

College of Pharmacy
Fourth year. Clinical Pharmacy

Treatment of acute decompensated heart failure (ADHF)

General Approach

1-**Acute decompensated heart failure** involves patients with **new or worsening signs or symptoms** (often resulting from volume overload and/or low CO) **requiring medical intervention**, such as emergency department visit or hospitalization.

2-Admission to an **intensive care unit (ICU)** may be required if the patient experiences hemodynamic instability requiring frequent monitoring of vital signs, invasive hemodynamic monitoring, or rapid titration of IV medications with close monitoring.

3-**Symptoms of volume overload** include dyspnea, orthopnea, PND, ascites, GI symptoms (poor appetite, nausea, early satiety), peripheral edema, and weight gain. **Signs of volume overload include** pulmonary crackles, elevated jugular venous pressure, HJR, and peripheral edema.

4-**Low output symptoms** include altered mental status, fatigue, GI symptoms (similar to volume overload), and decreased urine output. **Low output signs** include tachycardia, hypotension (more commonly) or hypertension, cool extremities, pallor, and cachexia.

5-Ascertain hemodynamic status to guide initial therapy. Patients may be categorized into one of **four hemodynamic subsets** based on **volume status** (**euvolemic** or “dry” vs **volume overloaded** or “wet”) and **CO** (**adequate CO** or “warm” vs **hypoperfusion** or “cold”).

6-**If fluid retention** is evident on physical exam, **start aggressive diuresis**, preferably with IV diuretics.

7-In the absence of cardiogenic shock or symptomatic hypotension, strive to continue all GDMT for HF. **β-blockers may be temporarily held or dose reduced** if recent changes are responsible for acute decompensation.

8-Other GDMT (**ACE inhibitors, ARBs, ARNI, and aldosterone antagonists**) **may also need to be temporarily withheld in the presence of renal dysfunction**, with close monitoring of serum potassium.

9-Place all patients with congestive symptoms **on sodium restriction** (<2 g daily) and consider fluid restriction for refractory symptoms.

10-Consider **noninvasive ventilation** for patients in respiratory distress due to acute pulmonary edema.

11-**Provide pharmacologic thromboprophylaxis** with unfractionated heparin or low-molecular-weight heparin for most patients with limited mobility; **consider mechanical thromboprophylaxis** with intermittent pneumatic compression devices in patients at high risk for bleeding.

12-Temporary **mechanical circulatory support** (MCS) with an **intraaortic balloon pump (IABP)**, **ventricular assist device (VAD)**, or **extracorporeal membrane oxygenation**

(ECMO) may be considered for hemodynamic stabilization until the underlying etiology has been corrected or until definitive therapy (eg, cardiac transplantation).

13-Temporary device implantation is used for patients awaiting heart transplantation. Permanent device implantation is used in patients ineligible for heart transplantation.

14-**Cardiac transplantation** is the best option for patients with irreversible advanced HF. New surgical strategies such **myocardial cell transplantation** offer additional options for patients ineligible for device implantation or heart transplantation.

Pharmacologic Therapy for ADHF

A-Loop Diuretics

1-Current guidelines **recommend IV loop diuretics** (furosemide, bumetanide) as first-line therapy for **ADHF patients with volume overload**.

2-Bolus administration **reduces preload** by functional **venodilation** within 5–15 minutes and **later** (>20 minutes) **via sodium and water excretion**, thereby improving pulmonary congestion.

3-**Diuretic resistance may be improved** by administering larger IV **bolus** doses, transitioning from IV bolus to continuous IV **infusions**, or **adding a second diuretic** with a different mechanism of action, such as a distal tubule blocker (eg, oral metolazone, oral hydrochlorothiazide, or IV chlorothiazide).

B-Vasopressin Antagonists

1-Vasopressin receptor antagonists affect one or two AVP (**antidiuretic hormone**) receptors, V1A or V2. Stimulation of V1A receptors (located in vascular smooth muscle cells and myocardium) results in vasoconstriction, myocyte hypertrophy, coronary vasoconstriction, and positive inotropic effects. V2 receptors are located in renal tubules, where they regulate water reabsorption.

- Tolvaptan** selectively binds to and inhibits the V2 receptor. It is an oral agent indicated for hypervolemic and euvolemic **hyponatremia in patients with HF**.

- Conivaptan** nonselectively inhibits both the V1A and V2 receptors. It is an IV agent indicated for hypervolemic and euvolemic hyponatremia due to a variety of causes but is not indicated for patients with HF.

2-**Monitor patients** closely to avoid an **excessively rapid rise in serum sodium** requiring drug discontinuation.

