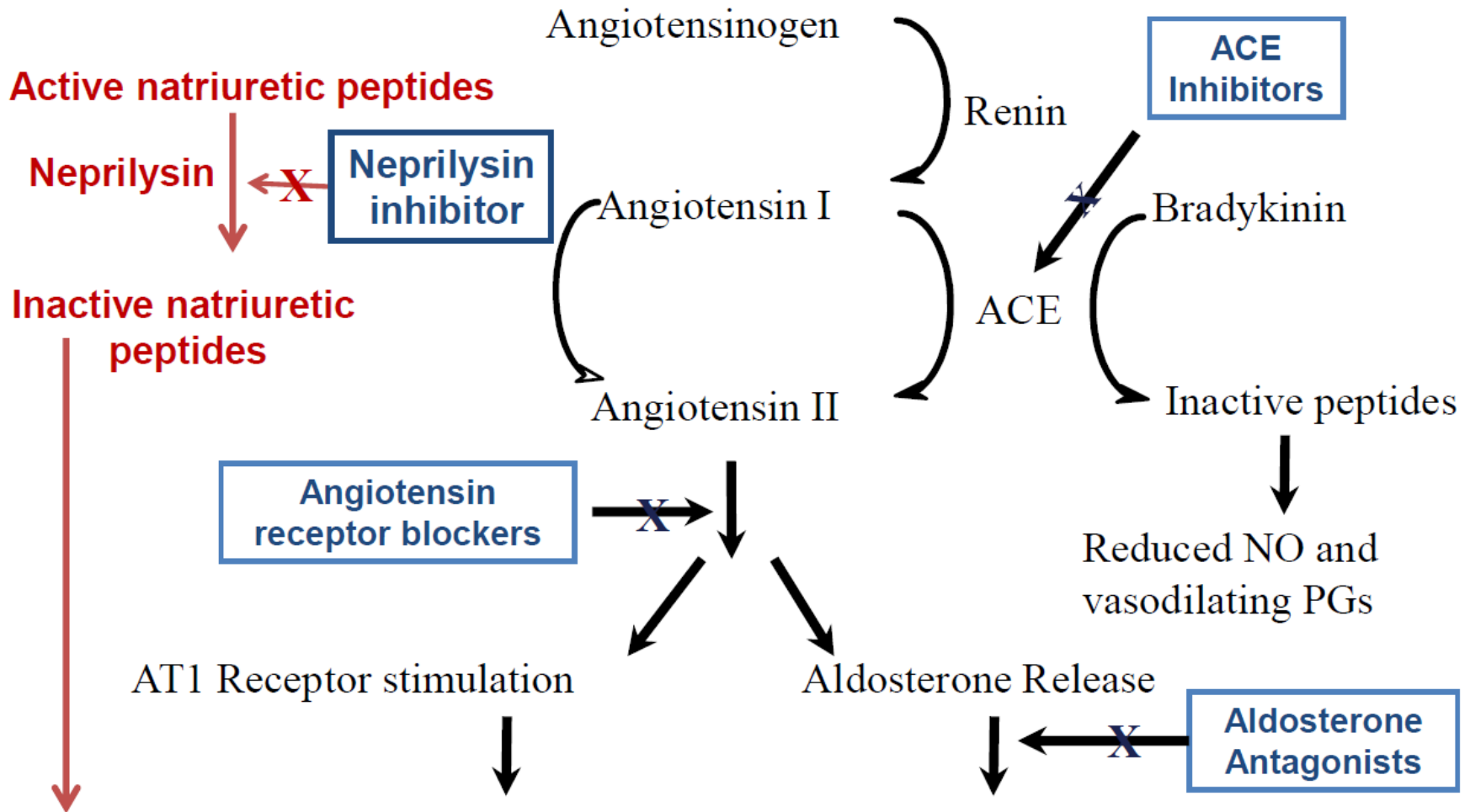
- (i) To detect reversible myocardial ischaemia
- (ii) As part of the evaluation of patients for heart transplantation and mechanical circulatory support
- (iii) To aid in the prescription of exercise training
- (iv) To obtain prognostic information.



