Acute Decompensated HF (or Acute HF)

Karen Kopacek MS, RPh

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Objectives

- Describe the 4 hemodynamic subsets of acute decompensated heart failure
- Given a case, determine the patient's hemodynamic subset based on s/sx and list appropriate therapies to treat acute heart failure
- Discuss treatment options for diuretic resistance
- List advantages and disadvantages of inotropes and vasodilators when used in acute decompensated heart failure

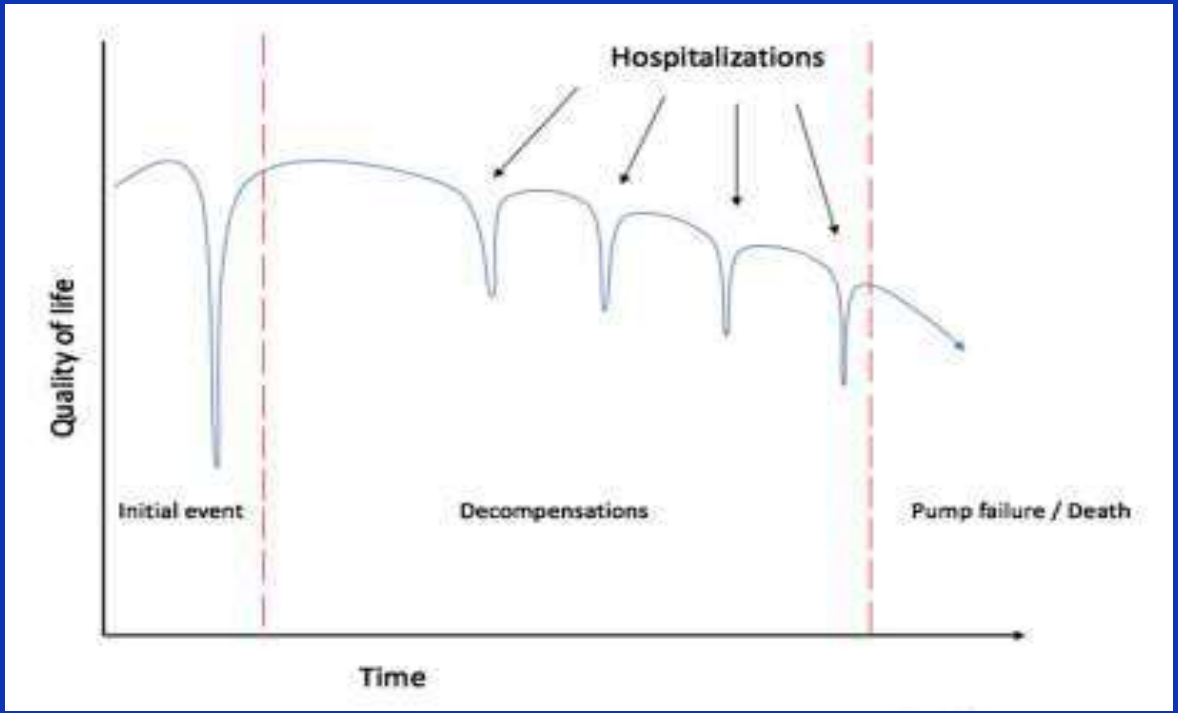
Definitions

- **Heart failure:**
  - Describes patients with established chronic HF whose symptoms may be graded by NYHA functional classification

- **Acute decompensated HF:**
  - Describes patients who present with worsening S/Sx of chronic HF that may be potentially life-threatening
  - Requires emergency treatment aimed at managing fluid overload and hemodynamic compromise
  - Hospital admission heralds poor prognosis with a high risk of readmission and death post-discharge

Kurmani S and Squire I. Curr Heart Fail Rep 2017;14:385-92

Natural History of HF



- Series of decompensations after which patient does not return to their prior baseline QOL and inherently requires a higher intensity of care.

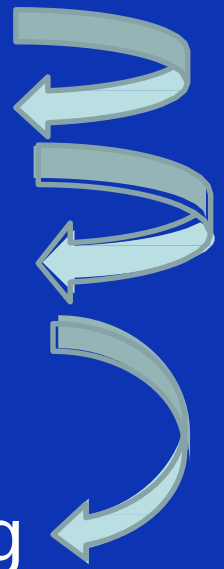
Causes of Acute Decompensation:

- Disease progression or Idiopathic
- New event:

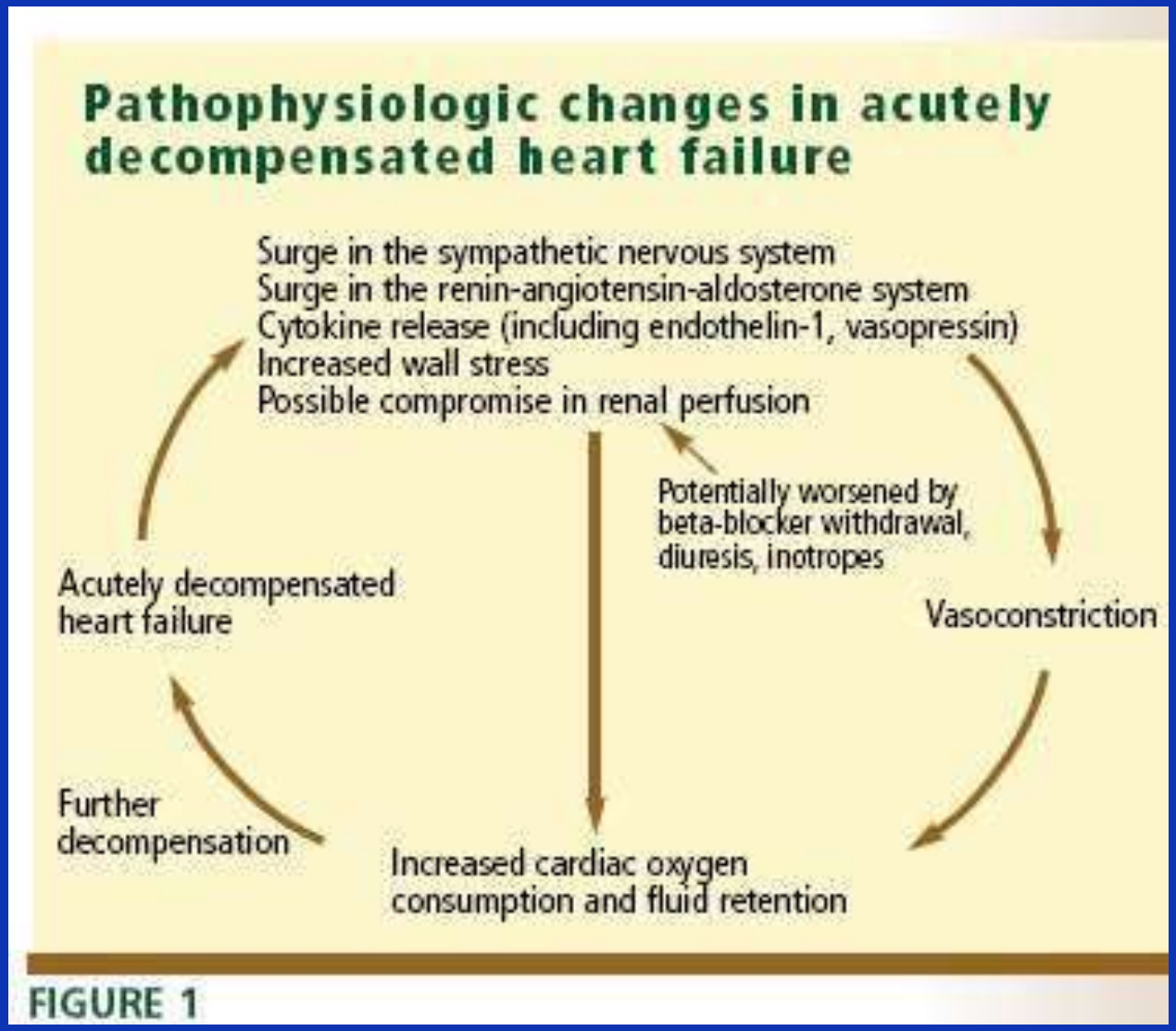
PUMP FAILURE	METABOLIC NEEDS
ACS	Infection
Arrhythmias (esp AF)	Anemia
Drugs	Hyperthyroidism
Sodium load + fluid retention	Non-adherence w/ HF meds
Uncontrolled hypertension	Renal failure
Non-adherence w/ HF meds	Alcohol or illicit drug binge
Renal failure	PE
Alcohol or illicit drug binge	COPD exacerbation
Valvular/congenital defect	

Pathophysiology of ADHF

- Event causes acute reduction in CO & BP
- Decreased perfusion to vital organs
- Compensatory catecholamines and ADH released to maintain HR, contractility, afterload, and volume
- Eventually, heart not able to keep up leading to:
  - Increased myocardial O2 demand
  - Shock: further vasoconstriction, cyanosis, hypoxia, anaerobic metabolism (lactic acidosis)



Pathophysiology of ADHF



Physiologic Outcomes: Hypoperfusion and Congestion!

Lab Assessment in Acute HF

- Electrolytes, blood glucose, CBC w/plts
- Renal function (SCr, BUN) & hepatic panel
- Lactic acid
- Troponin
- Thyroid function tests
- Urinalysis, toxicology screen
- ECG, chest X-ray
- **BNP or NT-proBNP**
  - Caution: ↑ in older age, renal dysfunction, pulmonary embolism, chronic pulmonary disease
  - Less elevated in diastolic dysfunction, obesity

BNP

Usefulness in ADHF Diagnosis

- Correlation with ↑ BNP level
  - ADHF diagnosis, disease severity, mortality

Evaluate BNP in context of clinical picture (acute dyspnea):

BNP < 100 pg/mL = ADHF highly unlikely

BNP 100 – 400 pg/mL = Consider HF history and other potential causes that may increase BNP

