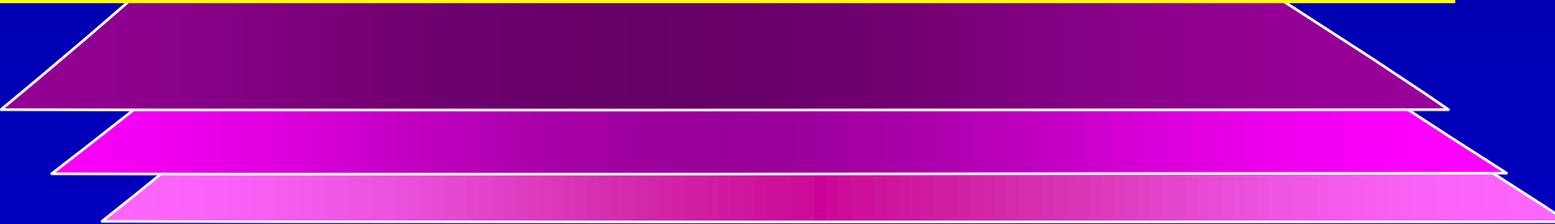




Initial Management of Heart Failure Exacerbations



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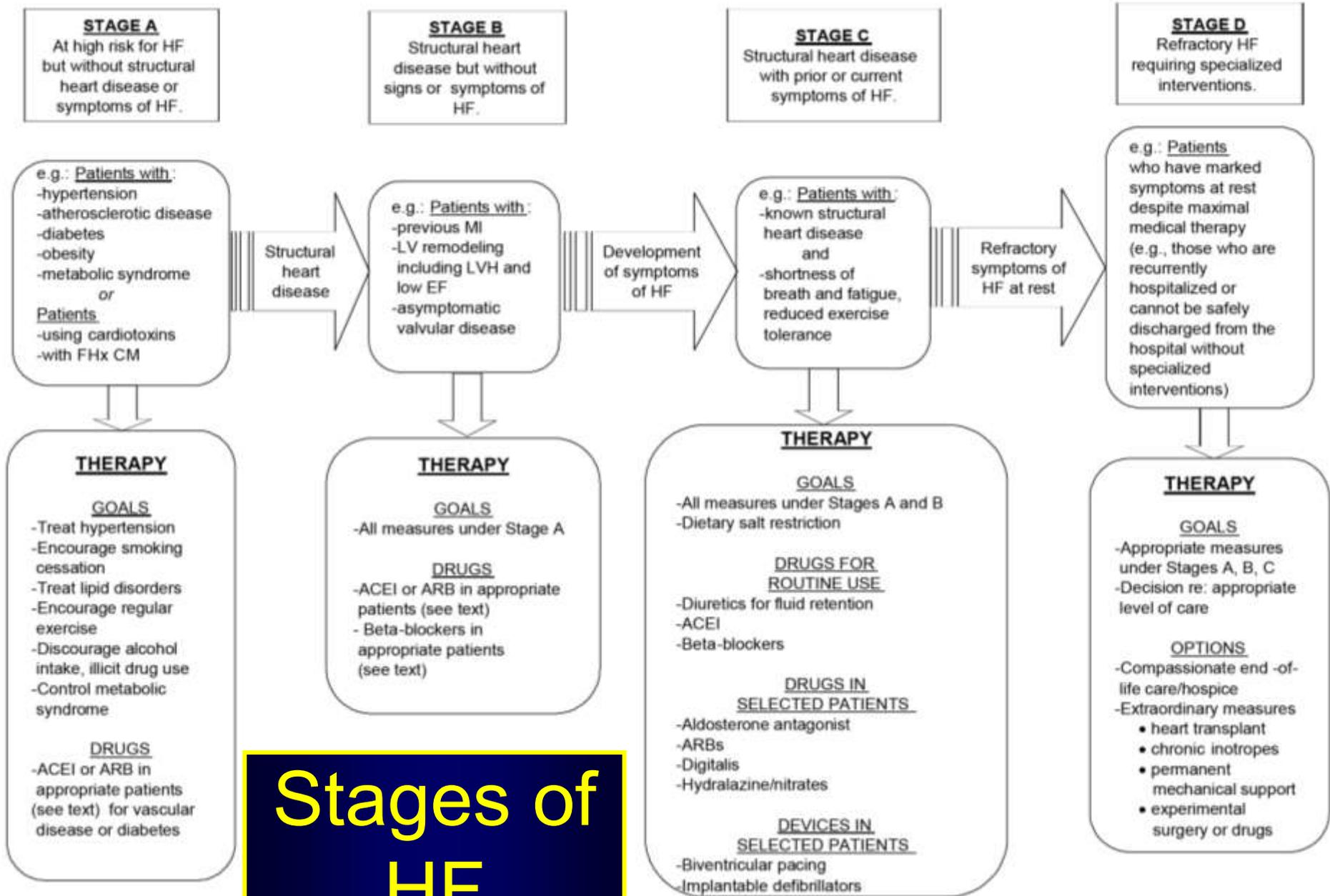
Definition: Heart Failure

- Syndrome of dyspnea or exercise intolerance or fluid retention resulting from the inability of the heart to provide output adequate for the needs of the body at a normal filling pressure
- Since some patients may not have fluid overload, the term congestive heart failure is not now favored
- May result from great vessel or pericardial disease or valvular disease, but most are LV dysfunction (systolic or diastolic)

ACC/AHA Guideline update for the diagnosis and management of chronic heart failure in the adult. Update 2009.

At Risk for Heart Failure

Heart Failure



Stages of HF

Topics

- Diagnosis (Is it HF? ... Why worsened?)
 - No prior HF
 - Known HF
- Prognosis
- Management
 - When to admit
 - Pharmacologic strategies

Decompensation of Cardiac Function

- HF progression: Pathophysiology
 - Neurohormonal abnormalities
 - Ventricular remodeling
 - Myocyte hypertrophy or slippage
 - Myocardial interstitial fibrosis
 - Progression of CAD
 - Worsening of valvular abnormalities (MR)
- Concomitant problems that cause decompensation of the patient

Heart Failure Society of America Guidelines: ADHF Diagnosis

- Primarily on signs and symptoms
- BNP may be helpful in clinical uncertainty

“Section 12: Evaluation and Management of Patients with Acute Decompensated Heart Failure.” Journal of Cardiac Failure. 2006;12:e86-e103.

