HeFSSA Practitioners Program 2019
"Challenges in Heart Failure Management"

- Dyspnoea and leg swelling, when is it heart failure?
- Management of acute decompensated heart failure
- Heart failure during pregnancy
- Refractory oedema in heart failure patient

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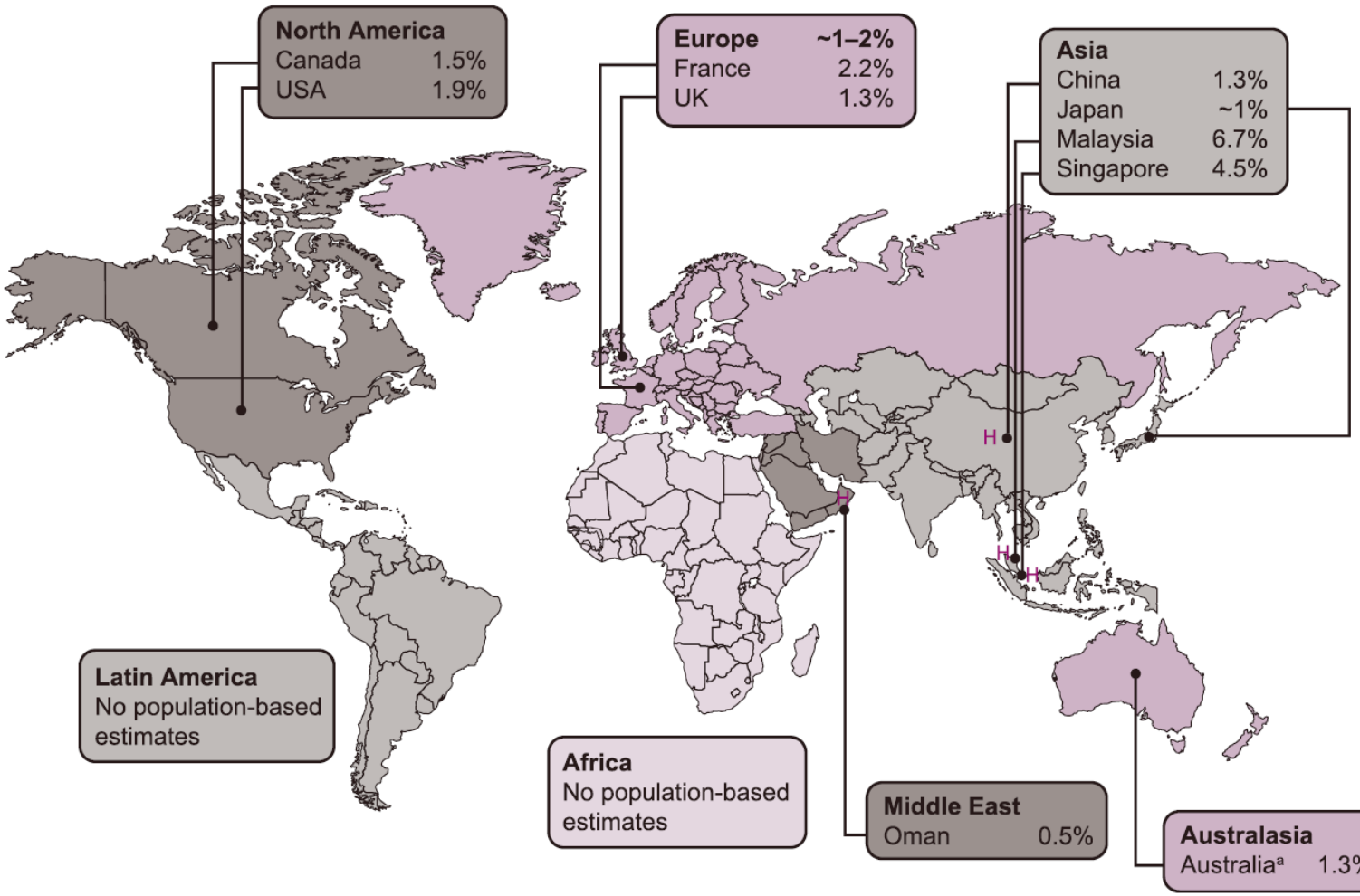
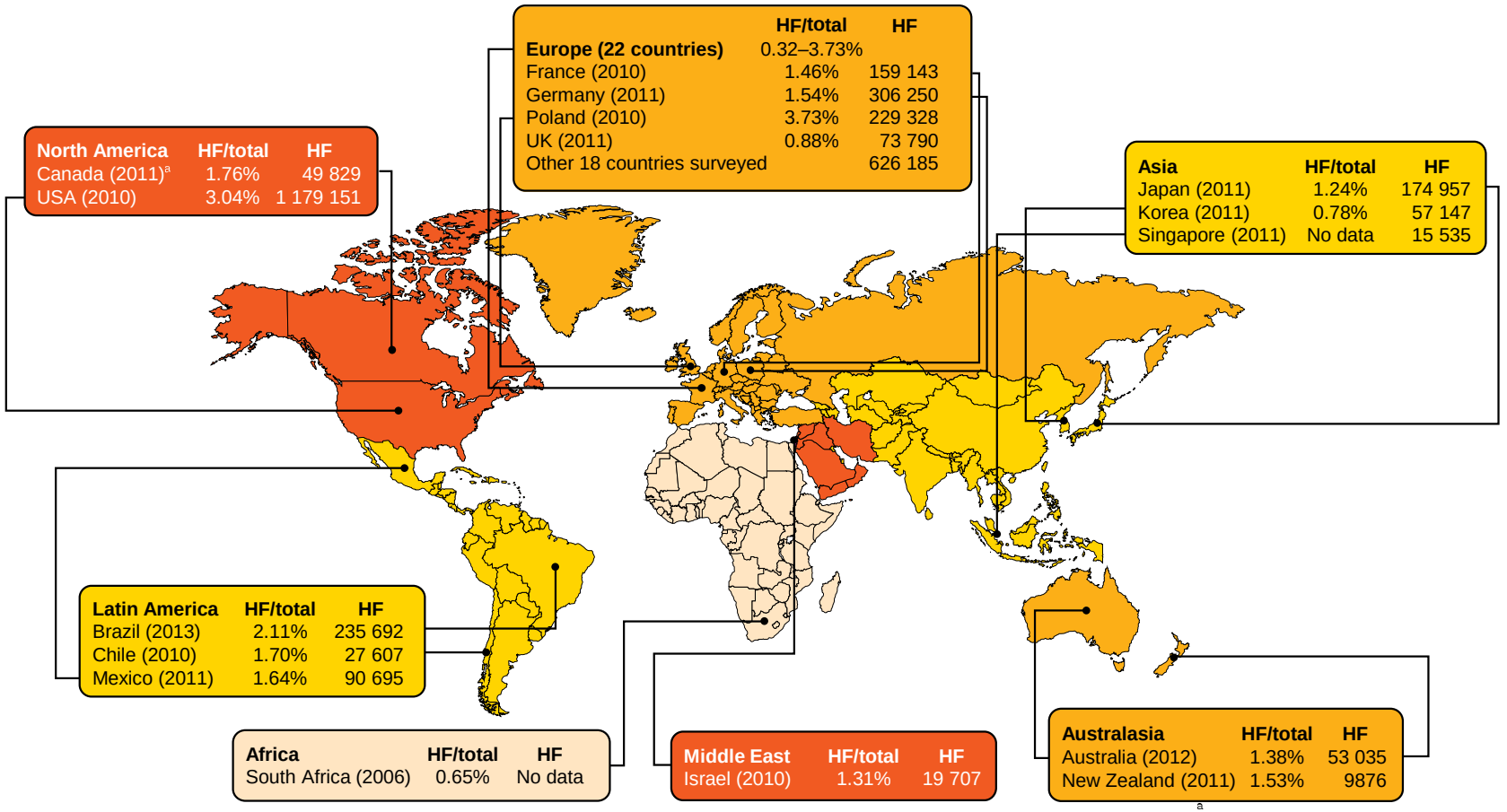
Prevalence of Heart Failure



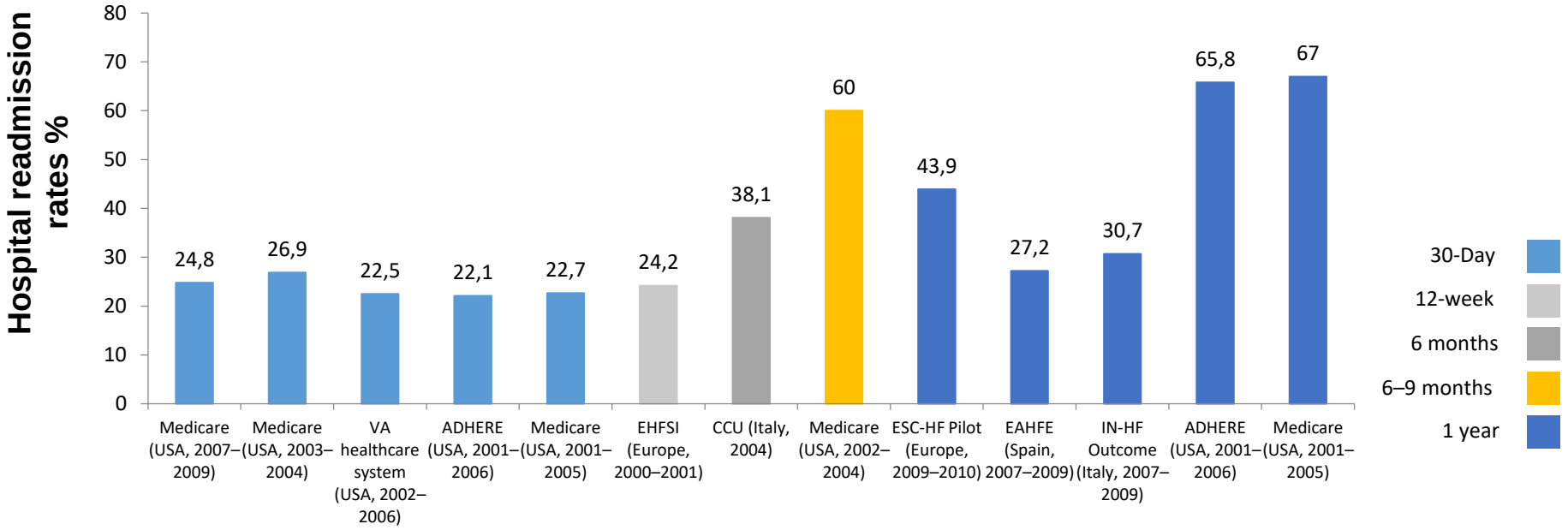
Ponikowski et al. ESC Heart Failure 2014; 1: 4–25