BNP > 400 pg/mL = ADHF highly likely

Gaggin and Januzzi. acc.org/cardiac biomarkers and heart failure

NT-proBNP

Usefulness in ADHF Diagnosis

- Correlation with ↑ NT-proBNP level
  - – ADHF diagnosis, disease severity, mortality

Evaluate NT-pro BNP in context of clinical picture (acute dyspnea):

NT-proBNP > 450 pg/mL for age < 50 years
NT-proBNP > 900 pg/mL for age 50-75 years
NT-proBNP > 1800 pg/mL for age > 75 years

Gaggin and Januzzi. acc.org/cardiac biomarkers and heart failure

Intensive Care Therapeutics

Patients may present with cardiogenic and/or respiratory failure that requires:

- ICU care
- Circulatory support (pharmacologic, mechanical)
- Ventilatory support or mechanical intubation
- **Pulmonary artery catheter placement to guide pharmacologic therapies**

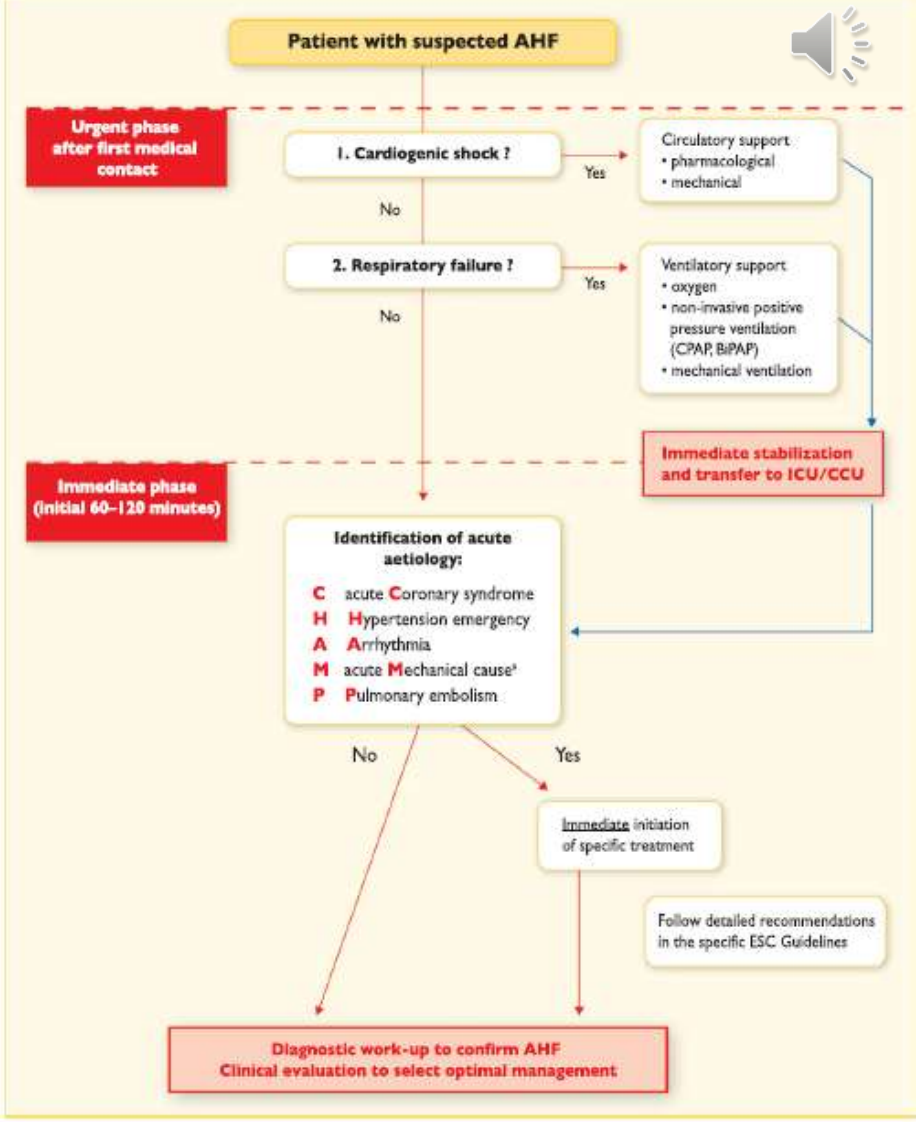
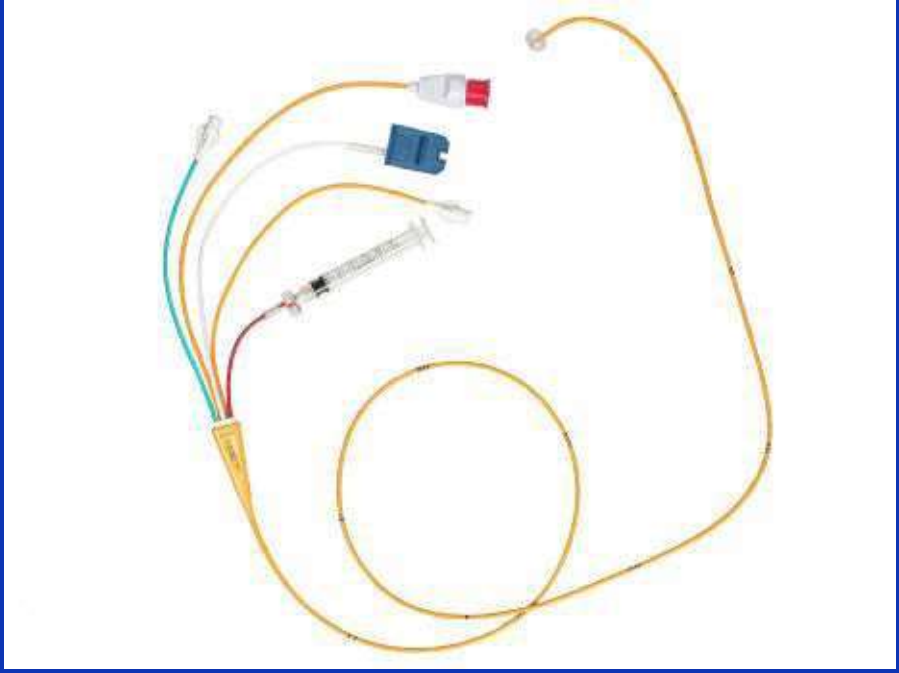