Diagnosis of HF in Patient Without Prior Known HF

- Presentation is usually dyspnea, but also cough or fatigue or swelling, usually gradual over days to weeks but maybe with recent acceleration over minutes to hours
- Patients may present with non-HF symptoms (MI or PE or arrhythmia)
- 19% of hospital admissions for HF had no prior diagnosis of HF*

Diagnosis of HF in Patient Without Prior Known HF - 2

- Accuracy of Diagnosis
 - False negative: call HF bronchitis or pneumonia in young because index of suspicion is low; cirrhosis in edematous patients with disproportionate right heart failure
 - False positive: diagnosing HF in patients with primary pulmonary problems as cause of dyspnea or patients with hepatic or renal failure as cause of fluid retention states
 - Risk factors for HF should be sought, and are present in most patients: Htn, DM, CAD, thyroid, valve dz, alcohol/drug, FH DCM

Diagnosis of HF in Patient Without Prior Known HF - 3

- Physical Exam: often hypertensive and tachycardic, JVP may be elevated, bilateral pulmonary crackles possible, most with S4, S3 occasionally, MR or AS murmur, edema
- JVP important in edema assessment (practice makes perfect)

Diagnosis of HF in Patient Without Prior Known HF - 4

- CXR important in dyspnea and cough (diffuse vs focal infiltrate)
- BNP important (if CXR and ECG and BNP are all normal, HF is unlikely*)

Diagnosis of HF in Patient Without Prior Known HF - 5

ECG is usually abnormal

- LVH
- MI, poor precordial R wave progression
- BBB/IVCD
- ST-T abnormalities
- If ECG is totally normal, EF is probably normal
- Is helpful in elucidating etiology and status (LAE may come and go with changes in PCW pressure)
- AFib may be present in about 1/3

Diagnosis of Decompensation in Patients With Known HF

- Reasons for decompensation (infection, change in diet or activity, medication, cardiac or renal or pulmonary function)
- Symptoms of dyspnea or fatigue or fluid accumulation, differentiate true cardiac decompensation from concomitant pulmonary or other problem causing symptoms similar to HF; HF most frequently gradual onset
- Exam, ECG, CXR, BNP

Pitfall in the Diagnosis of Decompensation in Heart Failure

- If a patient is on a weight reduction program or if he is unable to maintain adequate nutrition (nausea, early satiety, dyspnea, emesis), his dry weight may be decreasing and his water weight may be accumulating so that he can be volume overloaded without weight gain, and nutritional history will uncover this

¹Wilson Tang WH et al. J Am Coll Cardiol. 2003;41:1494

²Kwan HJ et al. Ann Intern Med 2003;138:807

Precipitants of Decompensation

- Patient related factors
- Acute cardiac events
- Acute noncardiac events
- Adverse medication effects

Precipitants of Decompensation: 1: Patient-related factors

- Nonadherence to medication
- Excessive salt intake
- Physical, emotional, and environmental stress
- Cardiac toxins: alcohol, cocaine

OSA needs CPAP
COPD is important

Precipitants of Decompensation: 2: Acute cardiac events

- RV Pacing
- Arrhythmia: AF with RVR, VT, marked bradycardia or conduction abnormalities
- Uncontrolled hypertension
- Myocardial infarction or ischemia
- Valve disease – progressive mitral regurgitation

Precipitants of Decompensation:

3: Acute noncardiac events

- Pulmonary embolism
- Anemia, bleeding
- Systemic infection, esp pulmonary
- Thyroid disorders

Precipitants of Decompensation:

4: Adverse medication effects

- **Fluid retention**
 - Steroids or NSAIDs
 - TZDs
- **Cardiac depression**
 - Nondihydropyridine calcium blocker
 - Type IA and IC antiarrhythmics
 - Doxorubicin or cyclophosphamide
 - Drugs that end in –ib or -ab
 - Pseudoephedrine?

Iatrogenic Causes of Decompensation in Heart Failure

- Initiation of thiazolidinedione agents in diabetics with HF is associated with fluid retention (17%), usually within the first few months of initiation, reversible with withdrawal of the agent, more likely peripheral than pulmonary, more in women and in patients on insulin¹
- TNF- α antagonists (etanercept TNF- α type 2 for some arthritis and infliximab for Crohn and for arthritis) reported in 47 patients to be associated with exacerbation or new dx of HF (formerly considered promising for treating HF!, but negative and adverse trials)²

¹Wilson Tang WH et al. J Am Coll Cardiol. 2003;41:1494

²Kwan HJ et al. Ann Intern Med 2003;138:807

Thiazolidinediones and HF

- Rosiglitazone and Pioglitazone are both contraindicated in NYHA Class III or IV heart failure
- In one study, 17% of TZD users developed edema, mainly peripheral edema which was reversible on discontinuation of agent
- More in women and in insulin users
- No relationship to NYHA Class or LV EF

Acutely Decompensated Heart Failure (ADHF) – One Example

- Study investigating presentation of patients with heart failure
- Included 293 patients admitted to a hospital in Spain in 2002-3
- Precipitating factors identified in 221 (75%)

Patient data

Age (years)	76.7±7.3
>75	192 (66%)
Gender	
Women	173 (59%)
Men	120 (41%)
Barthel Index	85.8±18.5
Charlson Index	1.79±1.5
Etiology	
Coronary artery disease	114 (39%)
Hypertensive heart disease	100 (33%)
Valvular heart disease	53 (16%)
Other	26 (9%)
Undetermined	21 (7%)
Baseline NYHA ^a functional class	
Class I	2 (0.6%)
Class II	96 (32.7%)
Class III	161 (54.9%)
Class IV	34 (11.6%)
Atrial fibrillation or flutter	123 (41%)

Values are expressed as number (percentage) or mean (standard deviation).