Proportion of HF hospitalisations across the globe



Ponikowski et al. ESC Heart Failure 2014; 1: 4–25

High rates of hospital readmission

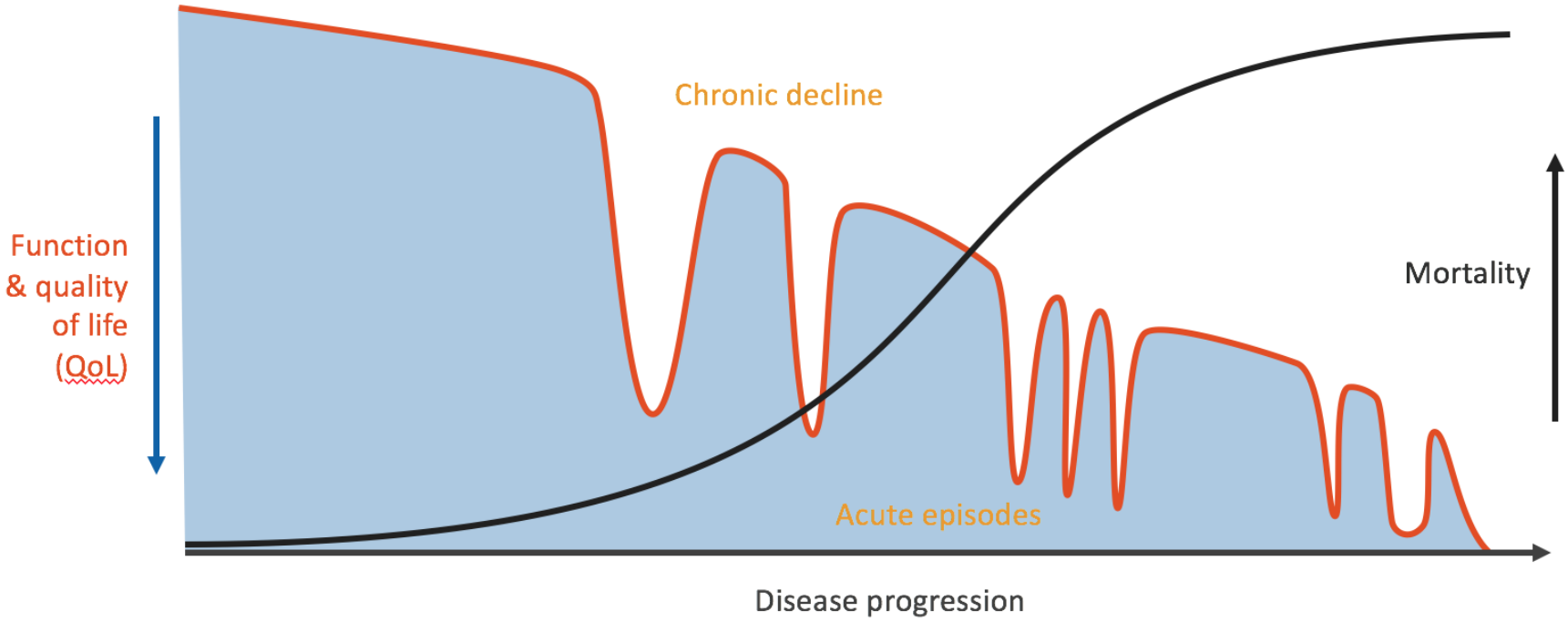


HF, heart failure

1. Cowie MR et al. ESC Heart Failure 2014;1:110–145

HFrEF Natural History

- Increasing frequency of acute events with disease progression leads to high rates of hospitalization and increased risk of mortality
- With each acute event, myocardial injury may contribute to progressive LV dysfunction



LV: left ventricular

Gheorghiade et al. Am J Cardiol 2005;96:11G–17G; Gheorghiade & Pang. J Am Coll Cardiol 2009;53:557–73

CASE STUDY:

Management of acute decompensated heart failure

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CASE STUDY

- Mr AB, 54 year old male – blue collar worker
- HFrEF on OMT – Diagnosed 9 months ago
- Metabolic syndrome – hypertensive, dyslipidaemia and type 2 diabetic (central obesity)
- Life style & dietary management
- Presents with a 6 week history of worsening shortness of breath on exertion
- Finds great difficulty walking up 2 flights of stairs

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Clinical Examination

- Body mass index – 28kg/m2
- Blood pressure – 100/68 mmHg at rest
- Pulse rate 88 beats/min
- Respiratory rate of 22 breaths/min at rest
- Bilateral Grade 3 peripheral oedema
- Raised jugular venous pressure
- Congested tender hepatomegaly

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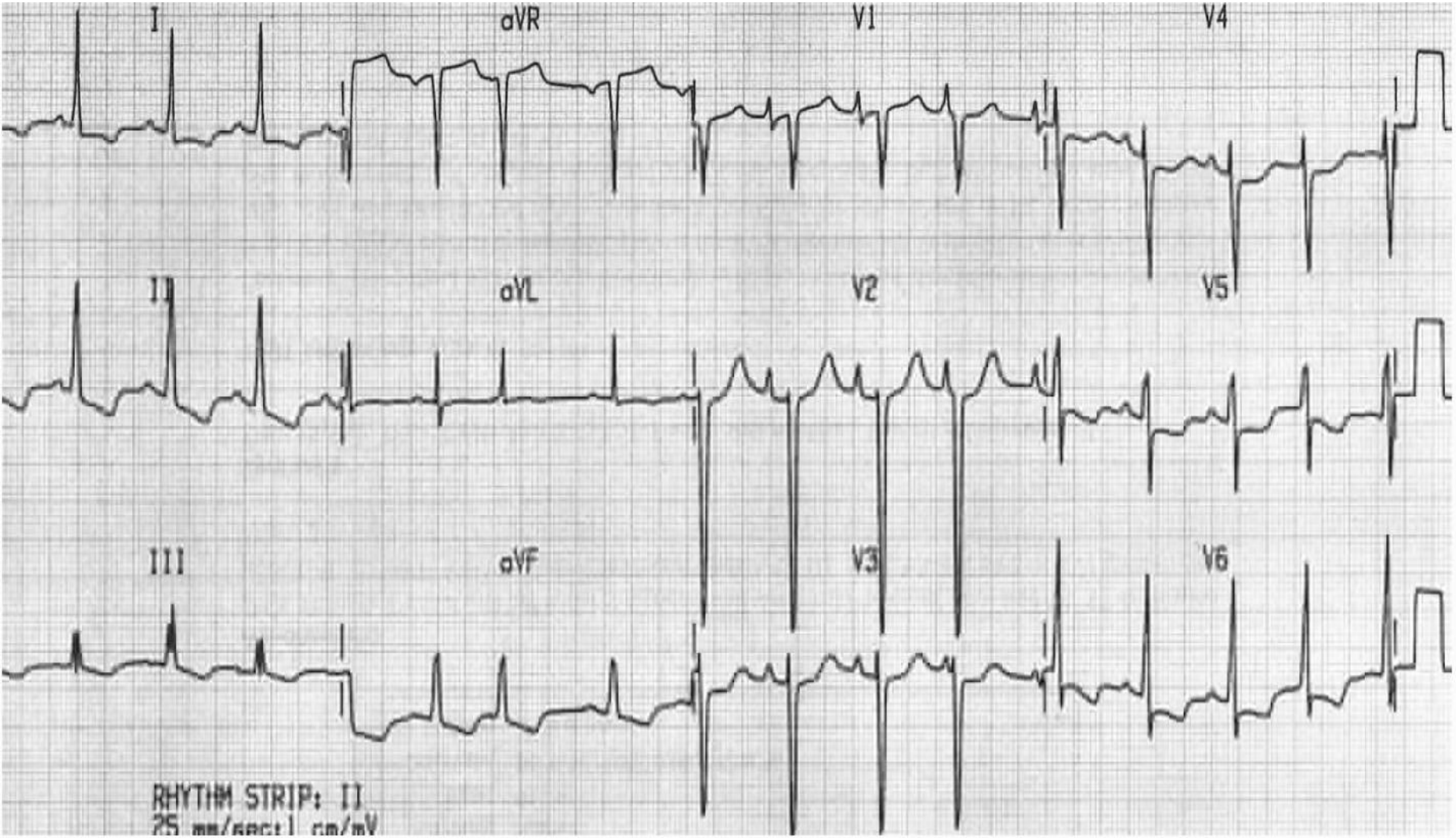
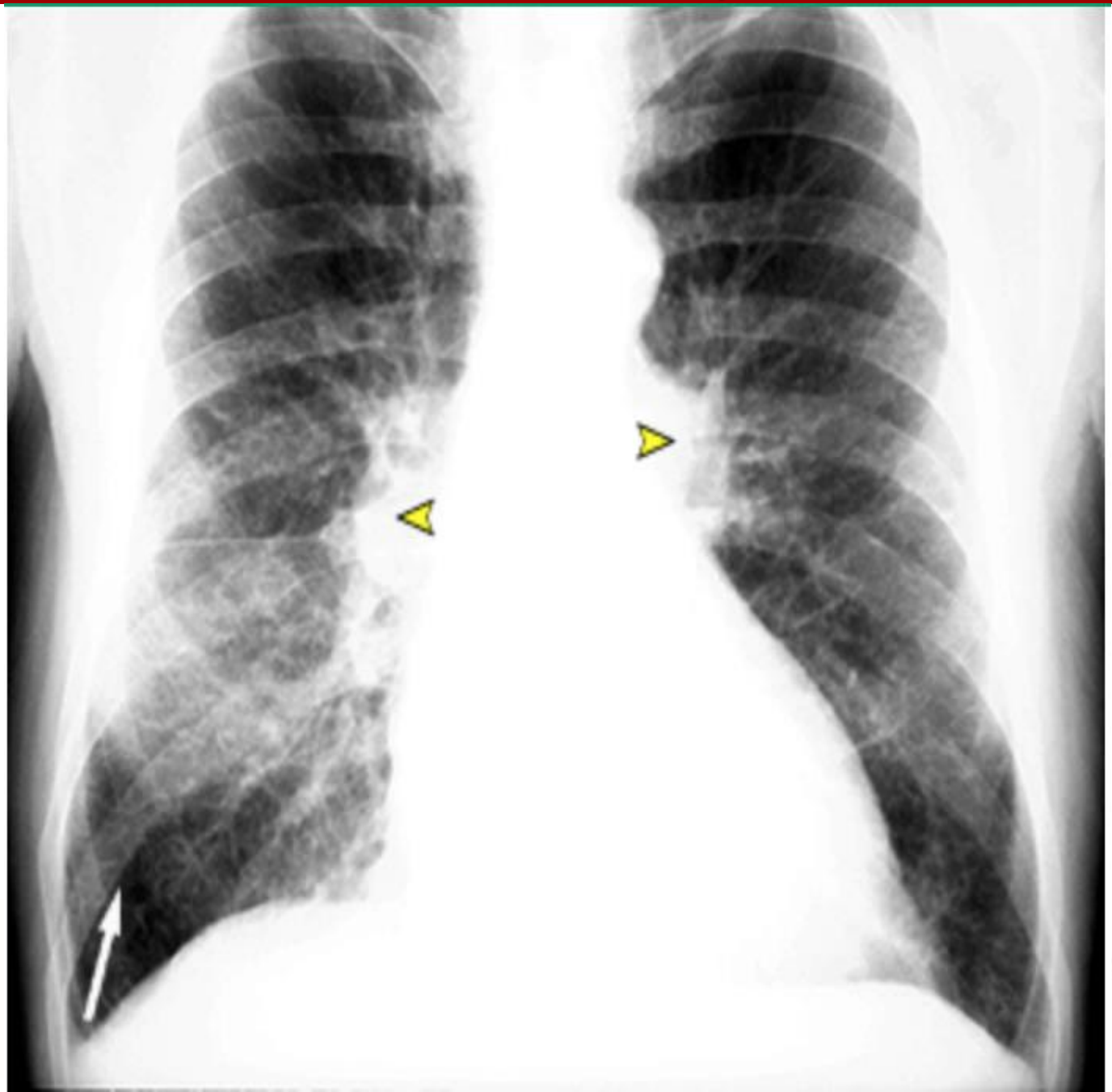
Electrocardiography