Natriuretic Peptides

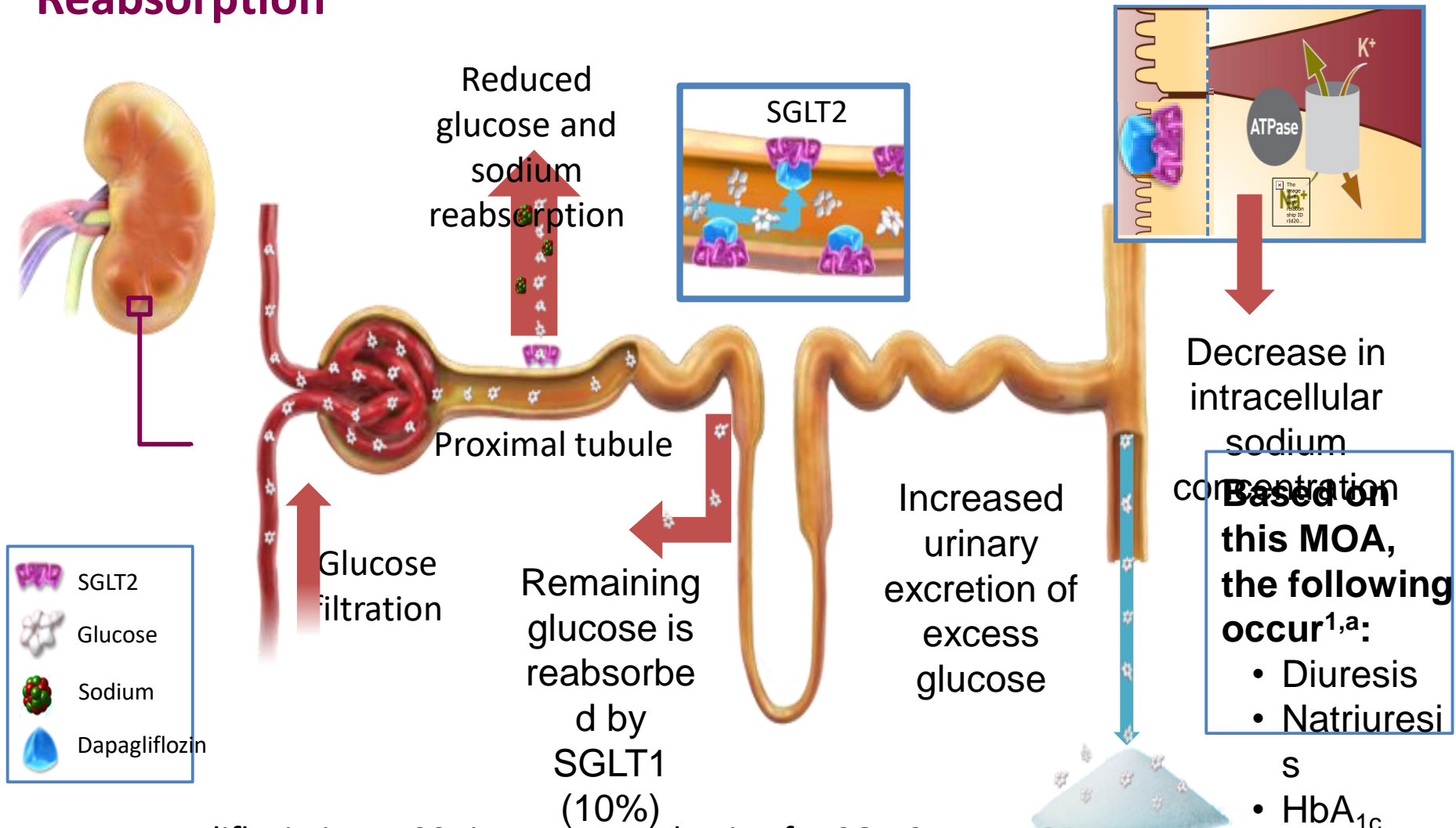


Neurohormonal blockade in HF – revisited



Vasoconstriction, Na retention, myocyte hypertrophy and apoptosis, endothelial dysfunction, sympathetic activation, free radical generation, etc

SGLT2 Inhibitors Block SGLT2 and Reduce Glucose and Na⁺ Reabsorption¹⁻³



- Dapagliflozin is >1400 times more selective for SGLT2 versus SGLT1^b

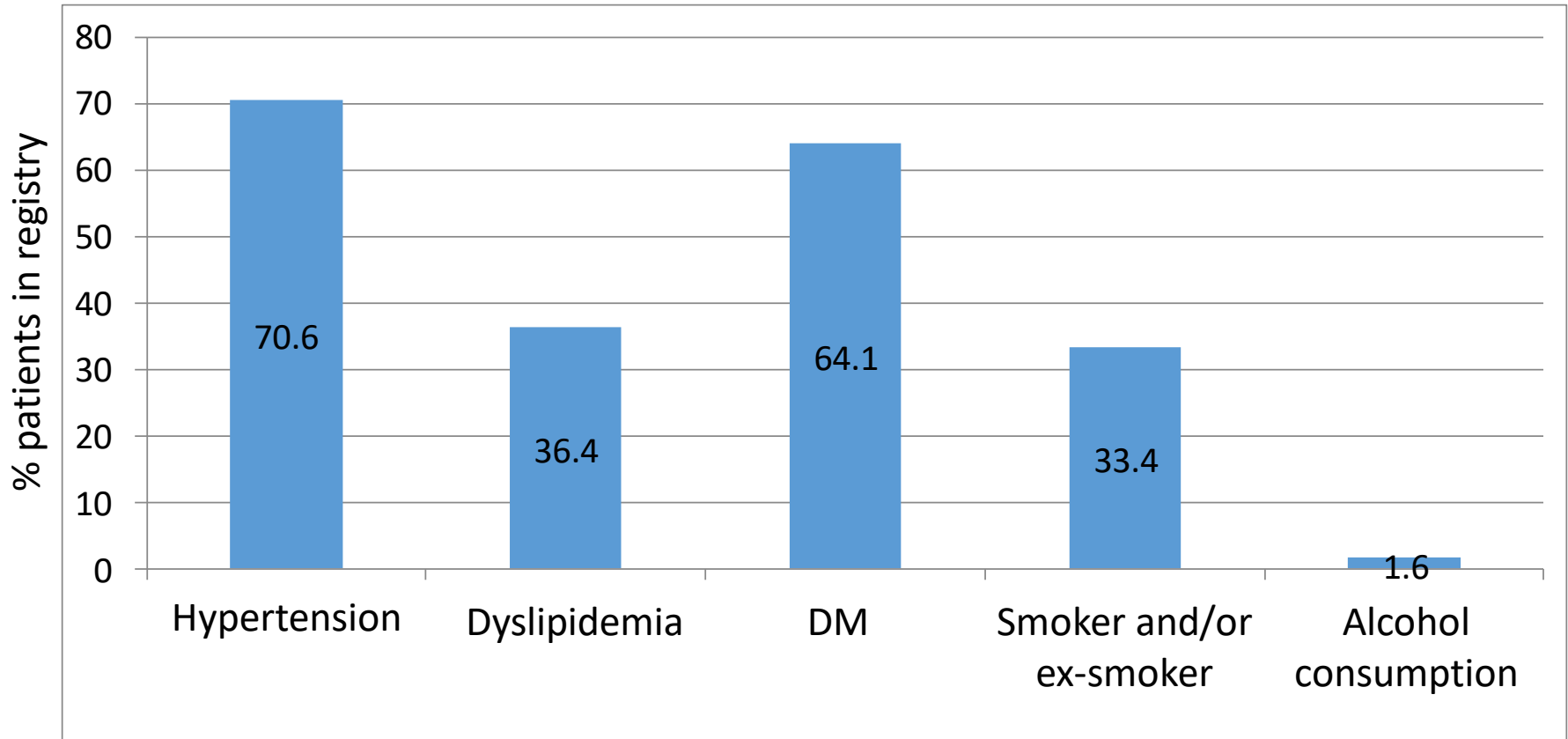
^aPlease note that dapagliflozin is only indicated to improve glycemic control; ^bIncreases urinary volume by only ~1 additional void/day (~375 mL/day) in a 12-week study of healthy subjects and patients with T2DM

The safety profile of SGLT2 inhibitors is currently under review by EMA PRAC. SGLT2 inhibitors are not marketed in France

SBP, systolic blood pressure; SGLT, sodium-glucose co-transporter; T2DM, Type 2 diabetes mellitus