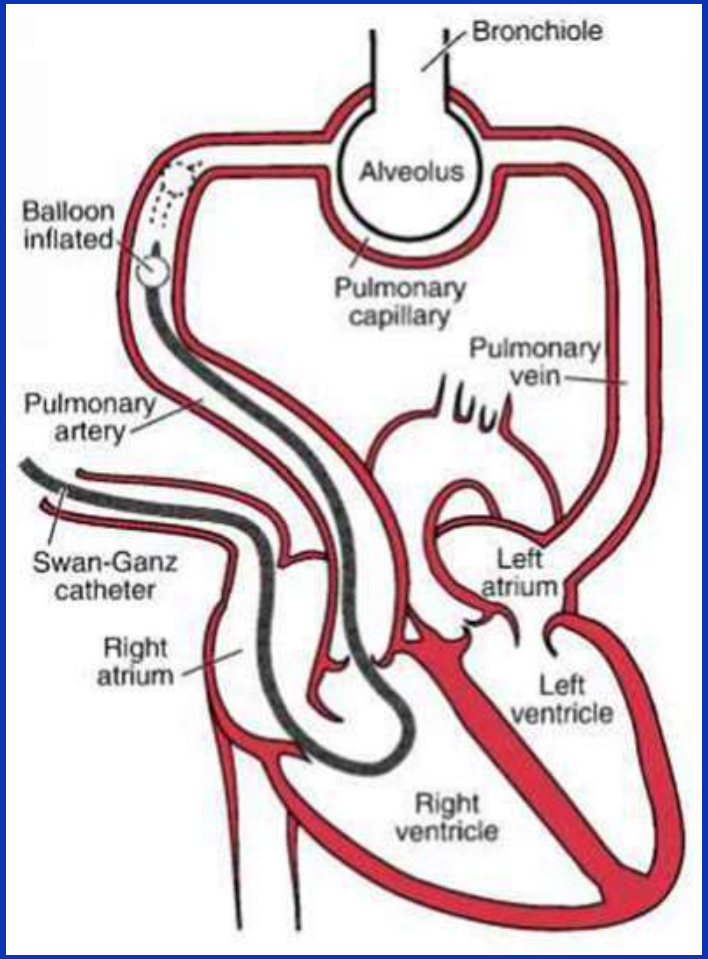
Figure 12.2 Initial management of a patient with acute heart failure. *Acute mechanical cause: myocardial rupture complicating acute coronary syndrome (free wall rupture, ventricular septal defect, acute mitral regurgitation), chest trauma or cardiac intervention, acute native or prosthetic valve incompetence secondary to endocarditis, aortic dissection or thrombosis, see above.

2016 ESC Guideline for Acute and Chronic HF

Swan-Ganz or PA Catheter

Measures pulmonary artery pressure, **PCWP, CO (cardiac index)**, CVP, SVR, and pulmonary vascular resistance





Hemodynamics – Cardiac Output

- Cardiac Output (CO) = HR x SV
  - Normal: 4 - 8 L/min
- **Cardiac index (CI)** relates CO to BSA, thus relating heart performance to body size
  - **Normal: 2.2 - 4 L/min/m^2**

Hemodynamics Continued

- SV = volume of blood ejected with each beat
  - Preload: left ventricular end diastolic volume, measured clinically as **pulmonary capillary wedge pressure (or PCWP)**
    - Normal: 5-15 mmHg
  - Afterload: force in which left ventricle must work against to eject blood, measured clinically as systemic vascular resistance (or SVR)
    - Normal: 800-1200 dynes/se/cm2

Review Questions:

- How is acute HF different from chronic HF?
- What are the two main physiologic problems patients exhibit with ADHF?
- How is fluid overload clinically measured? What is a normal value?
- What is cardiac index? What is a normal value?