^a NYHA: New York Heart Association.

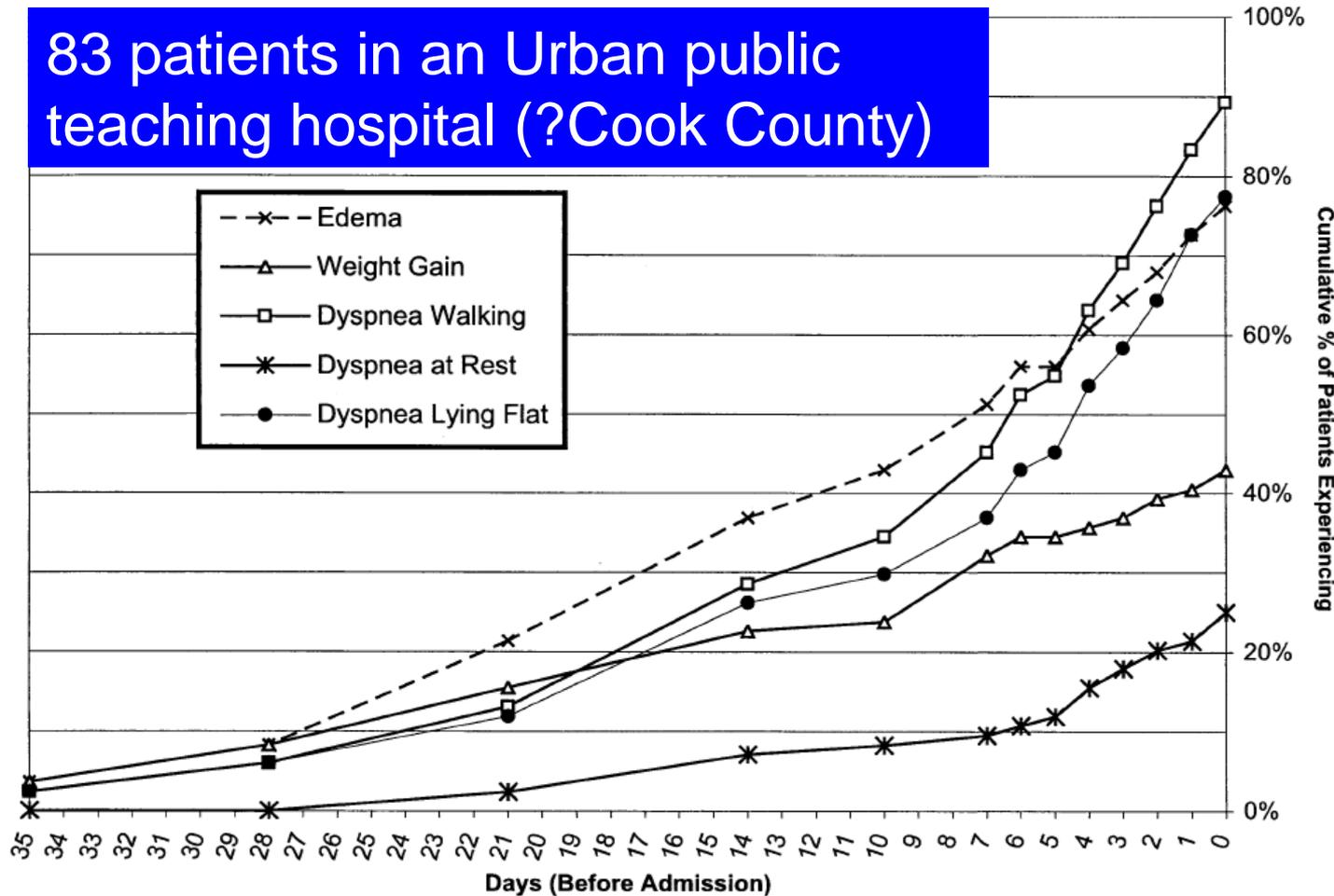
Table 2

Precipitating factors

	Number (%)
Preventable	
Poor dietary compliance	19 (6.5)
Poor medication compliance	35 (12)
Anemia	46 (15.7)
Use of harmful medications	19 (6.5)
Physical effort	8 (2.7)
Withdrawal of beneficial medications	4 (1.4)
Non-preventable	
Infections	84 (29)
Arrhythmias	64 (21.9)
Uncontrolled blood pressure	39 (13.3)
Myocardial ischemia	28 (10)
Emotional or stressful events	6 (2)
Others	4 (1.4)

Duration of Symptoms before Admission to Hospital: Another Example

83 patients in an Urban public teaching hospital (?Cook County)



Duration of Symptoms before Admission to Hospital: Another Example

Table 1. Frequency and Duration of Worsening Symptoms before Admission for Heart Failure (n = 83 Patients)

Symptom	Number (%) with Symptom Exacerbation	Duration of Worsening (days)	
		Mean \pm SD	Median (Interquartile Range)
Edema	64 (77)	12.4 \pm 11.1	11 (4–17.5)
Cough	57 (69)	10.1 \pm 9.3	7 (3–16.5)
Weight gain	34 (41)	11.4 \pm 9.4	7 (3.8–17.5)
Dyspnea walking	74 (89)	8.4 \pm 7.5	6 (2–14)
Dyspnea lying flat	67 (81)	8.4 \pm 7.7	6 (2–14)
Dyspnea at rest	21 (25)	6.4 \pm 6.3	4 (1.5–13.5)

Reasons for Decompensation

Table 2. Patient-Identified Factors Contributing to Worsening of Heart Failure*

Contributing Factor	Major Cause	Number (%)	
		Minor Cause	Not a Problem
Missed/skipped medication	28 (36)	14 (18)	36 (46)
Worry or stress	27 (33)	14 (17)	41 (50)
Got "sick" (e.g., from a cold)	33 (40)	5 (6)	44 (54)
Ran out of medication	20 (25)	4 (5)	56 (70)
No identifiable reason	13 (16)	1 (1)	69 (83)
Lapses in low-salt diet	10 (12)	24 (29)	49 (59)
Working too hard	6 (7)	10 (12)	67 (81)
Could not reach doctor	5 (6)	3 (4)	75 (90)
Could not get into clinic	3 (4)	3 (4)	77 (93)
Alcohol	5 (6)	0	78 (94)

* n = 83 in sample, but not all patients answered each question.