Chest X - Ray



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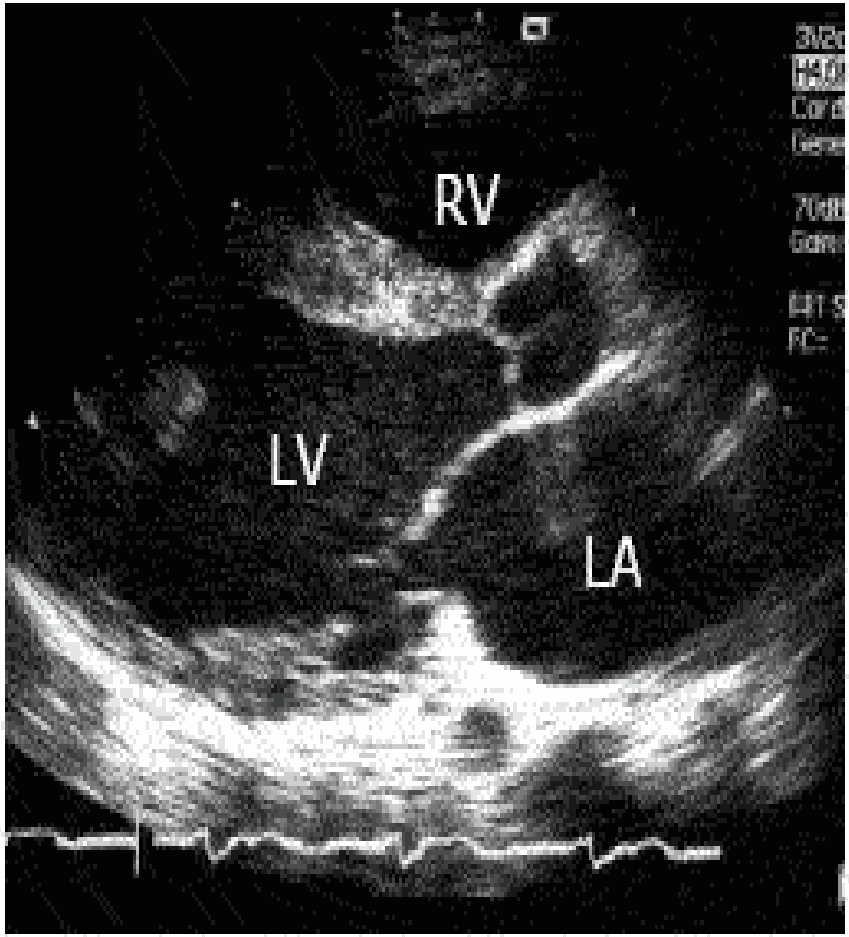
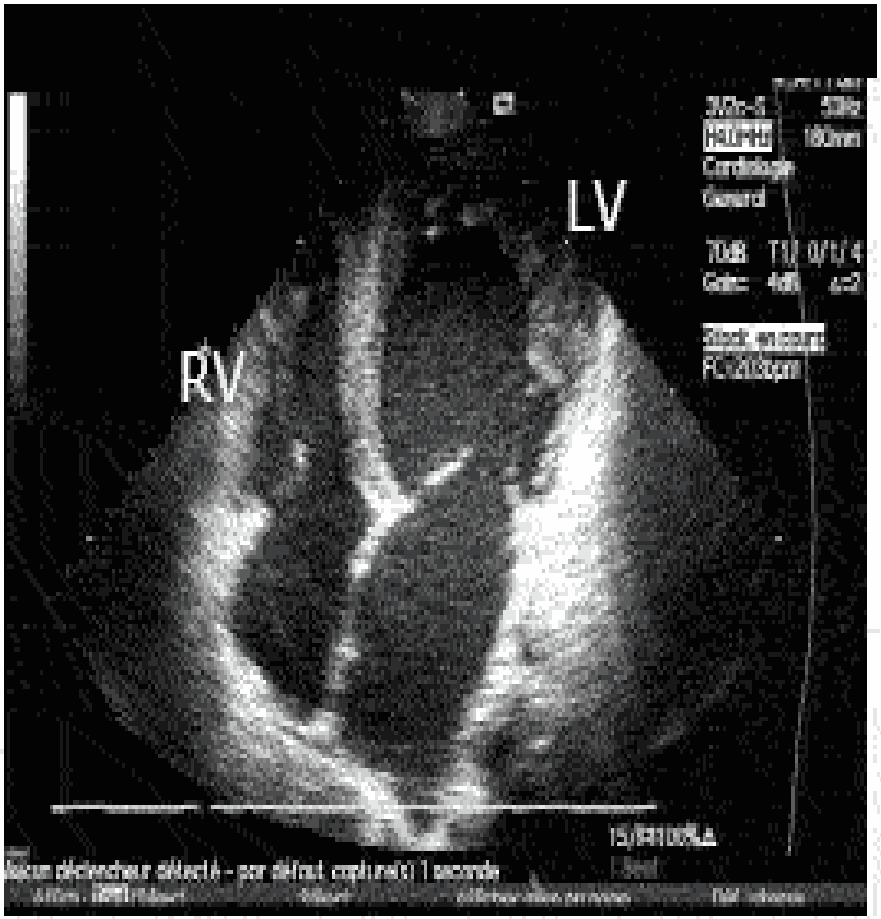
Echocardiography Findings





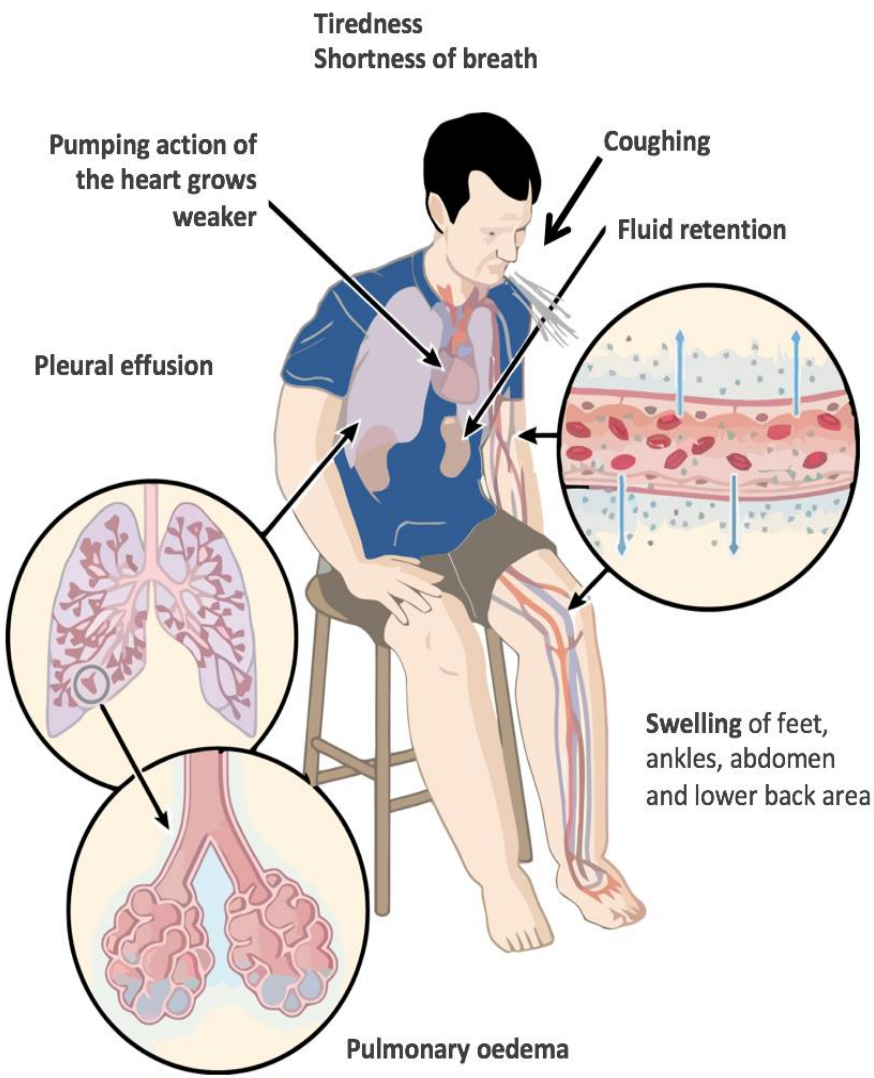
Typical Signs and Symptoms

Main symptoms

- Breathlessness
- Orthopnea
- Paroxysmal Nocturnal Dyspnea
- Reduced exercise tolerance
- Fatigue
- Ankle swelling

Main signs

- Elevated jugular venous pressure
- Hepato-jugular reflux
- Third heart sound
- Laterally displaced apical impulse
- Cardiac murmur



Current Management Strategy

- Metformin 850mg po BD
- Furosemide 40mg PRN
- Slow k 600mg po PRN when taking diuretic
- Enalapril 10mg po BD
- Carvedilol 25mg po BD
- Aldactone 25mg po BD

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How would you manage this patient?