ADHF Classification System

- Based on severity of presentation rather than underlying etiology of HF
- **Takes into account S/Sx of congestion and peripheral perfusion**
- **Patients are described as being:**
  - **Wet or dry depending on fluid status (PCWP)**
  - **Warm or cold depending on perfusion status (CI)**
- Combined clinical assessment allows patients to be categorized into one of 4 subsets that guides therapy and describes prognosis

Rapid Assessment of Hemodynamic Status

Congested? PCWP > 18 mmHg

Adequate perfusion? CI > 2.2 L/min/m2

	No (≤ 18)	Yes (> 18)
Yes (≥ 2.2)	**Warm & Dry** **Subset I**	**Warm & Wet** **Subset II**
No (< 2.2)	**Subset III** **Cold & Dry**	**Subset IV** **Cold & Wet**

S/Sx of Congestion:

- Orthopnea/PND
- Pulm congestion
- Hepatomegaly
- JVD, HJR
- Ascites
- Peripheral edema

Possible evidence of low perfusion:

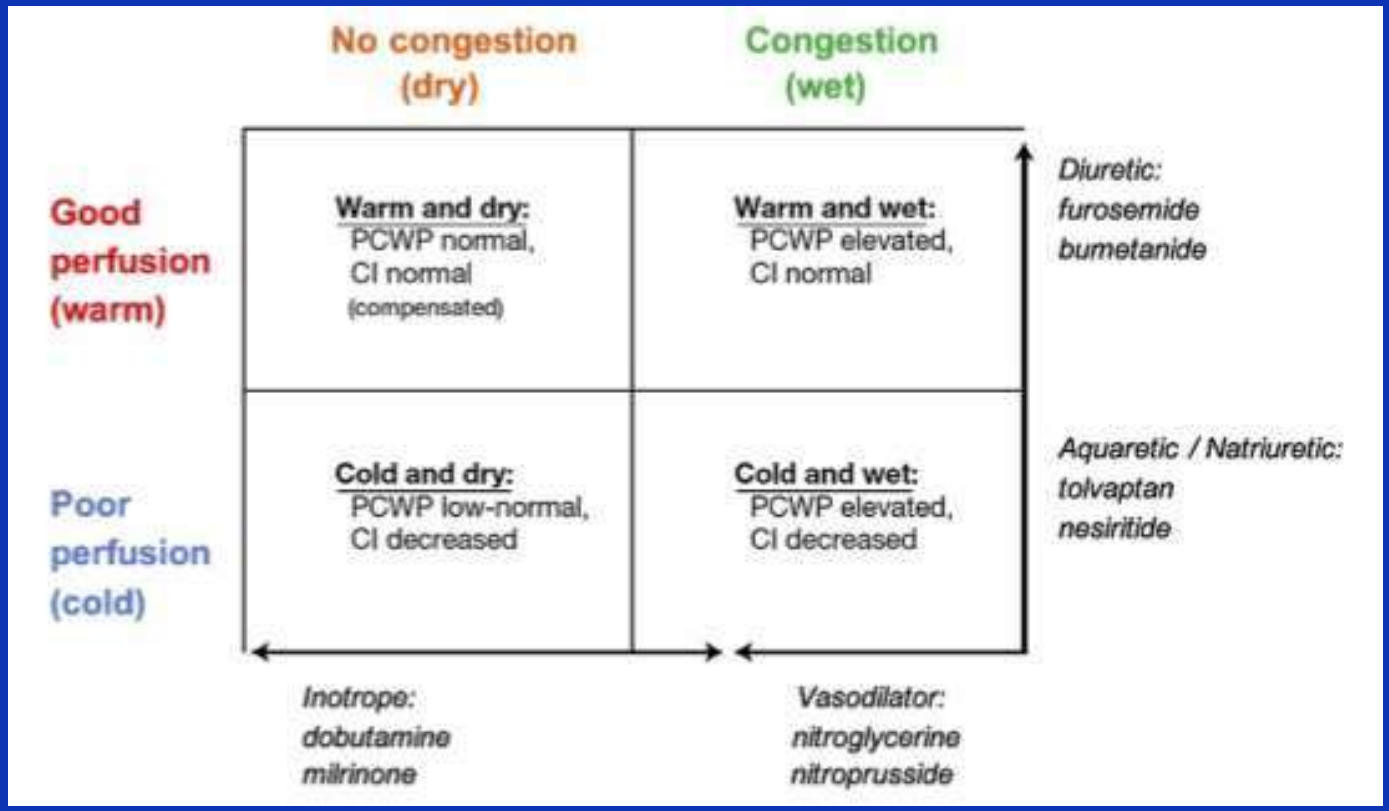
- Cool extremities
- Mental confusion
- Dizziness
- Narrow pulse pressure (SBP- DBP < 40 mmHg)
- Oliguria (UO < 0.5 L/kg/hr or < 500 ml in 24 hours)
- Lab abnormalities (elevated Scr & LA, met. acidosis)