Initial Approach to Care

ADHF: Treatment Goals

- Improve symptoms (congestion and low-output)
- Optimize volume status
- Identify etiology
- Identify precipitating factors
- Optimize chronic oral therapy

- Minimize medication side effects
- Identify appropriate revascularization candidates
- Educate: medications and self-assessment of HF
- Consider disease management program for HF

ED Management of HF

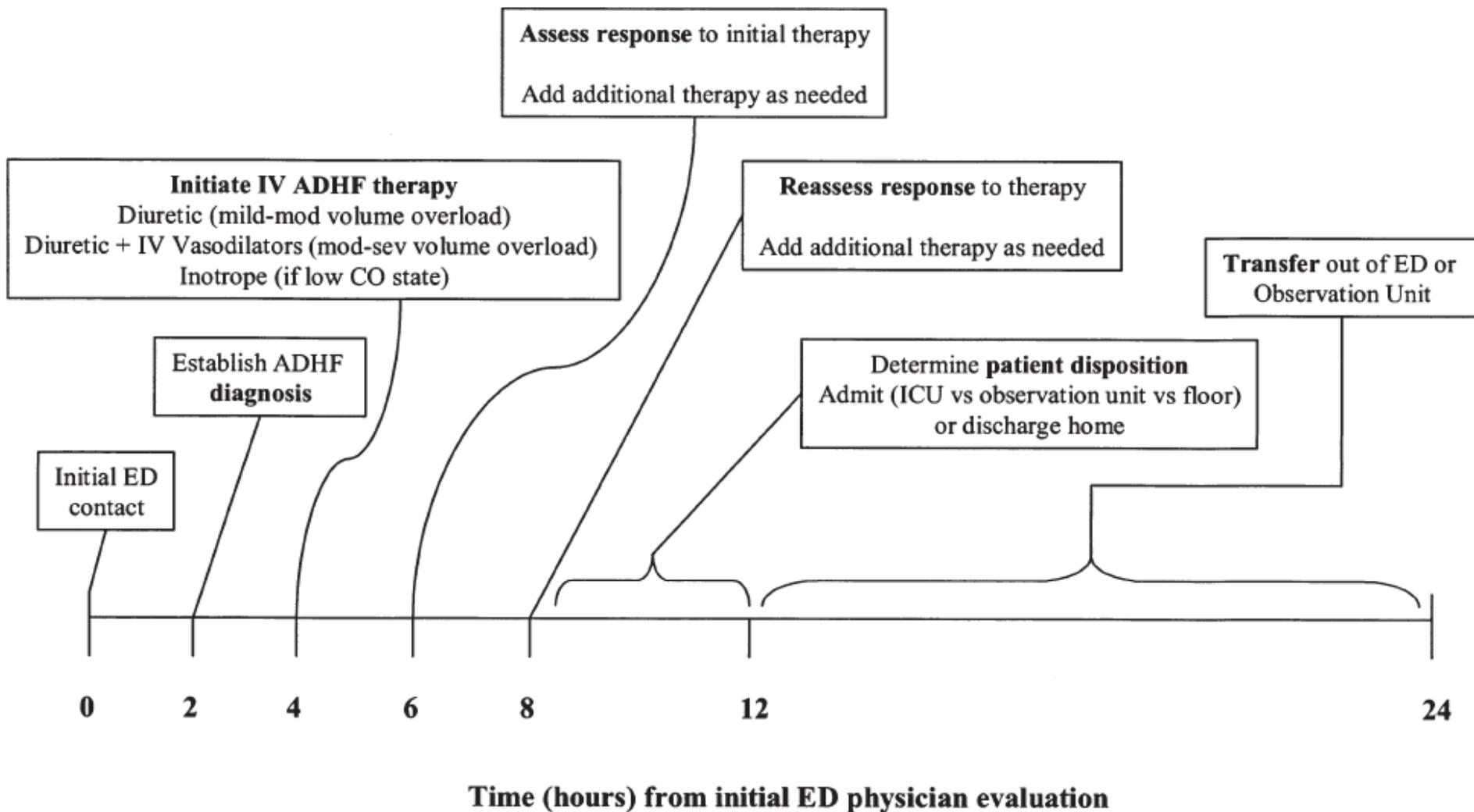


Figure 1. Timeline for the management of acute decompensated heart failure (ADHF) in the emergency department/observation unit. CO = cardiac output; ED = emergency department; ICU = intensive care unit; mod-sev = moderate to severe.

Dosing Diuretics

- No prior furosemide – 40 mg IV
- Prior outpatient PO furosemide – total daily outpatient dose as IV bolus (up to 180 mg)
- Goal urine output in 2 hours:
 - 500 cc if normal renal function
 - 250 cc if renal insufficiency
- Goal not met: double IV dose (up to 360 mg)

ADHF: Hospital Admission Recommended

- Severe HF: ↓BP, worsening renal function, altered mentation
- Resting dyspnea (tachypnea, sometimes O₂ sat <90%)
- Hemodynamically significant arrhythmias, particularly AF with RVR
- Acute Coronary Syndrome