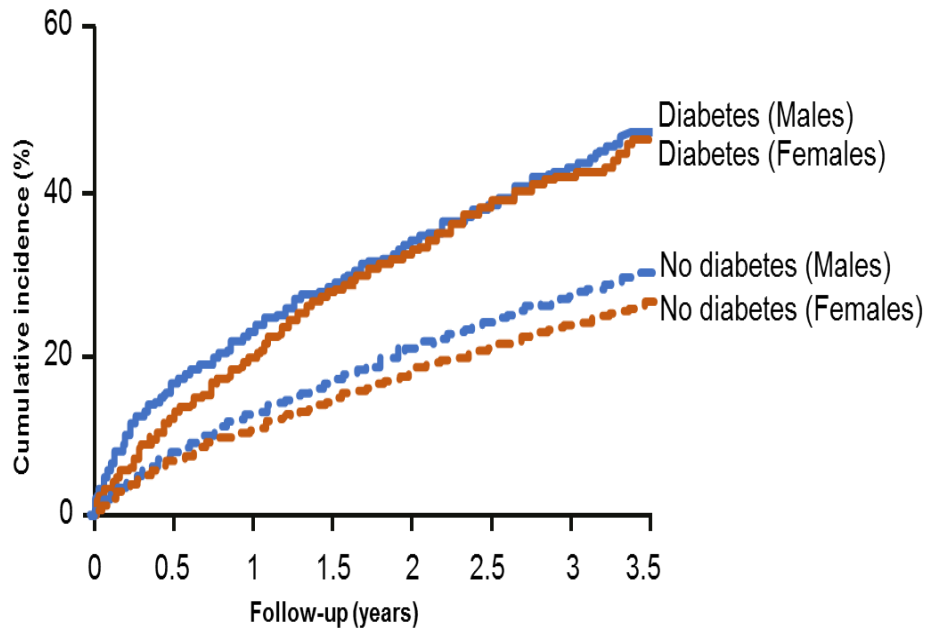
1. Marsenic O. *Am J Kidney Dis* 2009;53:875-885; 2. FORXIGA. Summary of product characteristics, 2014; 3. Mudaliar S, et al. *Diabetes Care* 2016;39:1115-1122

Risk factors/Comorbidities



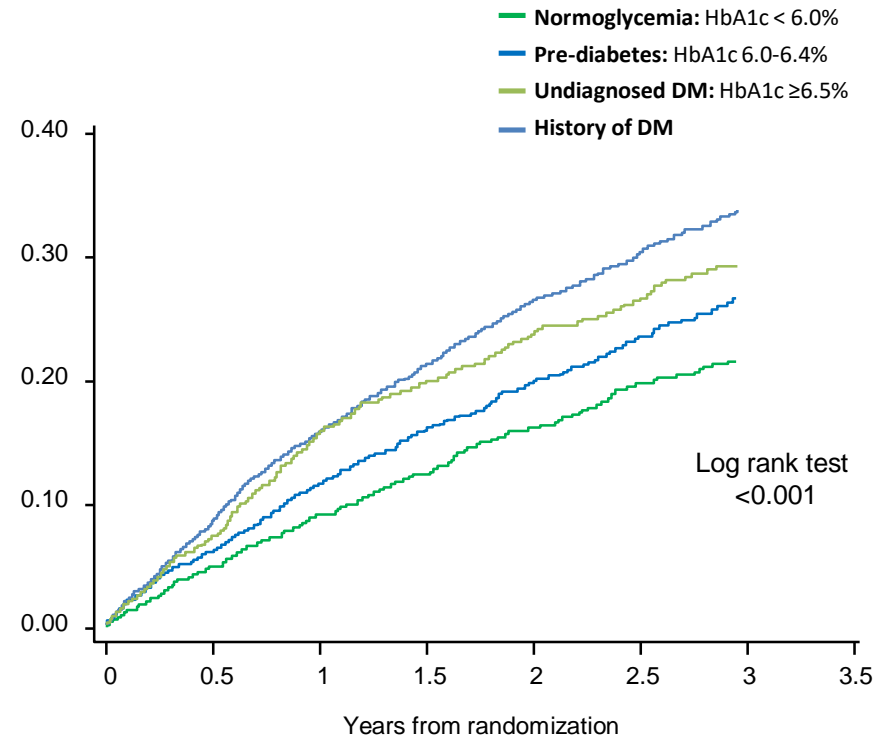
Association of HF and DM predicts worse outcomes than either disease would alone

CV death or HF hospitalization by DM status in patients with HF³



Data from CHARM trial program;

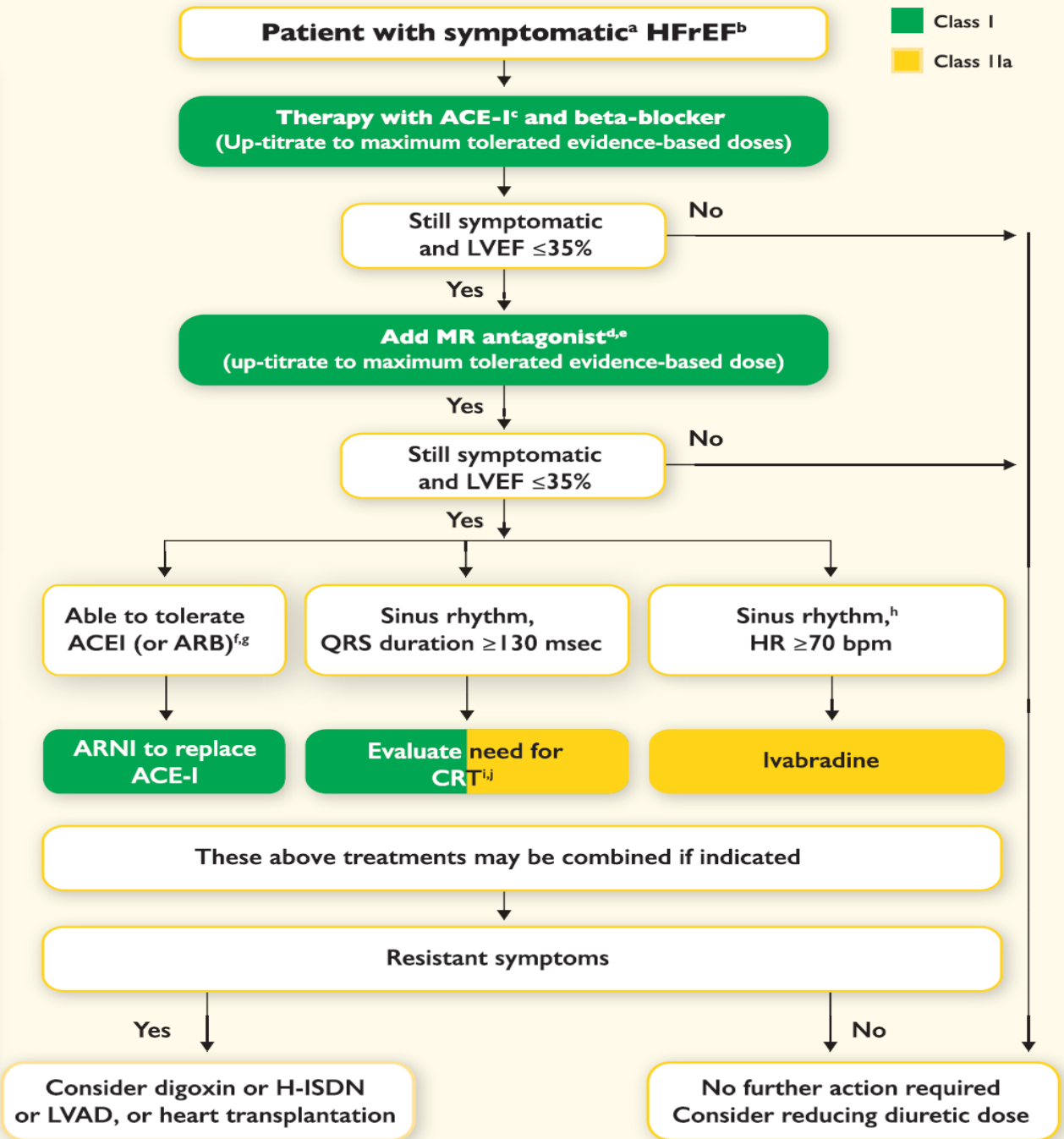
CV death or HF hospitalization by degree of dysglycemia in patients with HFrEF²