Acute decompensated heart failure

- ADHF (proposed definition)
- Sudden “denovo” or progressive (over a period of days or weeks) worsening HF
- Characterised by exacerbation of typical signs and symptoms
- Often leading to hospitalisation

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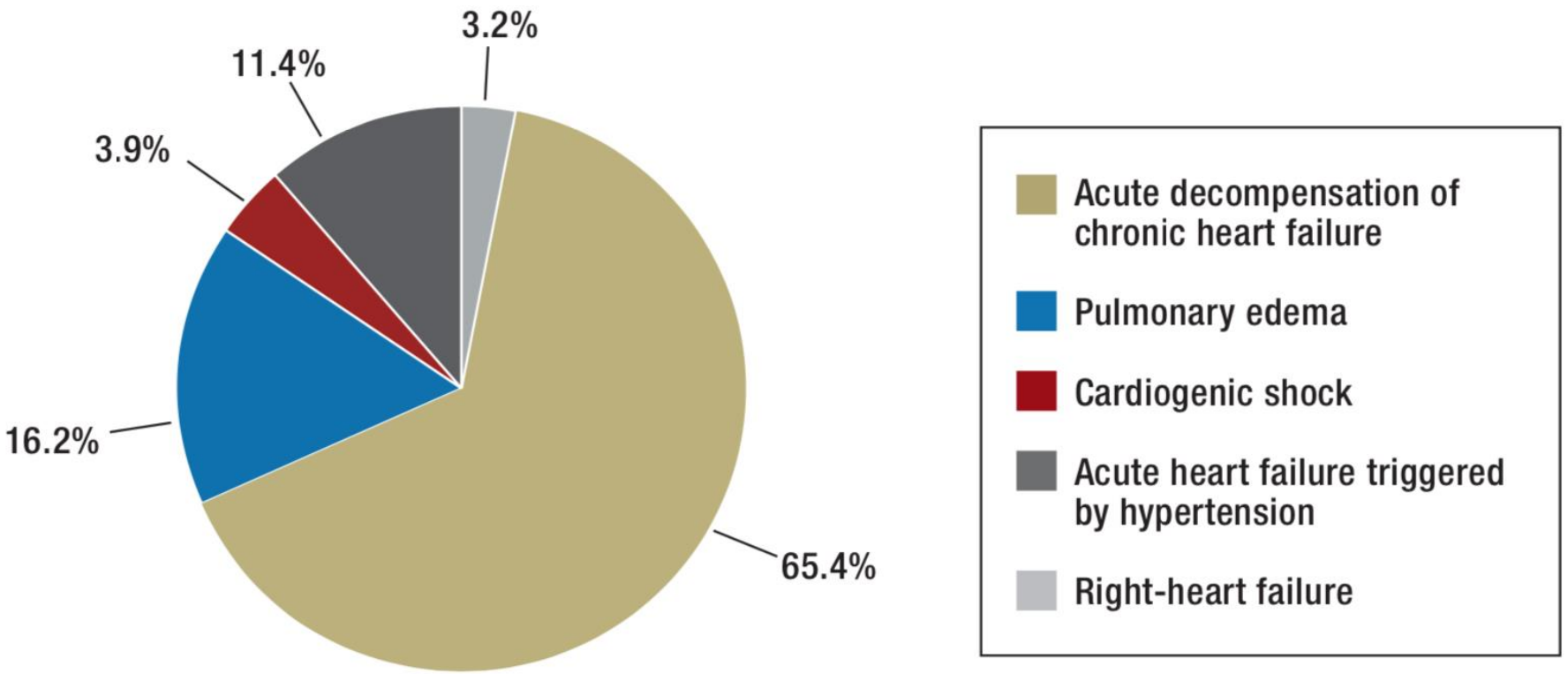
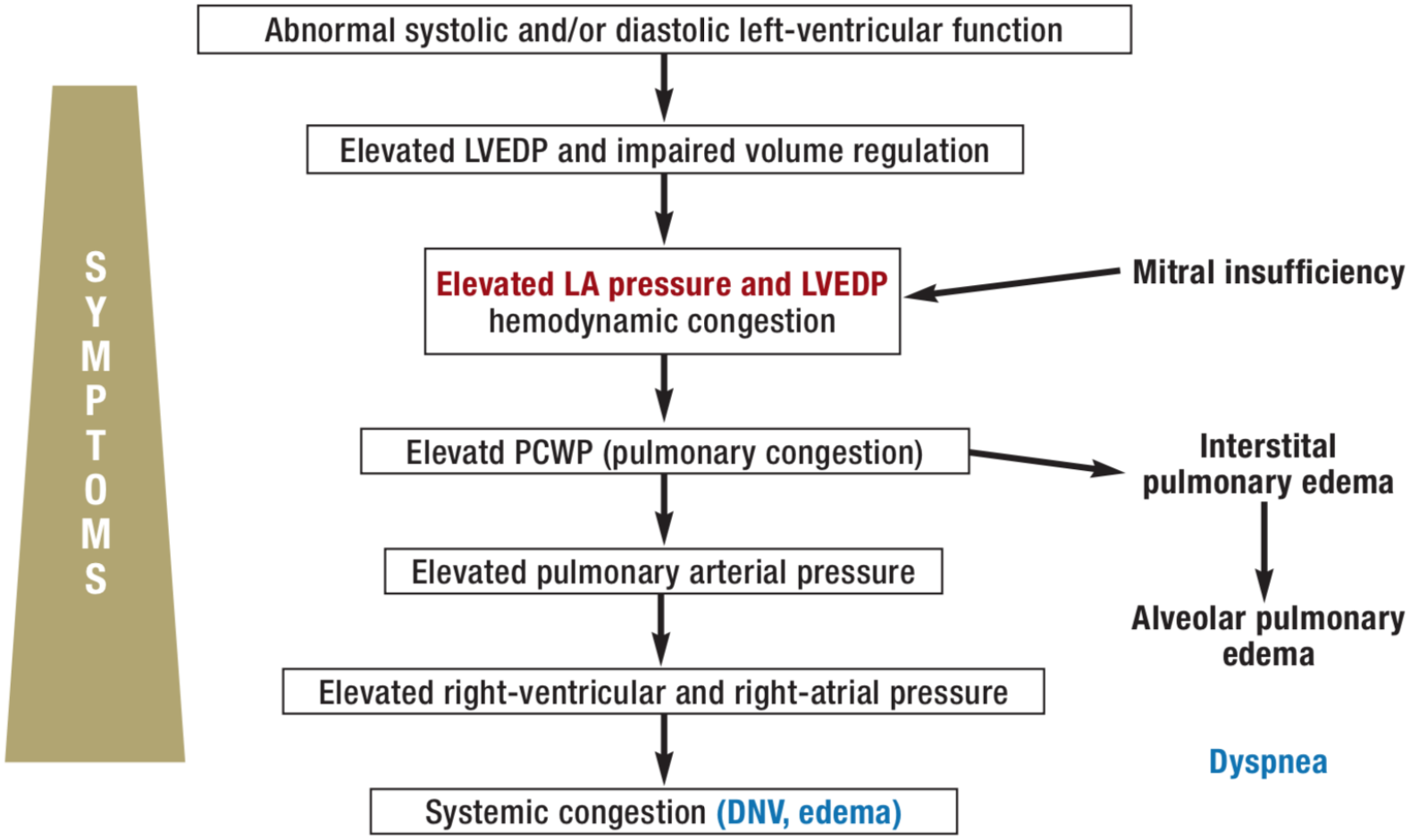
Rocha BML, Menezes Falcao L.. *Int J Cardiol.* 2016;223:1035-1044.

Frequency of subtypes of acute heart failure



Hummel A et al. *Dtsch Arztebl Int.* 2015;112(17):298-310

Pathophysiology of congestion



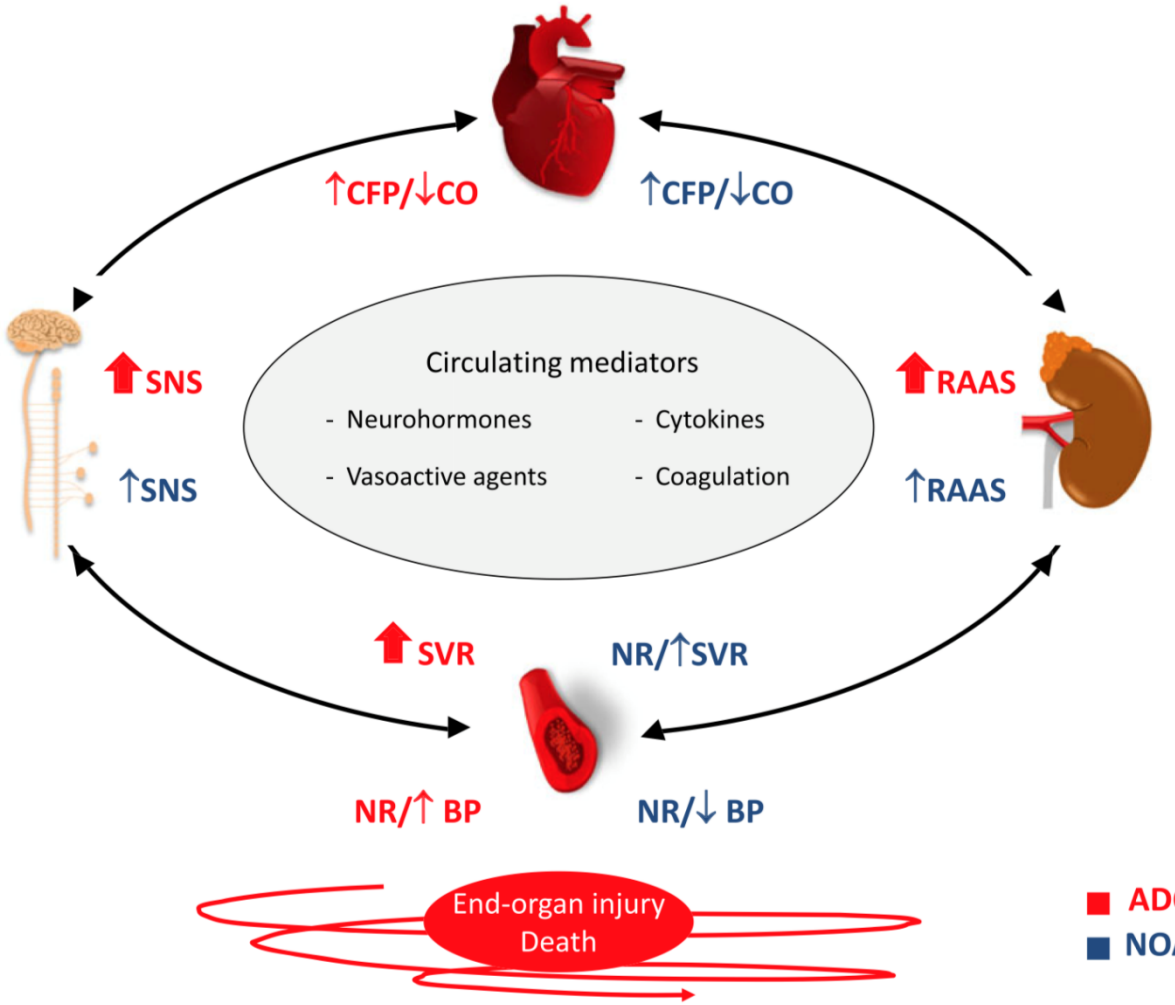
Hummel A et al. *Dtsch Arztebl Int.* 2015;112(17):298-310

ADHF Vs NOHF

Clinical, haemodynamic, and neurohormonal features	Acute decompensated chronic heart failure	New-onset acute heart failure
Blood pressure	Normal/hypertension	Low normal/hypotension
Systemic congestion	Moderate/severe	Absent/mild
Pulmonary congestion	Mild to severe	Mild to severe
Cardiac output	Depressed	Depressed
Cardiac filling pressure	Increased	Increased
Systemic vascular resistance	Very increased	Normal to increased
Sympathetic nervous system	Very increased	Increased
Renin–angiotensin–aldosterone system	Very increased	Increased
Cytokines/vasodilator mediators	Mild increase	Moderate/high increase