Nohira A et al. Am J Card 2005;96 (supp):32G-40G; 2016 ESC Guideline for Acute and Chronic HF

Patient Selection and Treatment

Decreasing PCWP

Increasing CI

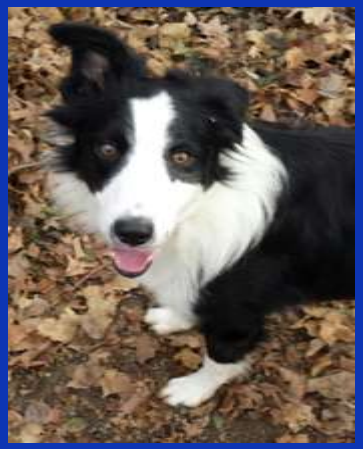


Pauly D. Cardiol Clin 2014;32:145-9

Subset I: Normal Hemodynamics "Purrfectly Compensated"

- CI > 2.2 L/min/m2 (warm)
- PCWP < 18 mmHg (dry)
- Mortality = 1-3%
- Therapy goal: **maintain status**
- Specific agents: no new therapy required, maximize oral therapy

Subset II: Pulmonary Congestion "Congested"



- CI > 2.2 L/min/m2 (warm)
- PCWP > 18 mmHg (wet)
- Mortality = 9-11%
- Therapy goal: decrease PCWP
- Specific agents: **diuretics**
- Treatment setting: ED (rare) or inpatient (common, admitted to non-ICU setting, typically do not require PA catheter to guide tx)

Subset III: Peripheral Hypoperfusion "Low Flow State"

- CI < 2.2 L/min/m2 (cool)
- PCWP < 18 mmHg (dry)
- Mortality = 18-23%
- Therapy goal: increase CI by increasing PCWP
- Specific agents: **volume (crystalloids, colloids), vasopressors, inotropes, mechanical cardiac support (intra-aortic blood pump)**
- Treatment setting: ICU

Subset IV: Pulm Congestion and Peripheral Hypoperfusion "Decompensated"

- CI < 2.2 L/min/m2 (cool)
- PCWP > 18 mmHg (wet)
- Mortality = 51-60%
- Therapy goal: increase CI and decrease PCWP
- Specific agents: **diuretics, vasodilators, inotropes, IABP**
- Treatment setting: ICU

Patient Case

- SB comes into clinic for urgent follow up for acute symptoms of HF. She's experiencing SOB even while sitting in a chair, and she can't wear shoes due to swelling. She is transferred to local hospital for admission to the ICU.

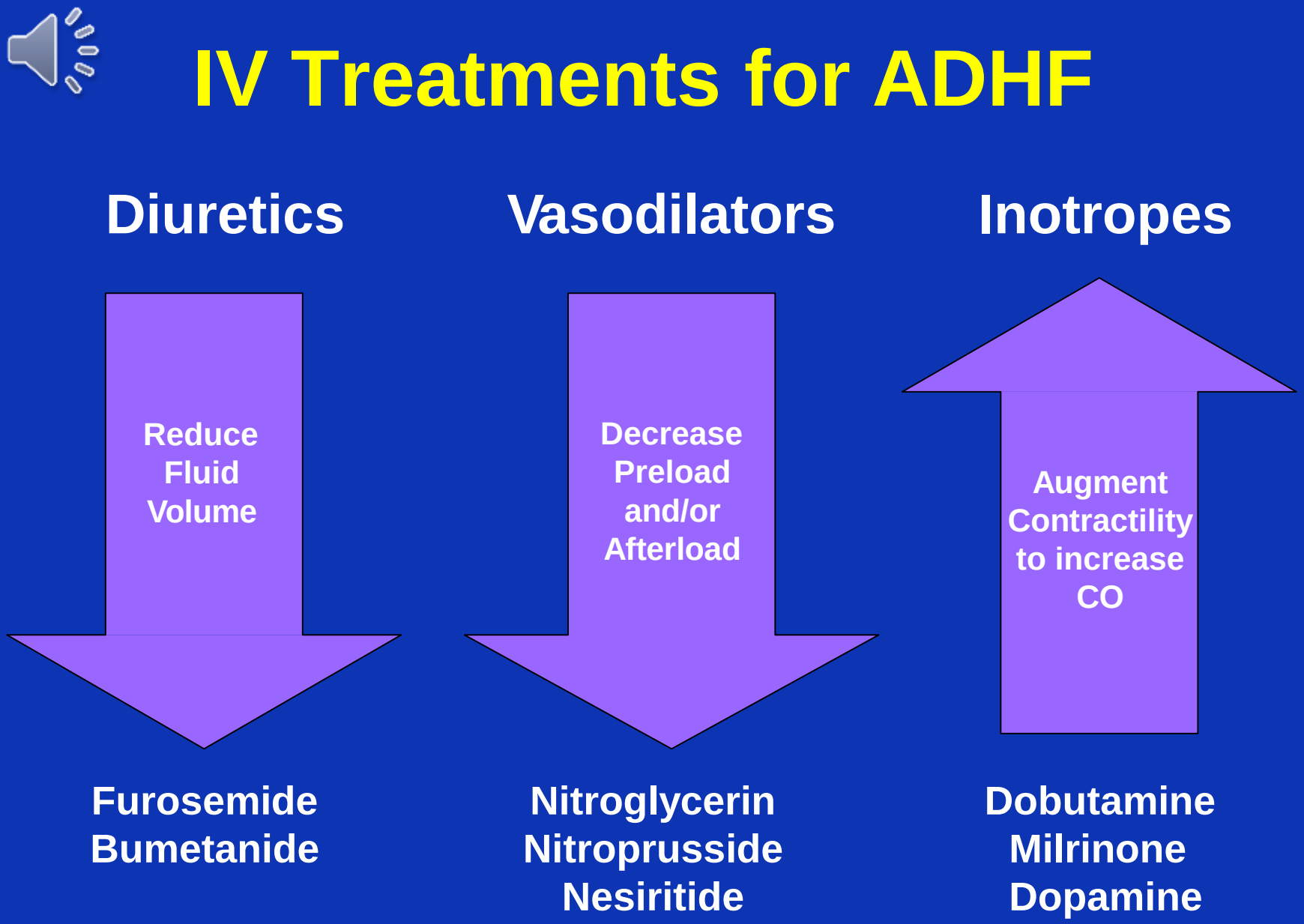
- Medications: aspirin 81mg QD, lisinopril 20mg QD, carvedilol 6.25mg BID, simvastatin 40mg QD, furosemide 40mg QD