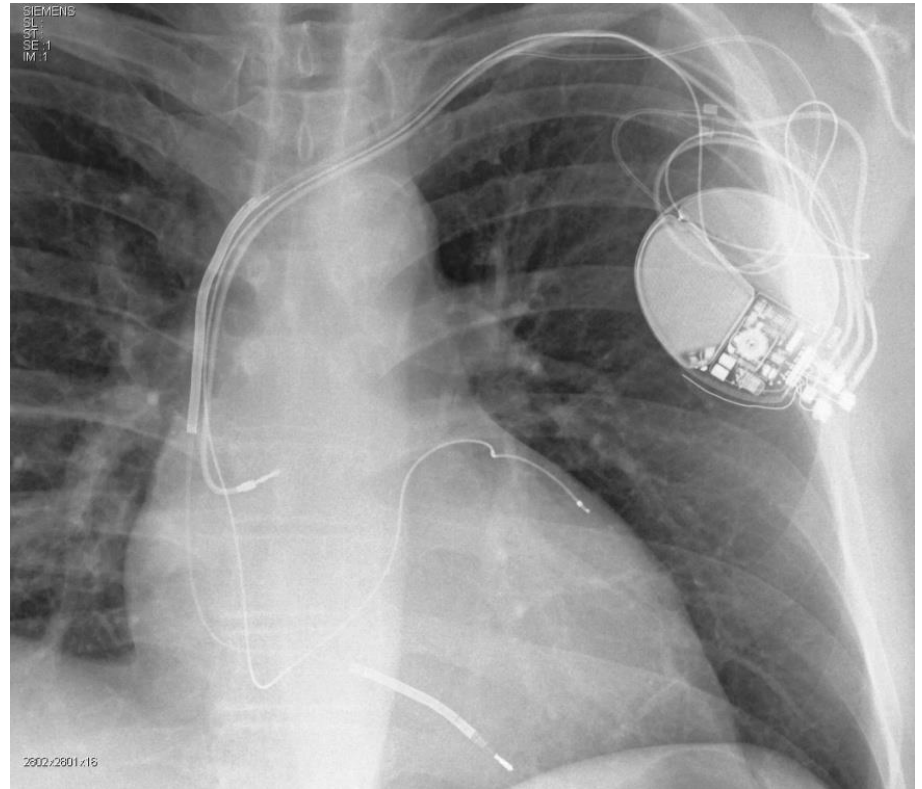
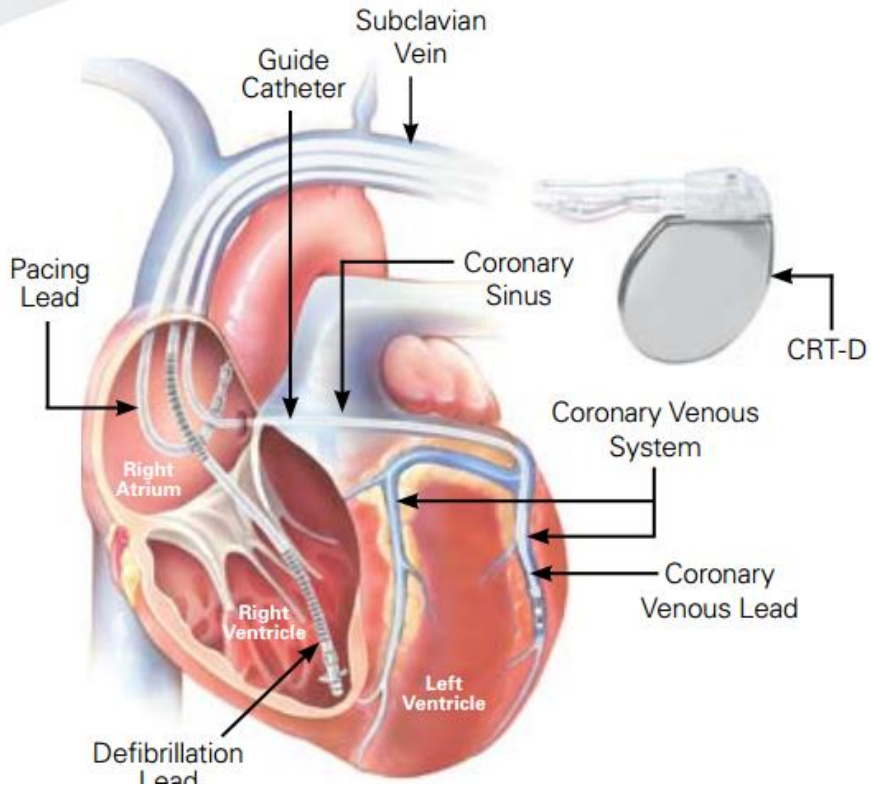
Data from PARADIGM-HF trial