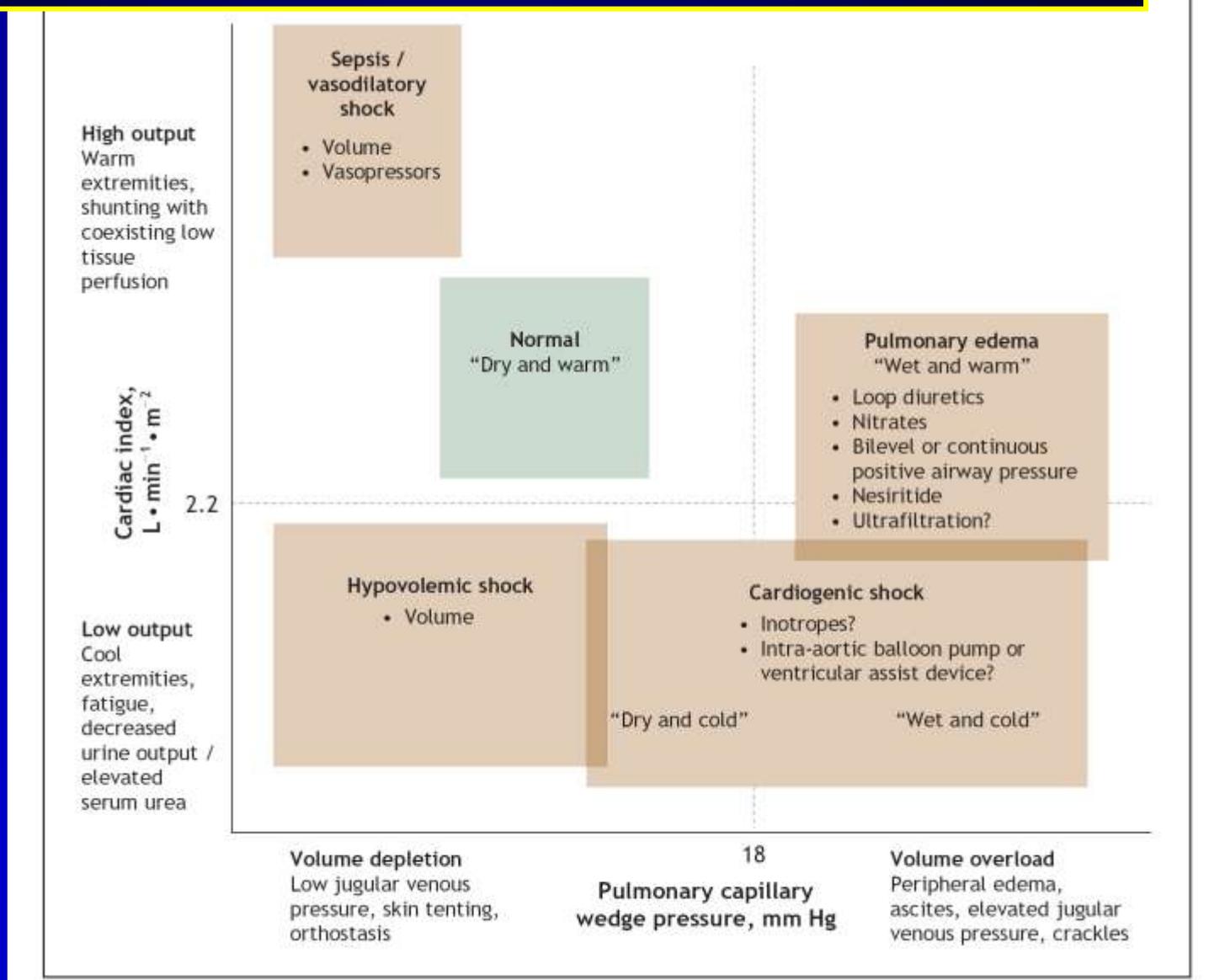
ADHF: Hospital Admission Should be Considered

- Worsened congestion (wt increase >5kg)
- Signs and symptoms of congestion (pulmonary or systemic) even if no wt gain
- Major electrolyte disturbance
- Associated comorbidity (pneumonia, PE, DKA, TIA or stroke)
- Multiple ICD discharges
- Prior undiagnosed HF with congestive signs or symptoms