- Pertinent PE findings: BP 100/62 mmHg, HR 102 bpm, JVP 11cm H_20, 3+ pitting edema, warm and well perfused

Patient Case Questions

- What stage and NYHA functional class is this patient in?
- What ADHF hemodynamic subset is SB in currently?
- What therapies are indicated for this subset?

IV Treatments for ADHF



Fonarow GC. *Rev Cardiovasc Med*. 2001;2(suppl 2):S7. Fonarow GC, et al. *Rev Cardiovasc Med*. 2003;4(suppl 7):S21.

Signs/Symptoms of ADHF

1. **Increased PCWP (Congestion)**
2. Decreased Cardiac Output (CI)

Medications for Congestion: Preload Reduction

- **Diuretics**
- Vasodilators

Loop Diuretics in ADHF

- Loop diuretics are the most widely used, the most potent, and effective at low CrCl (< 30 mL/min)
  - Furosemide (Lasix) most commonly used
- MOA: lowers preload (PCWP) by enhancing renal excretion of sodium and water
- Should be given as IV for rapid onset and better absorption
  - Conversions:
    - Furosemide 40mg PO = furosemide 20mg IV
    - Furosemide 40mg PO = bumetanide 1mg PO/IV

Loop Diuretics PK

Table 2. Pharmacokinetics of the Loop Diuretics[12-18]

Property	Furosemide	Bumetanide	Torsemide
Bioavailability (%)	10–100 (average = 50)	80–100	80–100
Affected by food	yes	yes	no
Metabolism	50% renal conjugation	50% hepatic	80% hepatic
Half-life (h)			
normal	1.5–2	1	3–4
renal dysfunction	2.8	1.6	4–5
hepatic dysfunction	2.5	2.3	8
heart failure	2.7	1.3	6
Onset (min)			
oral	30–60	30–60	30–60
intravenous	5	2–3	unavailable

Wargo and Banta. Annal Pharmacotherapy 2009;43:1836-47

Loop Diuretics Continued

- **New onset ADHF or diuretic naïve:**
  - Furosemide 20-40 mg IV bolus
  - Further doses based on urine output and s/sx congestion

- **On loop diuretic already:** initial IV dose should equal or exceed their chronic oral daily dose
  - Give as IV bolus every 12 hours or by continuous infusion (mg/hr) at the same dose in mg/day as home oral dose

2013 ACC/AHA Hospitalized Patient with HF Guidelines

Diuretic Dosing Example

- A patient receiving furosemide 100 mg po BID as an outpatient is admitted to the hospital with ADHF.
- You are asked by the medical team to assist with starting a furosemide drip.
- What infusion rate in mg/hour would you recommend?