Diuretics to relieve symptoms and signs of congestion

If LVEF \leq 35% despite OMT or a history of symptomatic VT/VF, implant ICD



Devices

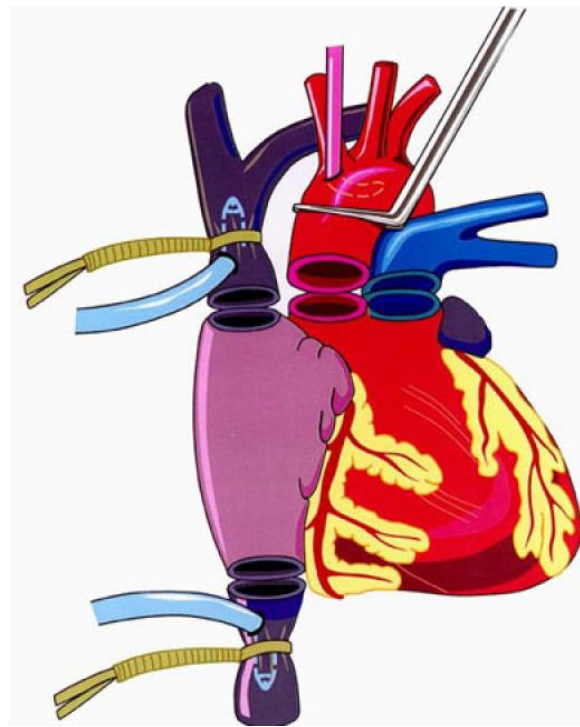


Advanced heart failure

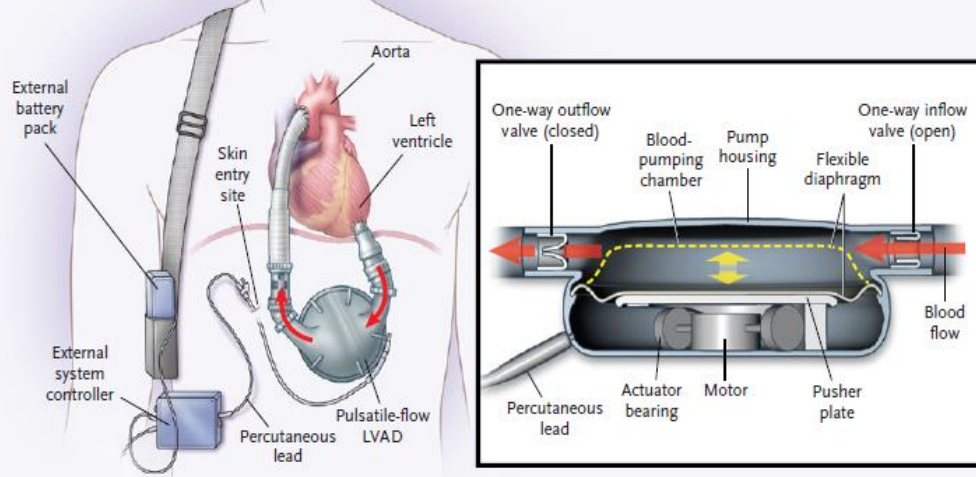
- *Defined* as persistent symptoms (NYHA class III–IV) that limit daily life despite routine therapy with agents of known benefit
- End-stage, refractory heart failure, probably accounts for 5% to 10% of the total population
- This group, consumes >60% of health-care expenditures for all patients with heart failure

Heart Transplantation

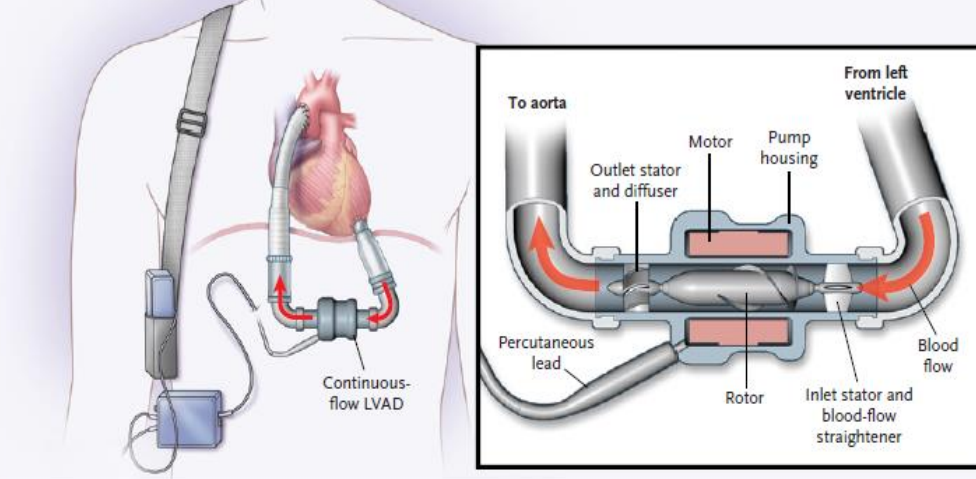
- Orthotopic cardiac transplantation remains the definitive therapy for terminal heart failure
- 5-year survival of 70%,
- 10-year survival of 60%,
- Markedly improved quality of life
- Donor organ availability has remained static even as the waiting list for heart transplant grows