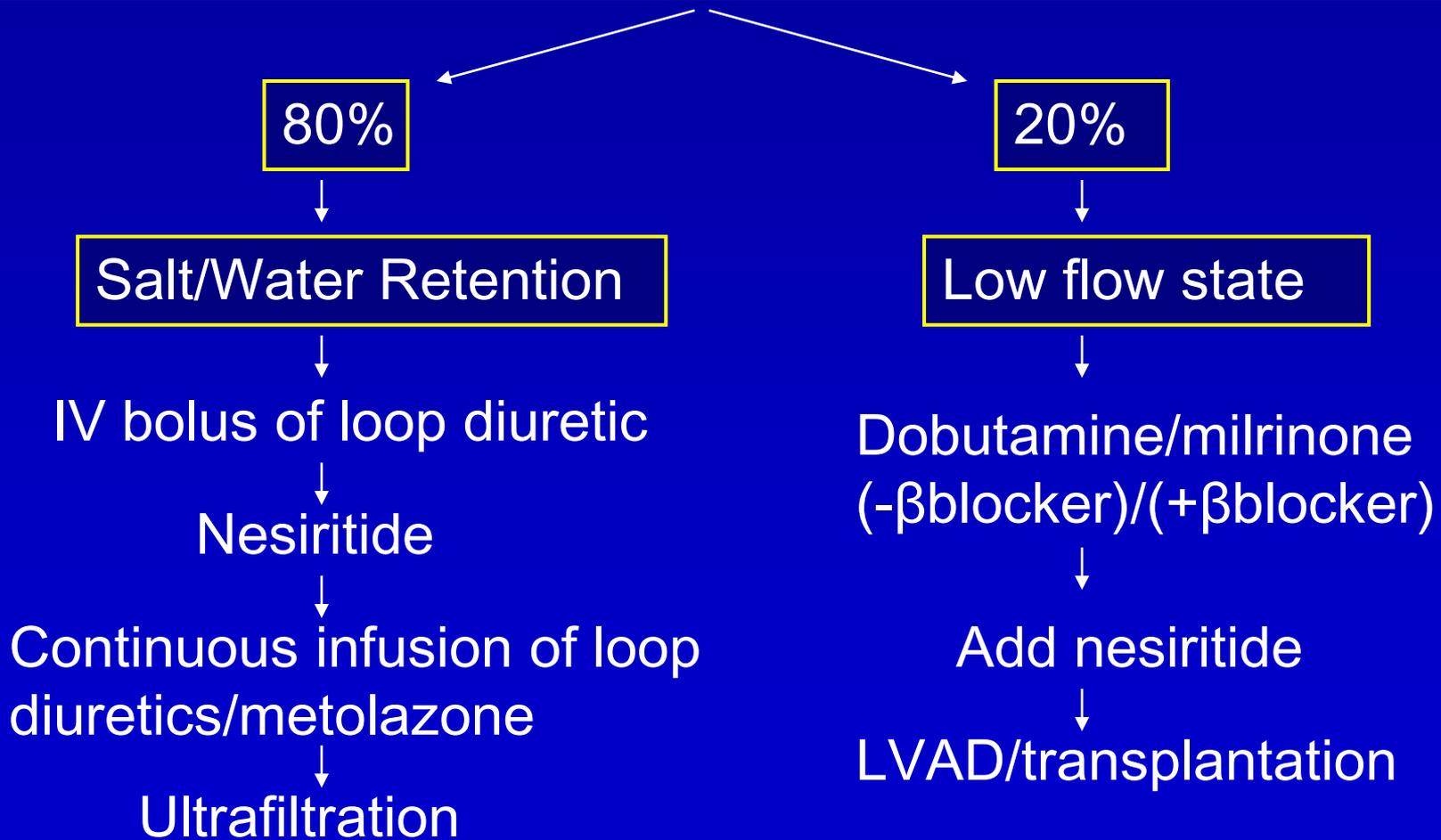
ADHF: Congestion

	Pulmonary	Systemic
Symptoms	Dyspnea Orthopnea PND	Edema Abdominal (hepatic) swelling or pain
Signs	Rales Wheezing Pleural effusion Hypoxemia Left sided S ₃ Worse MR	Edema Elevated JVP Hepatic enlargement and tenderness Ascites Right sided S ₃ Worse TR Hepatojugular Reflux

Hemodynamic/Clinical Approach



Approach to Decompensated HF



ADHF: Therapy - 1

- IV loop diuretic
- If refractory to IV loop diuretic
 - Na and fluid restriction
 - Higher dose of diuretic
 - Continuous infusion of diuretic
 - Add metolazone or aldosterone antagonist
 - Ultrafiltration may be considered
- If Na<130 may restrict fluid to <2 liter/da
- May consider: nitroglycerin, nitroprusside or nesiritide to improve symptoms if BP not low
- If acute pulmonary edema or severe hypertension, recommend diuretics with nitroglycerin or nitroprusside

ADHF: Therapy - 2

- Persistent severe HF despite therapy may consider nitroprusside, nitroglycerin or nesiritide
- May consider milrinone or dobutamine to improve perfusion (only if filling pressures are elevated), particularly if SBP<90 or intolerant of vasodilators, only with frequent BP monitoring and rhythm monitoring

ADHF: Ultrafiltration

- Study funded by CHF Solutions
- 200 patients randomized to diuretic or ultrafiltration (many exclusions)
- Wt loss at 48 hr greater with ultrafiltration 5.0 kg vs 3.1 kg
- Diuretic: daily IV dose at least twice the prehospital daily oral dose
- Ultrafiltration 241 ml/hr
- Diuretic 180 mg/day IV (1/3 continuous infusion)
- Similar dyspnea, creatinine, BP response (diuretic – more hypokalemia)
- Fewer rehospitalizations at 90 days

ADHF: Daily Monitoring in Hospital

- Symptoms – dyspnea, fatigue, cough
- Exam – JVP, rales, edema
- Weight – AM after voiding
- Intake & Output (no routine Foley)
- VS (incl orthostatic) more than daily
- Lytes incl Mg, BUN Cr

ADHF: Invasive Monitoring in Hospital

- Not Routine
- Consider in Special Circumstances
 - Refractory to initial therapy
 - Volume status and filling pressures unclear
 - SBP<80 or worsening renal function on therapy
 - Consideration of chronic outpatient inotrope infusion – documenting adequate hemodynamic response

Transplantation in CHF

Table 3. Indications for Cardiac Transplantation

Absolute indications

For hemodynamic compromise due to HF

Refractory cardiogenic shock

Documented dependence on IV inotropic support to maintain adequate organ perfusion

Peak VO_2 less than 10 mL per kg per min with achievement of anaerobic metabolism

Severe symptoms of ischemia that consistently limit routine activity and are not amenable to coronary artery bypass surgery or percutaneous coronary intervention

Recurrent symptomatic ventricular arrhythmias refractory to all therapeutic modalities

Relative Indications

Peak VO_2 11 to 14 mL per kg per min (or 55% predicted) and major limitation of the patient's daily activities

Recurrent unstable ischemia not amenable to other intervention

Recurrent instability of fluid balance/renal function not due to patient noncompliance with medical regimen

Insufficient Indications

Low left ventricular ejection fraction

History of functional class III or IV symptoms of HF

Peak VO_2 greater than 15 mL per kg per min (and greater than 55% predicted) without other indications

ADHF: Discharge Criteria

- At least near optimal volume status
- Transition from IV to oral diuretic completed
- Follow-up within 7-10 days
- Stable oral medical regimen for 24 hours
- Ambulation as inpatient to assess functional capacity
- Postdischarge management (scale, telephone follow-up arranged)

Predictors of Adverse Outcome

- Worse NYHA class
- Tachycardia
- Low BP
- Wide QRS complex
- Hyponatremia
- Renal insufficiency (BUN >34)
- Low hematocrit

- Low EF
- Low peak O₂ uptake
- Intolerance of conventional therapy
- Refractory volume overload

ACC/AHA Guideline update for the diagnosis and management of chronic heart failure in the adult. Update 2009, p. 16.