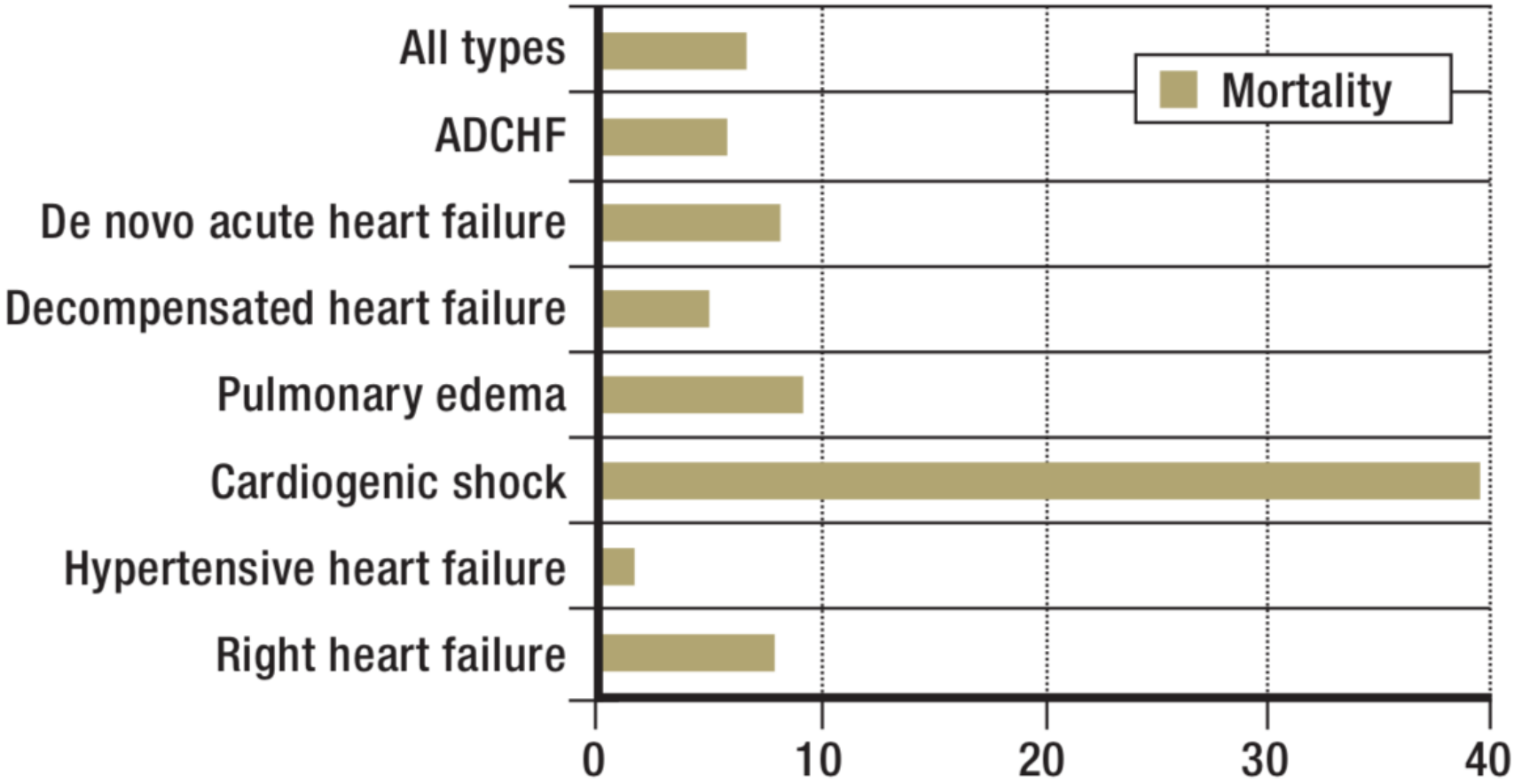
Ferreira J. *ESC Heart Fail.* 2017;4(4):679-685.

Pathophysiology of acute heart failure



Ferreira J. *ESC Heart Fail.* 2017;4(4):679-685.

In-hospital mortality associated with AHF



Hummel A et al. *Dtsch Arztebl Int.* 2015;112(17):298-310

Factors Triggering AHF

Events with acute clinical deterioration
(often, AHF)

- Coronary heart disease
  - Acute coronary syndrome
  - Mechanical complications of acute coronary syndrome, e.g., ventricular septal defect, acute mitral insufficiency, right-heart infarct
- Valvular diseases
- Myocarditis
  - Acute myokarditis
  - Peripartal cardiomyopathy
- Hypertension/arrhythmia
  - Hypertensive crisis
  - Tachycardia or severe bradycardia
- Circulatory failure
  - Acute pulmonary embolism
  - Pericardial tamponade
  - Aortic dissection
- Surgical interventions and perioperative complications

Events with delayed clinical deterioration
(often, acutely decompensated chronic heart failure [ADCHF])

- Infections, e.g., endocarditis
- Acute exacerbation of chronic obstructive pulmonary disease/asthma
- Anemia
- Worsening of renal failure
- Inadequate fluid and salt intake, non-compliance with prescribed medication
- Drug side effects and interactions, e.g., non-steroidal anti-inflammatory drugs, corticosteroids
- Uncontrolled arterial hypertension
- Hypo- or hyperthyroidism
- Alcohol and drug abuse

Hummel A et al. *Dtsch Arztebl Int.* 2015;112(17):298-310

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Precipitating factors of HF exacerbation

Worsening chronic heart failure
- Dietary indiscretion (excess fluid or salt intake)
- Medication related
  - Medication nonadherence
  - Use of medications with negative inotropic properties (e.g. diltiazem, verapamil)
  - Use of medications prepared with sodium or with sodium-retaining therapies (e.g., piperacillin-tazobactam, nonsteriodal anti-inflammatory agents)
- Uncontrolled hypertension
- Substance abuse (e.g., alcohol, other)
- Concurrent non-cardiac illness (e.g., infection especially pneumonia, pulmonary embolus, thyroid disease, renal failure)

New or worsening cardiac processes - Ischemia/Myocardial infarction - Arrhythmias (e.g., atrial fibrillation, ventricular tachycardia, other) - Hypertensive urgency/emergency
De novo heart failure - Large myocardial infarction - Sudden elevation in blood pressure - Stress-induced (takotsubo) cardiomyopathy - Myocarditis - Peripartum cardiomyopathy - Acute valvular insufficiency – stenosis, regurgitation, endocarditis - Aortic dissection
End-stage HF with progressive worsening of cardiac output

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Teerlink JR et al. *Curr Cardiol Rev.* 2015;11(1):53-62

Goals of Treatment in ADHF

Immediate (ED/ICU/CCU)
Improve haemodynamics and organ perfusion.
Restore oxygenation.
Alleviate symptoms.
Limit cardiac and renal damage.
Prevent thrombo-embolism.
Minimize ICU length of stay.
Intermediate (in hospital)
Identify aetiology and relevant co-morbidities.
Titrate therapy to control symptoms and congestion and optimize blood pressure.
Initiate and up-titrate disease-modifying pharmacological therapy.
Consider device therapy in appropriate patients.
Pre-discharge and long-term management
Develop a careplan that provides: • A schedule for up-titration and monitoring of pharmacological therapy; • Need and timing for review for device therapy; • Who will see the patient for follow-up and when.
Enrol in disease management programme, educate, and initiate appropriate lifestyle adjustments.
Prevent early readmission.
Improve symptoms, quality of life, and survival.

Ponikowski P et al. *Eur Heart J.* 2016;37(27):2129-2200.

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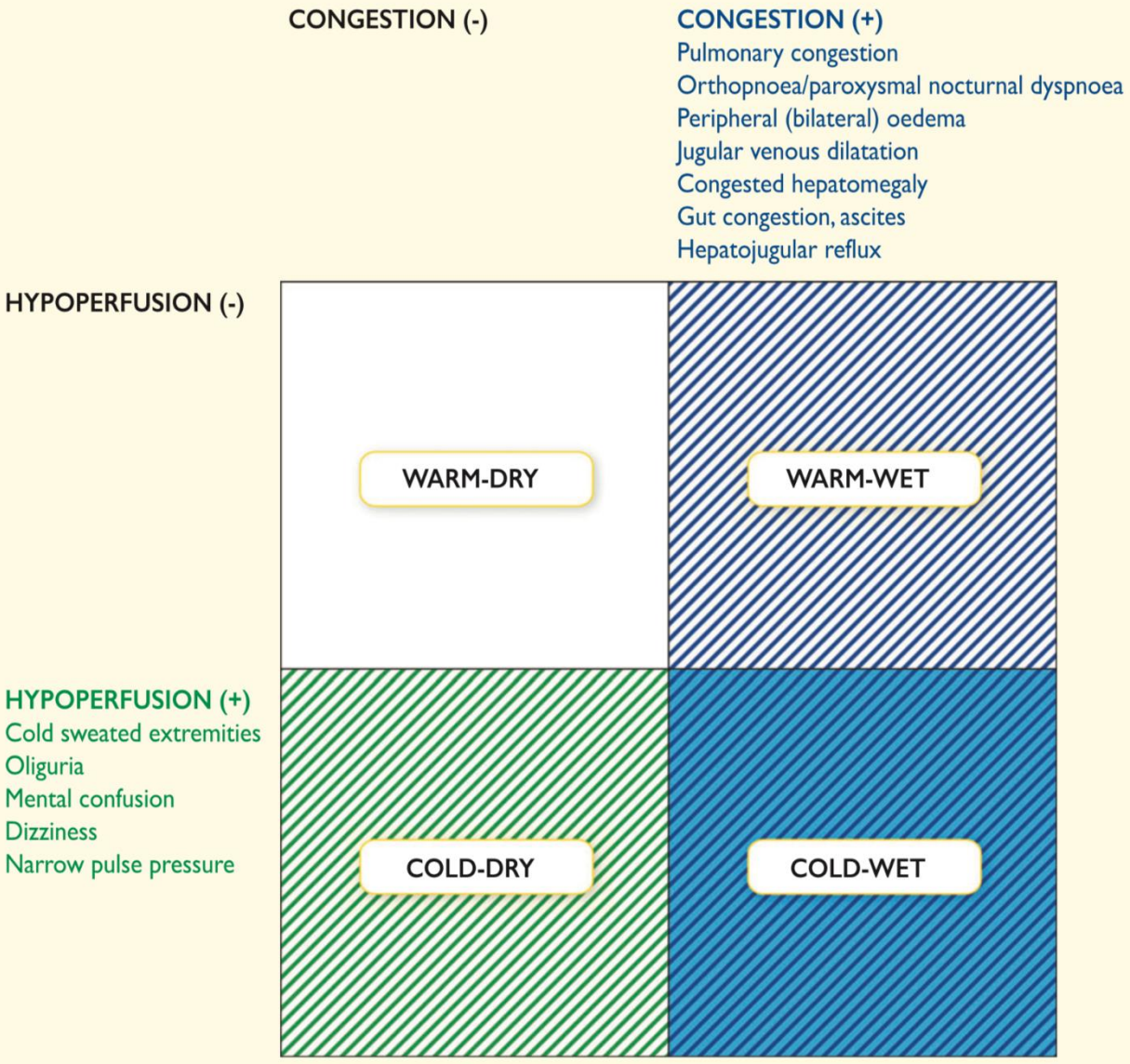
Clinical Profiles of Patients with ADHF



Hypoperfusion is not synonymous with hypotension, but often hypoperfusion is accompanied by hypotension.