A Pulsatile-Flow LVAD

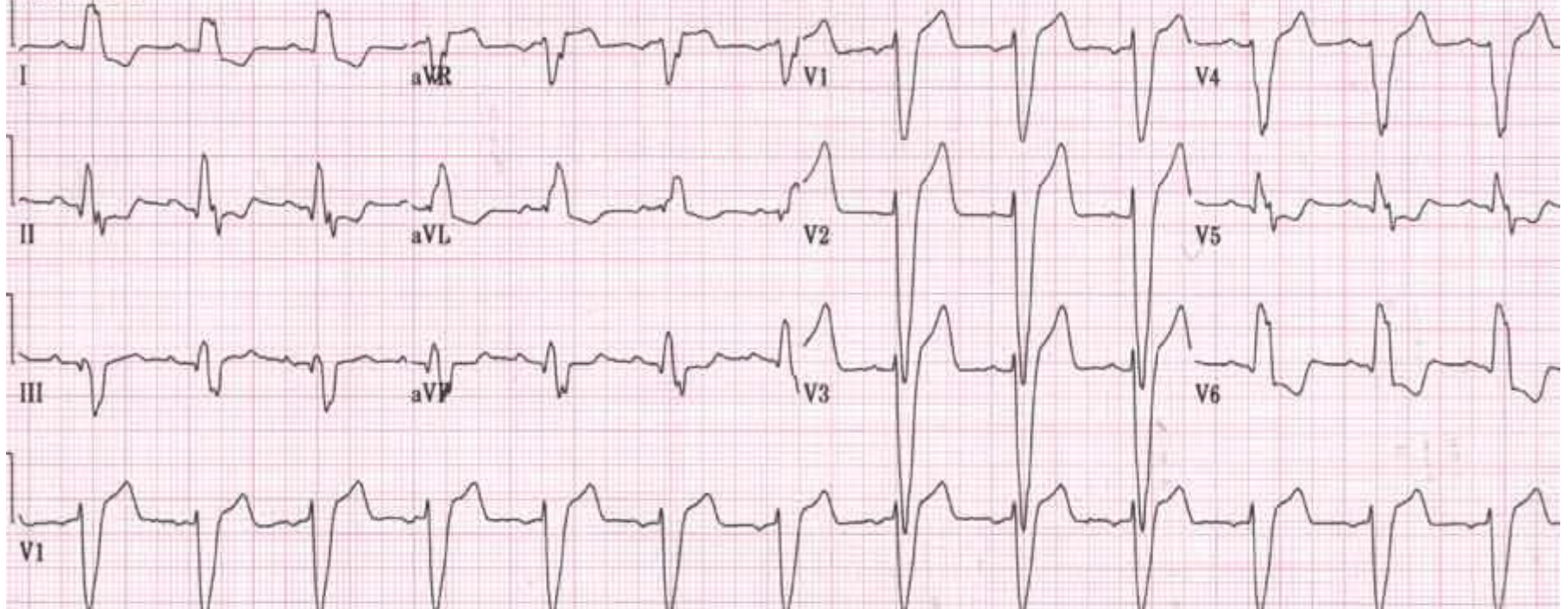


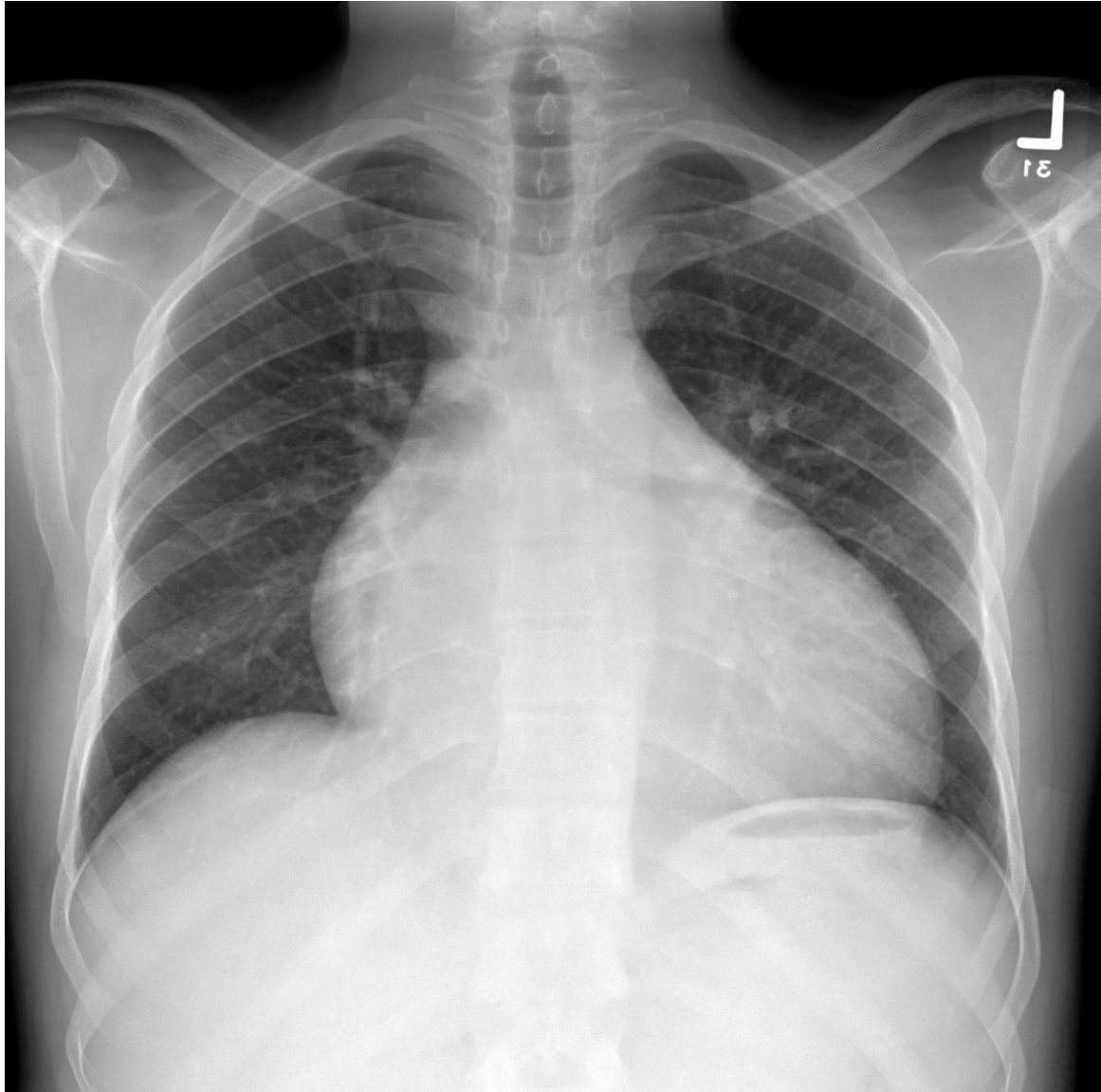
B Continuous-Flow LVAD



- 56 Y/O gentleman
- Diagnosed dilated cardiomyopathy
- LVEF 25%
- NYHA class II
- O/E B/P 112/68 HR 82 bpm
- JVP 7 cm water,
- Soft S3 and grade 2 PSM
- Chest clear,
- No LL edema and warm extremities