ADHF Treatments and Targets

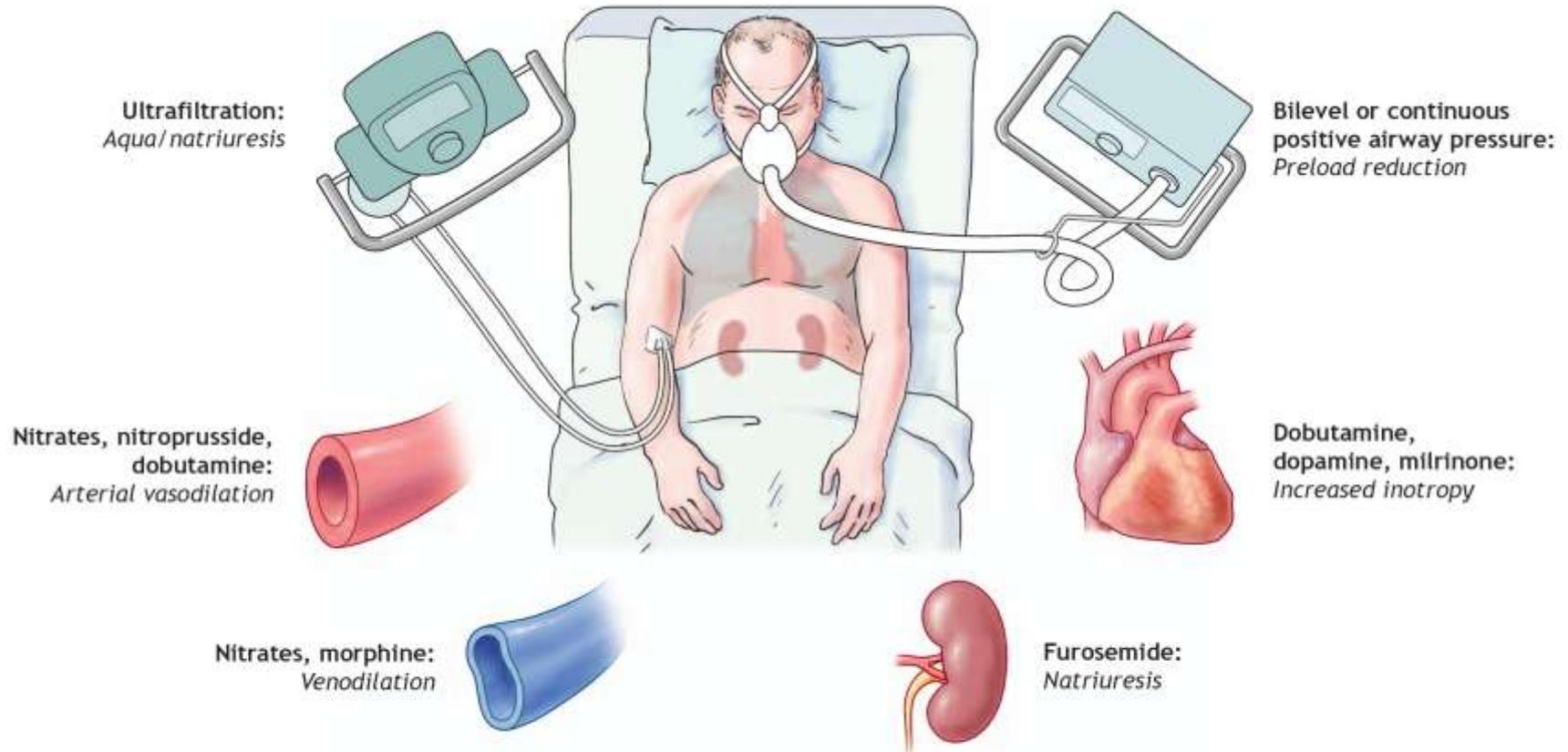


Fig. 2: Various targets for therapies used in the management of acute decompensated heart failure.

Treatment Options in ADHF

ADHF: Treatment Goals

- Improve symptoms (congestion and low-output)
- Optimize volume status
- Identify etiology
- Identify precipitating factors
- Optimize chronic oral therapy

- Minimize medication side effects
- Identify appropriate revascularization candidates
- Educate: medications and self-assessment of HF
- Consider disease management program for HF

Use of Pulmonary Artery Catheterization in HF

- ESCAPE (Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness): NHLBI multicenter randomized trial
- Hypothesis: Outcomes with PA catheter will be superior to clinical assessment alone over 6 months
- Endpoint: days alive and not hospitalized in 6 mo,
- 433 patients enrolled and PA catheter considered feasible and not mandatory, EF<30 (20%), HF>3 mo, SBP<125 (106), ED or hosp <6 mo; no change in endpoint; complic in 4.2%, PA catheter patients had fewer symptoms and walked farther

Pharmacologic Therapy in HF

- Patients should already be on ACE-I and β -blocker on arrival – generally continue them
- Stop β -blocker if systemic perfusion is inadequate
- Other IV agents to consider using: diuretic, nitroglycerine, nitroprusside, ACE-I, nesiritide, inotropes

Use of Diuretics in HF - 1

- IV furosemide – venodilation in 15 minutes, diuresis in 30 minutes lasting 1-2 hours, half life 6 hours (bumetanide is 40-50 times more potent, same mechanism of action, more bioavailable)
- Diuretic resistance – may consider adding thiazide or spironolactone or eplerenone acting more distally
- Monitor – urine output, BP, electrolytes, renal function
- Since the Frank Starling curve is flat in HF, the CO won't drop with decrease in filling pressure

Use of Diuretics in HF - 2

- One study showed furosemide infusion superior to bolus (JACC 1996), other studies not
- Adverse effects: electrolyte abnormalities and renal dysfunction (from changes in renal hemodynamics); activate RAAS and increase SVR, increase risk for hypotension with ACE-I
- Using vasodilator with diuretic is good for elevated SVR and low cardiac output but may increase hyponatremia if overdiuresed

Stepwise Approach to Loop Diuretic Resistance

- Enforce strict low-sodium diet
- Use effective doses of loop diuretics
- Combination administration of long-acting thiazide with loop diuretic to offset the antinatriuretic rebound effect observed with administration of short-acting loop diuretics
- Constant intravenous infusion of loop-diuretic
- Water restriction is an option (I do not favor)