Ponikowski P et al. *Eur Heart J.* 2016;37(27):2129-2200.

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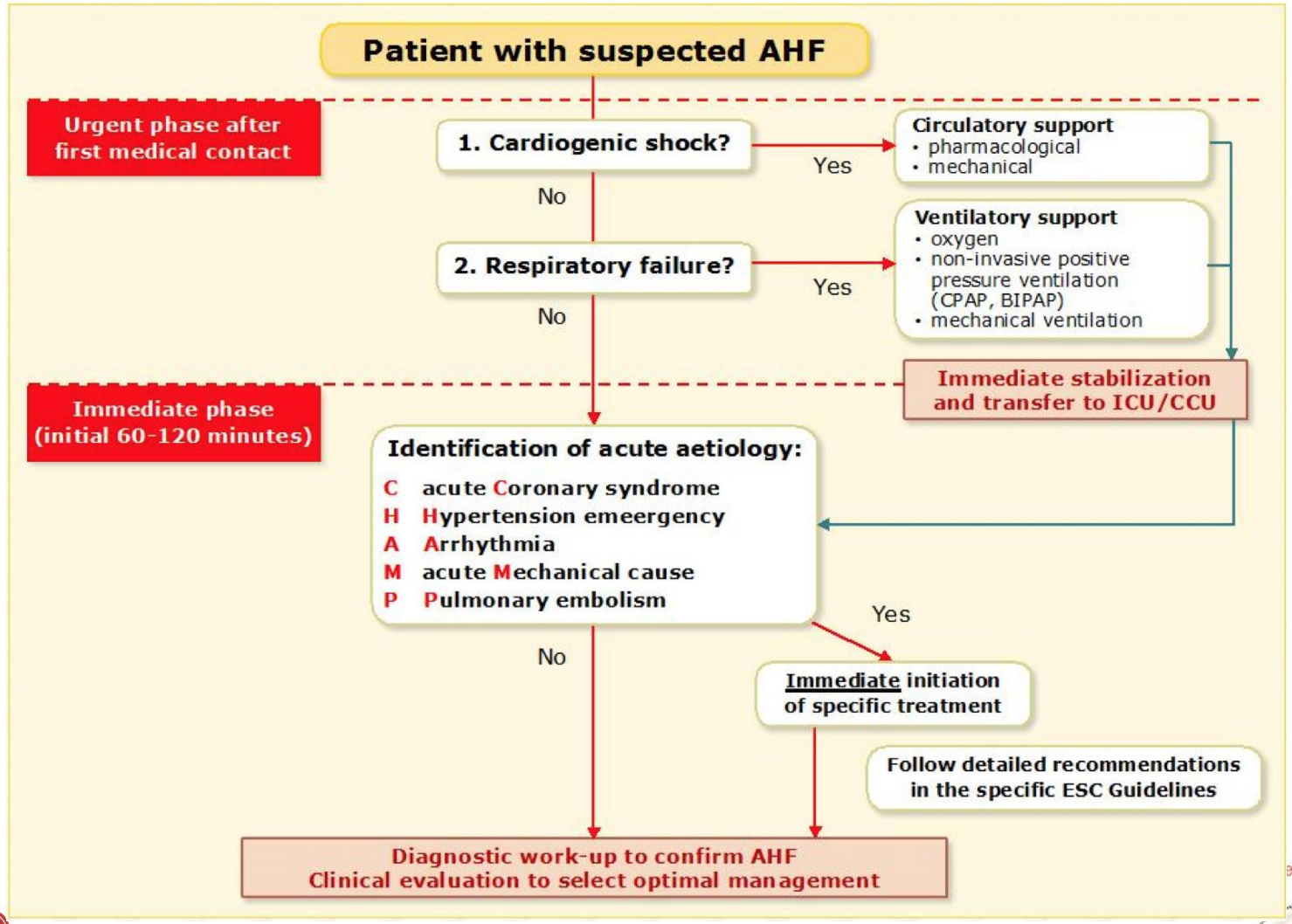
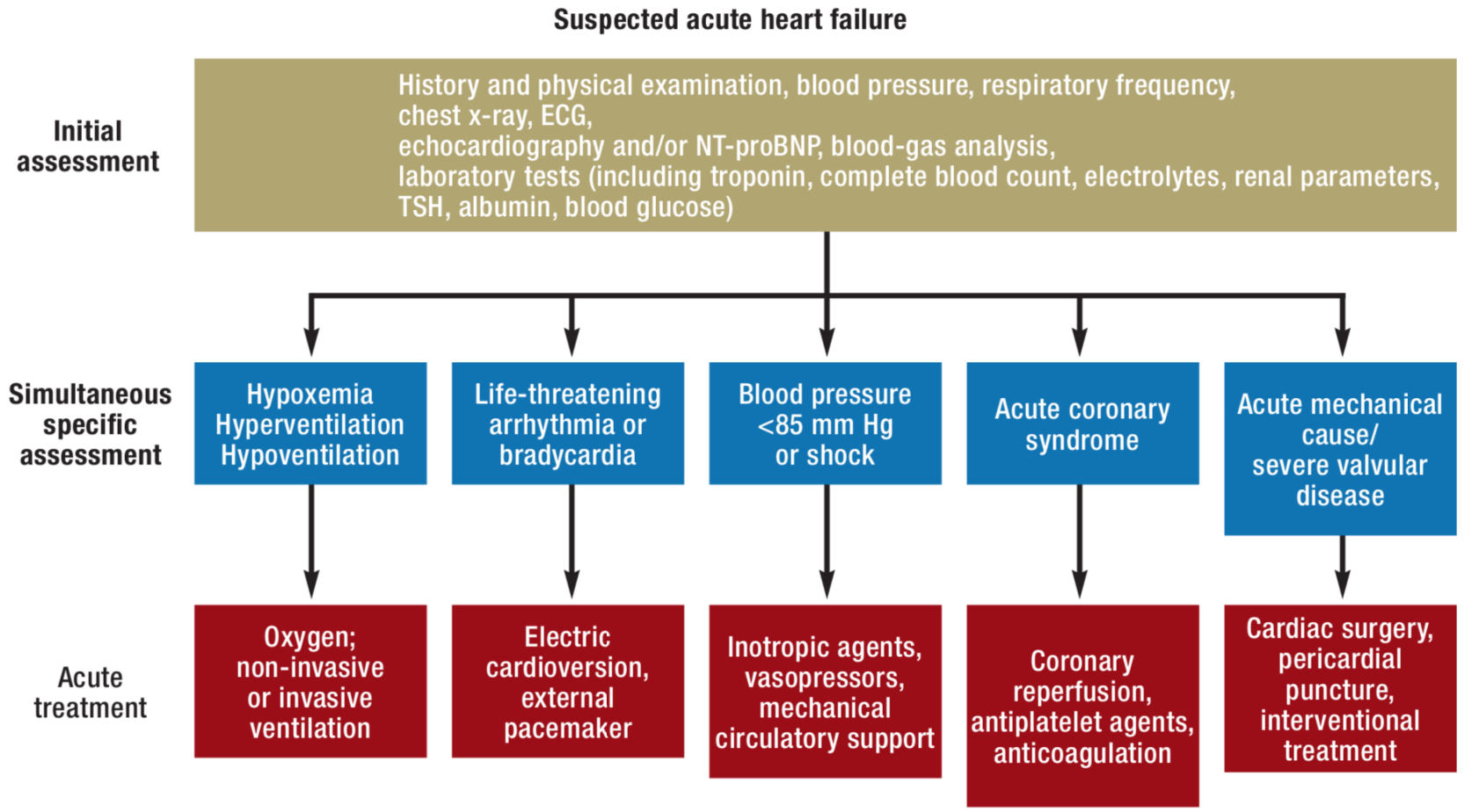
Initial Management of a patient with ADHF



Ponikowski P et al. *Eur Heart J.* 2016;37(27):2129-2200.

Suspected Acute Decompensated Heart Failure



Hummel A et al. *Dtsch Arztebl Int.* 2015;112(17):298-310.

Criteria for Inpatient Heart Failure Therapy

Recommend Hospitalization	Consider Hospitalization
Hypotension	Evidence of worsening congestion
	Increased liver function tests suggesting hepatic congestion
	Weight gain
Declining renal function	Electrolyte disturbances
Change in mental status	Comorbid conditions that can worsen heart failure • Pneumonia • Pulmonary embolism • Diabetes • Stroke or transient ischemic attack
Dyspnea at rest	Implantable cardiac defibrillator discharges
Arrhythmia	Newly diagnosed heart failure with signs and symptoms of congestion
Atrial fibrillation	
Ventricular tachycardia	
Acute coronary syndromes	

Krim SR et al. *Ochsner J.* 2015;15(3):284-289.

Treatment strategies for ADHF and NOHF

Acute decompensated chronic heart failure	New-onset acute heart failure
Decongestive therapy	Vasopressor
Loop diuretics	Norepinephrine
Renal replacement therapy	Dopamine
Vasodilator	Intrathoracic positive pressure
Nitrates	Non-invasive ventilation
Nitroprusside	Mechanical ventilation
Nesiritide	Fluid challenge
Inodilator	Circulatory assist device
Dobutamine	Intra-aortic balloon pump
Levosimendan	ECMO
Milrinone, enoximone	Ventricular assist device
Treatment of the precipitating cause	Treatment of the underlying cause

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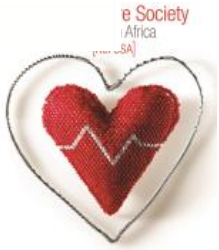
Ferreira J. *ESC Heart Fail.* 2017;4(4):679-685.



Management of oral therapy in ADHF

	Diuretics	ACE-i/ARB	Beta-blocker	MRA	Digoxin
Warm and dry Euvolemic, normal perfusion	Maintain or reduce, if possible	Maintain/increase checking renal function	Maintain/increase	Maintain/increase	Usually non needed. Maintain
Warm and wet Congestion, normal perfusion	Increase dosage or associate a second diuretic drug	Maintain, defer up-titration	Maintain, defer up-titration	Maintain, defer up-titration	Maintain Verify the plasma concentration
Cold and dry Euvolemic or hypovolemic, low perfusion	Reduce with caution/maintain	Reduce/withdraw	Reduce/withdraw Evaluate needing of inotropic support	Reduce/withdraw	Maintain Verify the plasma concentration
Cold and wet Congestion, low perfusion	Evaluate every single case	Withdraw	Withdraw Evaluate needing of inotropic support	Withdraw	Maintain Verify the plasma concentration

ACE-i: Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker; and MRA: Mineralocorticoid receptor antagonist.

Piepoli M et al. *Int J Cardiol.* 2014;176(2):321-326.