EMEDU



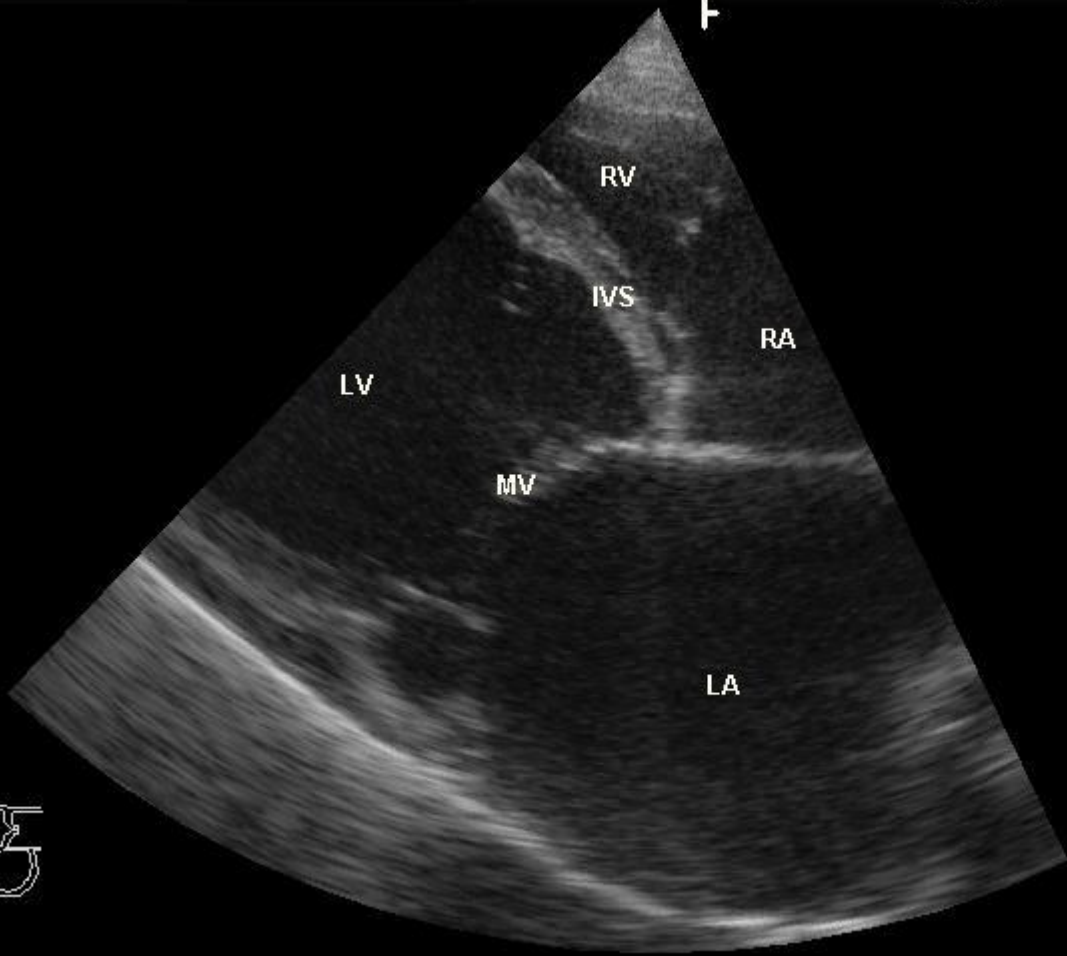


06/01/05 14:28:29
P80 4MHz S611

B5



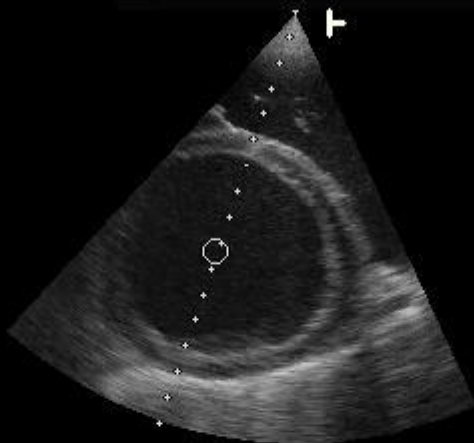
CN15
16cm
DB72
V 84



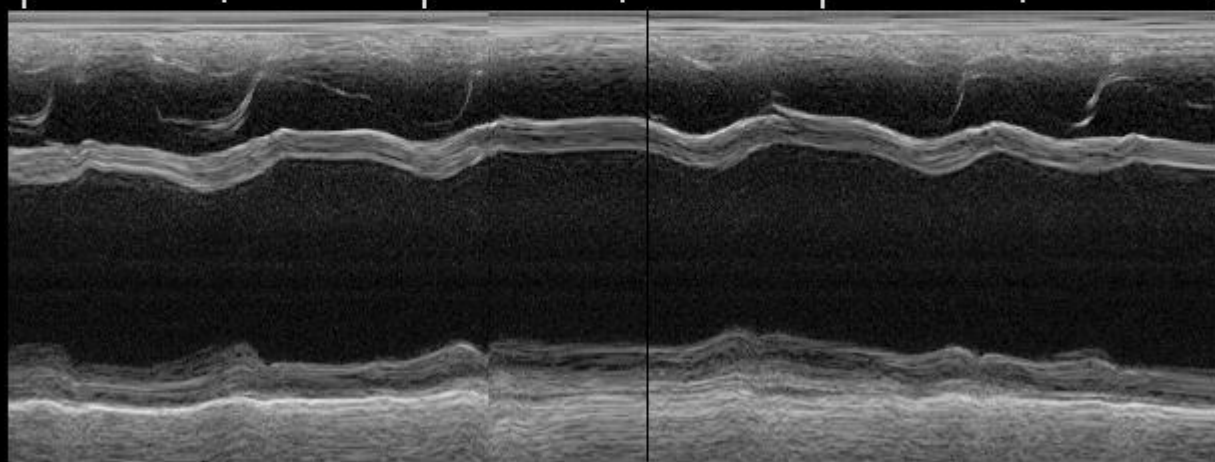
MI < 0.4

06/01/05 14:25:43

P80 4MHz S611



CN0
16cm
DB48
V 62



TIS<0.4

| | Starting dose (mg) | Target dose (mg) |
|------------------------------|--------------------|------------------|
| ACE inhibitor | | |
| Captopril ^a | 6.25 t.i.d. | 50 t.i.d. |
| Enalapril | 2.5 b.i.d. | 10–20 b.i.d. |
| Lisinopril ^b | 2.5–5.0 o.d. | 20–35 o.d. |
| Ramipril | 2.5 o.d. | 5 b.i.d. |
| Trandolapril ^b | 0.5 o.d. | 4 o.d. |
| Beta-blocker | | |
| Bisoprolol | 1.25 o.d. | 10 o.d. |
| Carvedilol | 3.125 b.i.d. | 25–50 b.i.d. |
| Metoprolol succinate (CR/XL) | 12.5/25 o.d. | 200 o.d. |
| Nebivolol ^c | 1.25 o.d. | 10 o.d. |
| ARB | | |
| Candesartan | 4 or 8 o.d. | 32 o.d. |
| Valsartan | 40 b.i.d. | 160 b.i.d. |
| Losartan ^{b,c} | 50 o.d. | 150 o.d. |
| MRA | | |
| Eplerenone | 25 o.d. | 50 o.d. |
| Spirolactone | 25 o.d. | 25–50 o.d. |

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

Recommendations

Thiazolidinediones (glitazones) should not be used as they cause worsening HF and increase the risk of HF hospitalization.