Diuretic Dosing Answer

- What furosemide rate in mg/hour would you recommend?
- Typical oral to IV conversion: 100mg po BID is 200mg/day (x 50%) = 100mg/day IV = 4mg/hour
  - Remember 50% bioavailability for oral
- **However, to treat THIS patient with ADHF: 200mg/day IV = 8mg/hour**
  - Round to the nearest whole number

Loop Diuretics Continued

- Monitoring:
  - Goal: **net diuresis of 1.5-2 L on Day 1**, decrease JVP to ≤ 8 cm, maintain SBP > 80 mmHg, **decrease weight by average 4-5kg**
  - >250-500 cc of urine output expected within 1st several hours (furosemide peak effect = 1-2 hours)
  - **Urine output, s/sx congestion and hypoperfusion, VS, weight daily at same time each day, daily electrolytes and BUN/SCr (increased BUN:SCr ratio > 20:1 when "pre-renal")**
- Inadequate response? Increase dose of IV loop diuretic or add thiazide

2013 ACC/AHA Hospitalized Patient with HF Guidelines

Diuretic Resistance

- Diuretic resistance – failure to achieve weight reduction of > 0.5 kg after several increasing bolus doses

- Causes:
  - Intravascular volume depletion
  - Neurohormonal activation
  - Rebound Na uptake after volume loss
  - Hypertrophy of distal nephron
  - Reduced tubular secretion (NSAIDS, renal failure)
  - Decreased renal perfusion (↓ output)
  - Impaired gut absorption of oral diuretic
  - Non-adherence with drugs or diet

Diuretic Resistance- Management

- Increase dose before increasing frequency of loop diuretic
  - Ceiling effect of IV furosemide is ~ 160-200mg
- Add a second diuretic with a different MOA
  - metolazone 2.5-5mg PO daily
  - chlorothiazide 250-500mg IV daily; consider for gut edema; $$$ so reserve for NPO status
- Change from intermittent dosing to cont. infusion
  - Furosemide initial infusion rate: 0.1 mg/kg/hr; double rate every 4-8 hours based on response, maximum rate 0.4 mg/kg/hr

Medications for Congestion: Preload Reduction

- Diuretics
- **IV Vasodilators**

ADHF Guidelines: IV Vasodilators

- May be considered in addition to IV loop diuretics to rapidly improve dyspnea in patients without symptomatic hypotension (or SBP > 90 mmHg)

- Benefits: decrease venous tone (to optimize preload) and arterial tone (decrease afterload)
  - No evidence/data to confirm their benefit

2013 ACC/AHA HF Guidelines; 2016 ESC HF Guidelines

Vasodilator Therapy for ADHF

	Nitroglycerin	Nitroprusside	Nesiritide (Natrecor®)
MOA	Vasodilator (venous > arterial)	Vasodilator (venous < arterial)	Vasodilator (venous and arterial)
Monitoring	Symptom relief, vital signs, urine output		
Limitations	Hypotension Headache Reflex tachycardia Titration required	Hypotension Thiocyanate Reflex tachycardia Difficult titration Coronary “steal”	Hypotension Unresolved issues (worsening renal function, mortality)

Therapeutic Goal: Decrease PCWP to 15-18 and keep SBP > 90 mmHg

DiDomenico et al. *Ann Pharmacother*. 2004;.38:649-60. Nieminen et al. *Eur Heart J*. 2005;.26:384-416. Adams KF et al. *J Card Fail*. 2006;.12:10-38.

Signs/Symptoms of ADHF

1. Increased PCWP
2. **Decreased Cardiac Output (CI)**

Medications for Hypoperfusion (low CO/CI)

- **Inotropes**
  - Dobutamine
  - Milrinone
  - Dopamine

ADHF Guidelines: IV Inotropes

- May be considered in patients with diminished peripheral perfusion or end-organ dysfunction, particularly if:
  - Marginal systolic blood pressure (< 90 mmHg)
  - Symptomatic hypotension exists despite adequate filling pressures, or
  - Unresponsive to, or intolerant of, IV vasodilators

- May be considered in similar patients with fluid overload if they respond poorly to IV diuretics or have worsening renal function

Lindenfeld J, et al. 2010 ADHF Guidelines. *J Card Fail* 2010;16:e134-e156.

Intravenous Inotropic Therapy

	Dobutamine	Milrinone
MOA	β-1agonist to increase contractility, slight peripheral vasodilation	PDE inhibitor, augments myocyte Ca++ utilization, moderate peripheral vasodilation
Indication	ADHF short-term management : “cold” or “cold & wet”	
Half-life	2 minutes	1 hour, prolonged 2-3 hours if CrCl < 50 ml/min
Other comments	Recommended if hypotensive	Recommended if receiving a β-blocker
Monitoring	Hypotension, increased myocardial oxygen demand, ventricular arrhythmias	

Patient Case

- SB comes into clinic for urgent follow up for acute symptoms of HF. She's experiencing SOB even while sitting in a chair, and she can't wear shoes due to swelling.
- Medications: aspirin 81mg qday, lisinopril 20mg qday, carvedilol 6.25mg bid, simvastatin 40mg qhs, furosemide 40mg qday
- Pertinent exam findings: BP 100/62 mmHg, P102 bpm, JVP 11cm H20, 3+ pitting edema, warm and well perfused
- Pulmonary artery catheter readings: CI 2.4 L/min/m^2, PCWP 22mmHg

Case Continued

- What dose of furosemide would you start?
- Unfortunately, we overshoot on the furosemide dose and now her PA readings are: CI 1.8L/min/m2, PCWP 15mmHg. What therapies could you start at this point?
- What if her readings were: CI 1.7L/min/m^2, PCWP 25mmHg?

Questions?

Thank you!