Diuretic therapies

	Furosemide	Bumetanide	Torsemide	Metolazone	Chlorothiazide
Mechanism of action	Loop Diuretic	Loop diuretic	Loop diuretic	Thiazide-like diuretic	Thiazide diuretic
Bioavailability	40%–70%	80%–95%	80%–90%	65%	N/A
Dose Equivalents	PO: 40 mg, IV: 20 mg	1 mg	20 mg	N/A	N/A
Usual oral dosing	40-80 mg one or twice daily, max 600 mg/d	1-2 mg once or twice daily, max 10 mg/d	20-40 mg once or twice daily max 200 mg/d	2.5-5 mg once daily, max 10 mg/d	N/A
Usual intravenous bolus dosing	Diuretic naïve: 40-80 mg q8-24h Diuretic PTA: 1-2.5 x PO dose PTA*, May repeat in 2-3 hours, max 600 mg/d	Diuretic naïve: 0.5-1 mg q8-24h Diuretic PTA: 1-2.5 x PO dose PTA*, May repeat in 2-3 hours, max 10 mg/d	Diuretic naïve: 10-20 mg q8-24h Diuretic PTA: 1-2.5 x PO dose PTA*, May repeat in 2-3 hours, max 200 mg/d	N/A	250 mg-500 mg q12-24h, max 2 gm/day
Usual intravenous continuous infusion dosing	40-80 mg IVB load, then 5-10 mg/hr, max 40 mg/hr	1-2 mg IVB load, then 0.5-2 mg/hr, max 2 mg/hr	20-40 mg IVB load, then 5-20 mg/hour, max 20 mg/hour	N/A	N/A
Duration of action	4–6 hours	6–8 hours	12–16 hours	12-24 hours	6-12 hours

IVB =intravenous bolus, PO = oral, PTA = prior to admission.
*See text regarding selection of 1, 2, or 2.5 x PO dose PTA

Teerlink JR et al. *Curr Cardiol Rev.* 2015;11(1):53-62

Vasodilator therapies

	Nitroglycerin	Nitroprusside	Nesiritide
Mechanism	Increase NO synthesis and cGMP	Increase NO synthesis and cGMP	Activate guanylate cyclase–linked NP receptor A to increase cGMP
Clinical effects	Vasodilator (venous > arterial)	Vasodilator (venous = arterial)	Vasodilator (venous = arterial)
Indication	Warm & wet, Cold & wet, HTN Crises, ACS	Warm & wet, Cold and wet, HTN Crises	Warm & wet, Cold & wet
Usual dosing	10–30 mcg/minute and titrate by 10–20 mcg/ minute every 10–20 minutes, to max 200 mcg/kg/min	0.1–0.2 mcg/ kg/minute and titrate by 0.1–0.2 mcg/kg/minute every 10–20 minutes, to max 2 mcg/kg/min	0.01 mcg/kg/minute and titrate by 0.005 mcg/kg/minute every 3 hours, to max 0.03 mcg/kg/min
Onset, Half-life	1-5 minutes, 1-4 minutes	< 1 minute, < 10 minutes	15-30 minutes, 20 minutes
Elimination	Inactive metabolites in urine (no renal/hepatic adjustment)	Cyanide (hepatic), thiocyanate (renal)	NP receptor C (no renal/hepatic adjustment)

ACS = acute coronary syndrome, cGMP = cyclic guanosine monophosphate, HTN = hypertensive, NO = nitric oxide, NP = natriuretic peptide.

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Teerlink JR et al. *Curr Cardiol Rev.* 2015;11(1):53-62.

Inotropic therapies

	Dobutamine	Milrinone
Mechanism	Beta agonist, increases AC to convert cATP to cAMP	PDE-III inhibitor, blocks degradation of cAMP
Clinical effects	Positive inotropic effect, slight peripheral vasodilation	Positive inotropic effect, moderate peripheral and pulmonary vasodilation
Indication	Cold and wet Cold and dry	Cold and wet Cold and dry
Usual intravenous dosing	2.5–5 mcg/ kg/minute and titrate by 2.5 mcg/kg/minute every 10–20 minutes, to max 20 mcg/kg/min	0.1–0.375 mcg/ kg/minute and titrate by 0.125–0.25 mcg/ kg/minute every 6–12 hours (intravenous bolus dose generally avoided)
Onset, Half-life	5-10 minutes, 2 minutes	90 minutes, 1 hour, prolonged 2-3 hours if CrCl < 50 ml/min
Other comments	-Recommend if hypotensive - May cause hypotension and tachyarrhythmias	-Recommend if receiving a beta-blocker and SBP > 90 mmHg -May cause hypotension -Elimination prolonged with renal dysfunction

AC = adenyl cyclase, cAMP = cyclic adenosine monophospate, cATP = cyclic adenosine triphosphate, CrCl = creatinine clearance, PDE = phosphodiesterase, SBP = systolic blood pressure.

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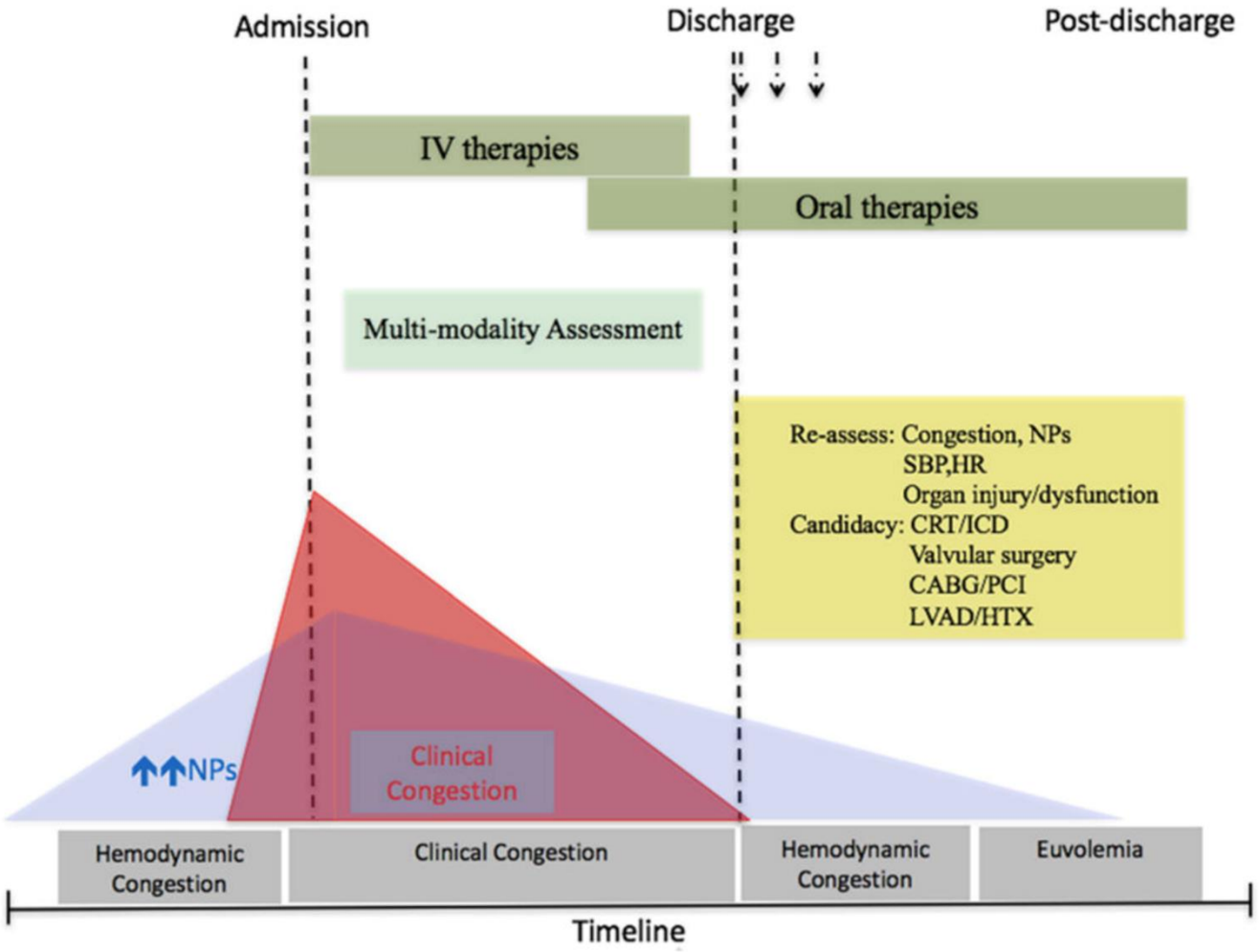
Teerlink JR et al. *Curr Cardiol Rev.* 2015;11(1):53-62.

ADHF Inpatient flow



Njoroge et al. *Heart Fail Rev.* 2018;23(4):597-607.

Discharge planning goals

- ☐ 1. Guideline-directed medical therapy has been reviewed and patient has been stable for 24 hours.
- ☐ 2. Potential exacerbating/confounding comorbidities have been addressed.
- ☐ 3. Exercise tolerance has returned to New York Heart Association Class II.
- ☐ 4. Volume status has been optimized.
- ☐ 5. Education has been provided.
- ☐ 6. Clinic follow-up has been scheduled.

Krim SR et al. *Ochsner J.* 2015;15(3):284-289.

Discharge performance measures

1. Left ventricular function was assessed during hospitalization or within the past 6 months.
2. Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker therapy was prescribed for patients with heart failure with reduced ejection fraction.
3. Beta blocker therapy was prescribed for patients with heart failure with reduced ejection fraction.
4. Postdischarge appointments have been scheduled.

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Krim SR et al. *Ochsner J.* 2015;15(3):284-289.

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Underutilised HF therapies

Therapy	Recommendation	Supporting trials
Digoxin	Use in refractory HFrEF in addition to GDMT to decrease rate of rehospitalization	DIG Trial (1997)
MRAs	HFrEF patients with NYHA III–IV symptoms HFpEF patients with normal renal function	RALES (1999) TOPCAT (2014)
Torsemide	Consideration of torsemide over furosemide as oral loop diuretic therapy in patients with difficult to treat congestion or diuretic resistance	TRANSFORM-HF (current)
Thiazides	Use in combination with loop diuretics in diuretic resistant patients	CLOROTIC (current)
Ivabradine	HFrEF patients on maximal GDMT with standing HR > 70BPM	SHIFT (2010)
ARNIs	HFrEF patients in place of ACEI	PARADIGM-HF (2014) PIONEER-HF (current)
Ultrafiltration	In ADHF with congestion refractory to medical therapy (level of evidence: C)	RAPID-CHF (2005) CARRESS-HF (2012)

Njoroge et al. *Heart Fail Rev.* 2018;23(4):597-607.