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.

NSAIDs and COX-2 Inhibitors should be avoided if possible as they may cause sodium and water retention, worsening renal function and worsening HF.

The addition of an ARB (or renin inhibitor) to the combination of an ACE inhibitor AND a mineralocorticoid antagonist is NOT recommended because of the risk of renal dysfunction and hyperkalaemia.

Acute Heart Failure

- **FACTORS THAT MAY PRECIPITATE ACUTE DECOMPENSATION OF CHRONIC HEART FAILURE**

Events usually leading to rapid deterioration

- Rapid arrhythmia or severe bradycardia/conduction disturbance
- Acute coronary syndrome
- Mechanical complication of acute coronary syndrome (e.g. rupture of interventricular septum, mitral valve chordal rupture, right ventricular infarction)
- Acute pulmonary embolism
- Hypertensive crisis
- Cardiac tamponade
- Aortic dissection
- Surgery and perioperative problems
- Peripartum cardiomyopathy

Events usually leading to less rapid deterioration

- Infection (including infective endocarditis)
- Exacerbation of COPD/asthma
- Anaemia
- Kidney dysfunction
- Non-adherence to diet/drug therapy
- Iatrogenic causes (e.g. prescription of an NSAID or corticosteroid; drug interactions)
- Arrhythmias, bradycardia, and conduction disturbances not leading to sudden, severe change in heart rate
- Uncontrolled hypertension
- Hypothyroidism or hyperthyroidism
- Alcohol and drug abuse

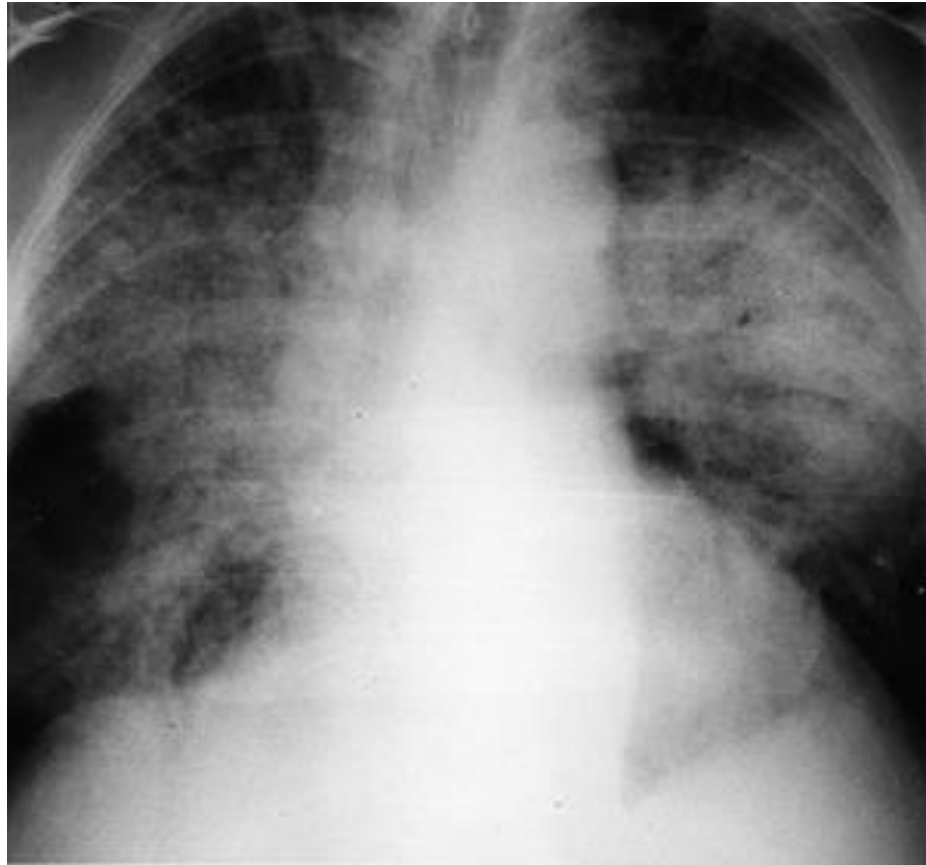
Two Minute Assessment of Hemodynamic Profile

| | | Congestion at rest? | |
|-----------------------------------|-----|-----------------------------------|-----------------------------------|
| | | NO | YES |
| Low perfusion at rest? | NO | <i>Warm & Dry</i> A | <i>Warm & Wet</i> B |
| | YES | <i>Cold & Dry</i> L | <i>Cold & Wet</i> C |

| | |
|--|--|
| <p><u>Evidence for low perfusion</u> Narrow pulse pressure⁺ Cool extremities⁺ May be sleepy, obtunded Suspect from ACEI hypotension and low Serum Sodium One cause of worsening renal fn</p> | <p><u>Evidence for Congestion</u></p> <p>Orthopnea⁺ Elevated JVP[±] Edema (25%) Pulsatile hepatomegaly Ascites Rales (rare in chronic HF) Louder S3</p> <p>P2 radiation leftward Abdomino-jugular reflex Valsalva square wave</p> |
|--|--|

** Most helpful*





Suspected acute heart failure

History/examination
(including blood pressure and respiratory rate)

| | |
|--------------------------------|-------------------|
| Chest X-ray | ECG |
| Echocardiogram or NP (or both) | Oxygen saturation |
| Blood chemistry | Full blood count |

Simultaneously assess for

Ventilation/
systemic
oxygenation
inadequate?^a

Life-threatening
arrhythmia/
bradycardia?^b

Blood pressure
<85 mmHg
or shock^c

Acute
coronary
syndrome^d

Acute
mechanical
cause/severe
valvular disease^e

**Urgent
action
if present**

- Oxygen
- NIV
- ETT and invasive ventilation

- Electrical cardioversion
- Pacing

- Inotrope/
vasopressor
- Mechanical circulatory support (e.g. IABP)

- Coronary reperfusion
- Antithrombotic therapy

- Echocardiography
- Surgical/
percutaneous intervention

ECG = electrocardiogram; ETT = endotracheal tube; IABP = intra-aortic balloon pump; NIV = non-invasive ventilation; NP = natriuretic peptide.

^aFor example, respiratory distress, confusion, SpO₂ <90% or PaO₂ <60 mmHg (8.0 kPa).

THANK YOU & GOOD LUCK