Use of Nitrates in HF - 1

- Primary direct venodilator
 - Low dose, venodilator only
 - Higher dose, arterial dilator also
- Decrease afterload so increases stroke volume
- Mechanism is through conversion to NO which binds to guanylate cyclase and increases production of cGMP
- SL dose is bolus of 400 μg , starting IV is 5 $\mu\text{g}/\text{min}$, can titrate every 3-5 min and half life is about 3 min

Use of Nitrates in HF - 2

- Oral isosorbide dinitrate 60 mg po qid with hydralazine was good, superior to ACE-I in African American
- Nitrate added to ACE-I is reasonable if inadequate afterload reduction with high dose or if intolerant of ACE-I
- Nitrate tolerance in 24 hours, 20% are resistant to NTG at first, so if no response to 200 µg, no point in increasing further
- Nitrates can cause hypotension (particularly in RV MI and significant aortic stenosis) and tachycardia

Use of Nitroprusside in HF

- Balanced arterial and venous dilator
- Marked decrease in afterload, also preload
- Continuous BP monitoring needed, and PA catheter if PCWP not known to be elevated
- Start 0.1-0.2 $\mu\text{g}/\text{kg}/\text{min}$ and increase q 5 min, taper to avoid rebound
- May worsen V/Q mismatch in advanced COPD or pleural effusions, so worsen hypoxia
- In ischemia NTP may cause coronary steal (NTG would be better for those patients with active ischemia)
- Use only in patients with adequate renal function (thiocyanate toxicity if $>10\mu\text{g}/\text{ml}$ in blood can give abdominal pain and mental status changes), and hepatic (cyanide toxicity can be treated with hydroxycobalamin); also methemoglobinemia can result from NTP

Use of ACE-I in HF

- Enalaprilat
 - Reduces supine and standing SBP and DBP, not much orthostasis
 - Onset in about 15 minutes, maximal effect in 1 to 4 hours, duration single dose 6 hours
 - Generally use only in NPO patients
 - Renal: antagonize efferent arteriolar constriction mediated by angiotensin II, so lower GFR and rise in creatinine
- Captopril orally onset in 15-30 min and peak effect in 30-120 minutes, dose at q6h or q8h, shorter action than enalaprilat, so safer

Use of Nesiritide in HF

- Recombinant human BNP (hBNP) – activates guanylyl cyclase in target tissues increasing cGMP (not cAMP so not an inotrope and probably no increase in mortality)
- Natural BNP released by stretch of ventricles, counterregulatory to activation of sympathetic NS and RAAS
- Normal subjects BNP action: increase venous capacitance and decrease arterial tone (by decrease sympathetic stimulation, direct RAAS inhibition, direct arterial vasodilation)
- No tolerance like NTG but 25% unresponsive, 50% not improved in dyspnea
- Similar hypotension to IV NTG (4-5%) but longer
- Std dose is 2 µg/kg bolus and infusion start is 0.01 µg/kg/min infusion, with doses up to 0.015 and 0.030, usually limited by hypotension
- Not arrhythmogenic

Use of IV Inotropes in HF

- Not shown to improve clinically relevant endpoints, so only use when refractory to aggressive therapy with multiple drugs
- Inotropes are used because patients may be refractory to diuretics or vasodilators and have hypotension
- Milrinone and dobutamine give tachyarrhythmias, ischemia, hypotension
- If SBP<90 no milrinone or dobutamine, but dopamine

Use of Dobutamine in HF

- Stimulates β_1 and β_2 receptors in 3:1 ratio, upregulates adenylyl cyclase and increase cAMP, increasing systolic Calcium release from sarcoplasmic reticulum, increasing force of contraction and stroke volume
- Therapeutic effect attenuated by β -blockers
- Low dose mainly β_2 as vasodilator, higher more β_1 with increase afterload
- Start at 1-2 $\mu\text{g}/\text{kg}/\text{min}$ and titrate, dose may be limited by tachycardia
- Tolerance can develop due to downregulation of β receptors, so taper and then monitor 48 hours after d/c
- Dobutamine is associated with arrhythmia and other adverse outcomes in some studies

Use of PDE Inhibitors in HF

- Milrinone selective inhibitor of phosphodiesterase III (catalyzes breakdown of cAMP to AMP), increases availability of Calcium to actomyosin directly without β -receptor
- Reduction of afterload by arterial vasodilation and reduction of preload by increasing venous capacitance, also potent pulmonary vasodilator
- Hypotension is common and may be severe and sustained
- Renal clearance, half life 2.5 hr is increased to 6-8 hours in renal insufficiency
- Can be added to dobutamine
- No data showing improved outcomes (OPTIME-CHF)

Use of Levosimendan in HF

- Calcium-sensitizing agent increases sensitivity of troponin-C to calcium, but also PDE inhibitor
- Hemodynamically similar to milrinone: increase SV and decreases PVR and SVR and filling pressures from venodilation
- Can cause tachycardia and ventricular arrhythmias

Use of Dopamine in HF

- Endogenous catecholamine with selective renal and mesenteric vasodilation at doses $<3\mu\text{g}/\text{kg}/\text{min}$ via dopaminergic receptor (?)
- Use for pressure support
- More tachycardia and arrhythmia than dobutamine
- Increasing dose is positive inotrope via β_1 receptor
- Doses $7-10\mu\text{g}/\text{kg}/\text{min}$ is α -stimulant with increase afterload

Use of Vasopressin Receptor Blocking Agents in HF

- Arginine vasopressin causes
 - vasoconstriction via cAMP independent V_1 receptors
 - Renal water reabsorption via cAMP dependent V_2 receptors
- Blockade of these receptors might cause vasodilation and free water excretion
- Conivaptan IV (V_{1A} and V_2 blocker) reduced PAW and RA pressure, no change in BP or HR or SVR or PVR or C.O., diuresis did occur
- Tolvaptan oral (V_2 blocker) in a study resulted in increased urine output and increased Na especially in hyponatremia
- Not currently available

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