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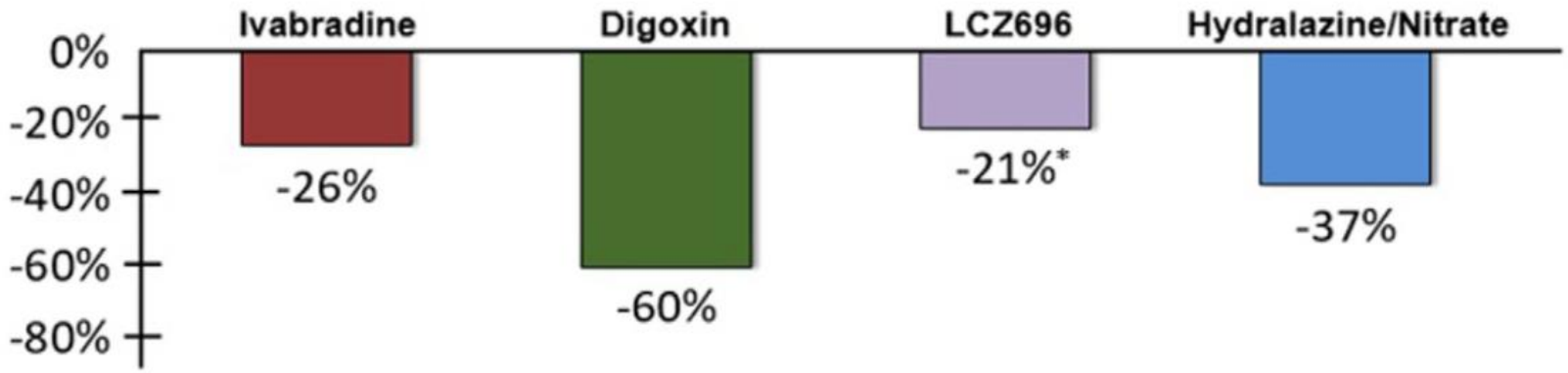
HF hospitalisation rate reduction



	Ivabradine	Digoxin	LCZ696	Hydralazine/Nitrate
Study	SHIFT[87] Ivabradine vs Placebo	Main DIG trial[84] Digoxin vs Placebo	PARADIGM-HF[88] *LCZ696 vs Enalapril	A-HeFT[89] Hydralazine/Nitrate vs Placebo
Population	Chronic HFrEF, SR, heart rate≥70bpm, NYHA II-IV	Chronic HFrEF, SR, NYHA I-IV	Chronic HFrEF, NYHA II-IV	Self-identified blacks, Chronic HFrEF, NYHA III-IV
N	6558	6800	8442	1050
Outcome measurement	Median follow-up (22,9 months)	30-days after randomization	Median follow-up (27 months)	Median follow-up (15 months)

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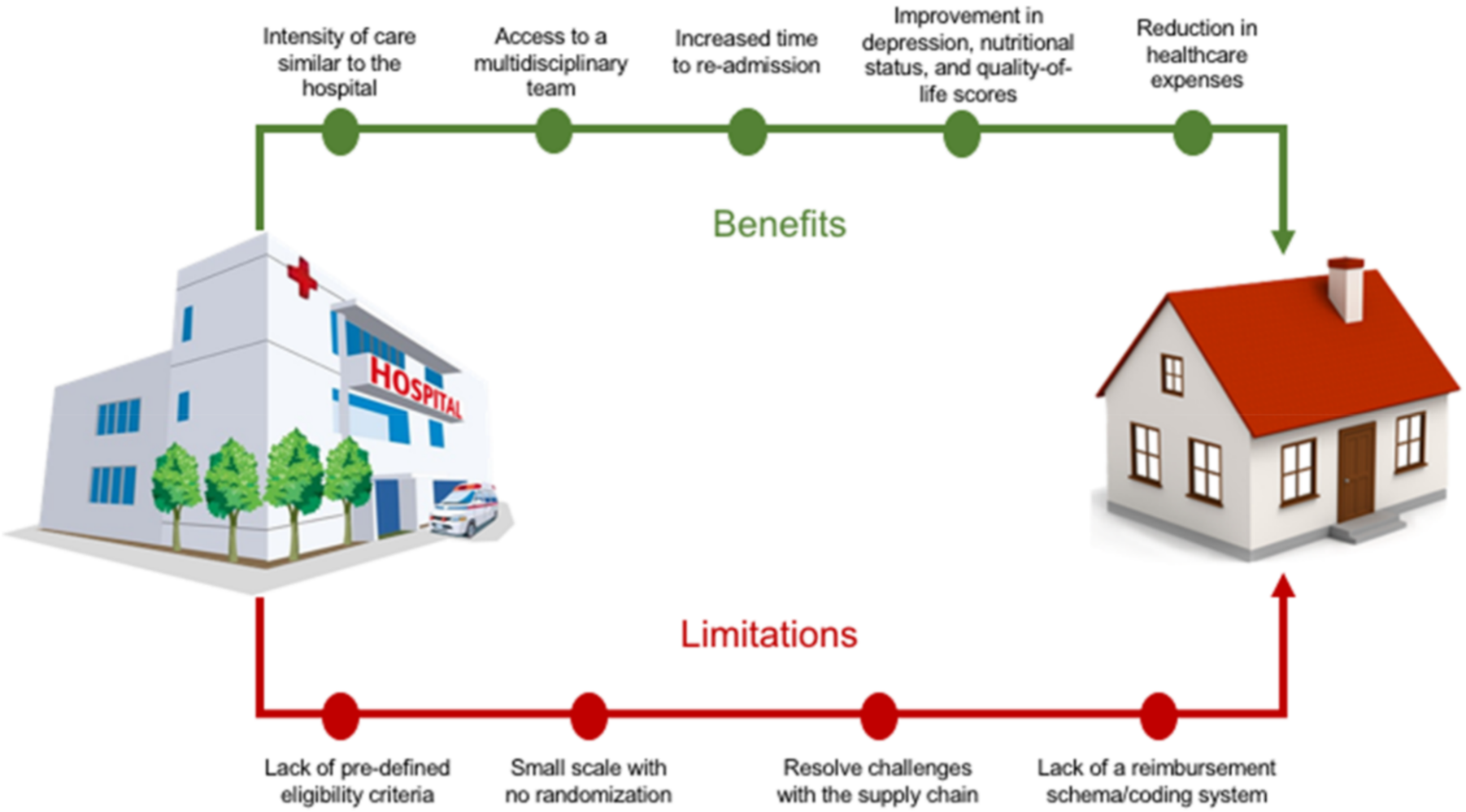
of South Africa [HeFSSA]

Rocha BML, Menezes Falcao L.. *Int J Cardiol.* 2016;223:1035-1044.

Home hospitalisation model



Voudris KV, Silver MA. *Healthcare.* 2018;6(2).

Investigational therapies for ADHF

Therapy	Mechanism of Action
Aliskiren	Direct renin inhibitor with favorable neurohormonal and hemodynamic effects
Caperitide	Recombinant atrial natriuretic peptide; diuretic, natriuretic, and vasodilatory activity
Cenderitide (CD-NP)	Chimeric protein which causes cGMP-mediated venodilation
Cinaciguat	Vasodilator that activates soluble guanylyl cyclase, leading to increased cGMP and venous and arterial vasodilation
Clevidipine	Calcium channel blocker that selectively dilates arteries with no significant effect on myocardial contractility
Istaroxime	Inhibits sodium-potassium ATP activity and stimulates SERCA2a, thereby increasing lusitropy and inotropy
Omecamtiv mecarbil	Cardiac-specific activator of myosin, improves myocardial efficiency and performance
Serelaxin	Recombinant human relaxin 2, modulates cardiovascular and renal adaptations during pregnancy
Ularitide	Recombinate atrial natriuretic peptide hormone; natriuretic and diuretic activity

ATP = cyclic adenosine triphosphate, cGMP = cyclic guanosine monophosphate, SERCA2a = sarco/endoplasmic reticulum Ca^{2+} ATPase.

Teerlink JR et al. *Curr Cardiol Rev.* 2015;11(1):53-62.

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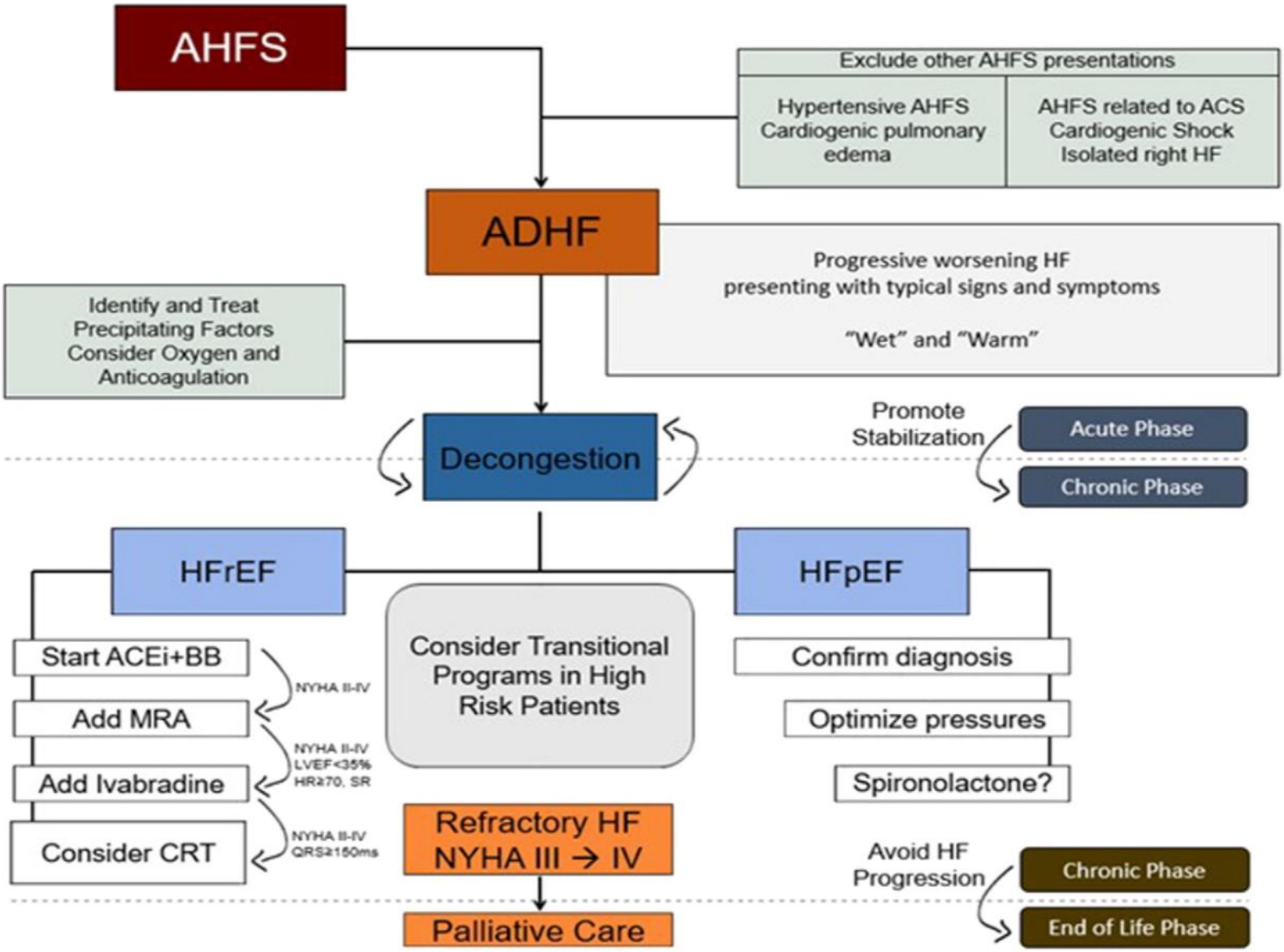
Summary Slide



THANK YOU