3-**The role of vasopressin receptor antagonists in the long-term management of HF is unclear. Results of studies do not support routine use of tolvaptan in ADHF and it should be reserved for managing severe hyponatremia.**

C-Vasodilators

1-**Venodilators reduce preload** by increasing venous capacitance, and improve symptoms of pulmonary congestion. **Arterial vasodilators decrease afterload and causing increased CO. Mixed vasodilators** act on both arterial resistance and venous capacitance vessels, **reducing congestive symptoms while increasing CO.**

2-IV **vasodilators should be considered before positive inotropic** therapy in patients with low CO and elevated SVR. However, **hypotension may preclude their use in patients with preexisting low BP or SVR.**

3-IV **nitroglycerin is often preferred for preload reduction in ADHF**, especially in patients with pulmonary congestion. Nitroglycerin displays potent coronary vasodilating properties making it the vasodilator of choice for patients with severe HF and ischemic heart disease.

- **Hypotension and excessive decrease in pulmonary capillary wedge pressure (PCWP) are important dose-limiting side effects.** Tolerance to the hemodynamic effects may develop over 12–72 hours of continuous administration.

6-**Sodium nitroprusside is a mixed arteriovenous vasodilator.** **Hypotension** is an important dose-limiting adverse effect of nitroprusside, and its use should be primarily reserved **for patients with elevated SVR.**

- **Nitroprusside-induced cyanide and thiocyanate toxicity** are unlikely at low dose and short duration except in patients with significant renal impairment

D-Inotropes

1-Prompt correction of low CO in patients with “cold” subsets (III and IV) is required to **restore peripheral tissue perfusion and preserve end-organ function.**

2-Although IV inotropes can improve hypoperfusion by enhancing cardiac contractility, potential adverse outcomes limit their use to select patients with refractory ADHF.

3-**Inotropes should be considered only as a temporizing measure to maintain end-organ perfusion** in patients with cardiogenic shock or severely depressed CO and low systolic BP (ie, ineligible for IV vasodilators).

- Dobutamine is a β 1- and β 2-receptor agonist with some α 1-agonist effects; its positive inotropic effects are due to effects on β 1-receptors. Cardiac Index (CI) is increased because of inotropic stimulation, arterial vasodilation, and a variable increase in HR. **It causes relatively little change in mean arterial pressure (MAP).** Dobutamine should be considered over milrinone when a significant decrease in MAP might further compromise hemodynamic function. Dobutamine’s major **adverse effects are tachycardia and ventricular arrhythmias.**

- Milrinone inhibits phosphodiesterase III and produces positive inotropic and arterial and venous vasodilating effects (an **inodilator**). It has supplanted use of amrinone, which has a higher rate of thrombocytopenia.

- Milrinone also lowers pulmonary PCWP by venodilation and **is particularly useful in patients with a low CI and elevated LV filling pressure.** Use milrinone cautiously in severely hypotensive HF patients because it does not increase, and may even decrease, arterial BP.

5-**Norepinephrine** (stimulates α 1- and β 1-adrenergic receptors) and **dopamine** [endogenous precursor of norepinephrine that stimulates α 1, β 1, β 2, and D1 (vascular dopaminergic) receptors) have combined inotropic and vasopressor activity.

- Although therapies that increase SVR are generally avoided in ADHF, they may be **required in select patients where marked hypotension precludes use of traditional inotropes** (eg, septic shock, refractory cardiogenic shock).

Evaluation of therapeutic outcomes

Chronic Heart Failure

1-Ask patients about the **presence and severity of symptoms** and how symptoms affect daily activities.

2-**Evaluate efficacy of diuretic treatment** by disappearance of the signs and symptoms of excess fluid retention. Focus the physical examination on **body weight**, extent of JVD, and presence and severity of pulmonary congestion (crackles, dyspnea on exertion, orthopnea, and PND) and peripheral edema.

3-**Other outcomes** are improvement in exercise tolerance and fatigue, decreased nocturia, and decreased HR.

4-**Monitor BP** to ensure that symptomatic hypotension does not develop as a result of drug therapy.

5-**Body weight** is a sensitive marker of fluid loss or retention, and patients should weigh themselves daily and report changes of (1.4–2.3 kg) to their healthcare provider so adjustments can be made in diuretic doses.

6-**Symptoms may worsen initially on β -blocker therapy**, and it may take weeks to months before patients notice symptomatic improvement.

7-**Routine monitoring** of serum electrolytes (especially potassium and magnesium) and renal function (BUN, serum creatinine, eGFR) is mandatory in patients with HF.

Acute Decompensated Heart Failure

1-**Assess the efficacy of drug therapy with daily** monitoring of weight, strict fluid intake and output measurements, and HF signs/symptoms.

2-**Monitor frequently for** electrolyte depletion, symptomatic hypotension, and renal dysfunction. Assess vital signs frequently throughout the day.

3-**Optimize GDMT in hemodynamically stable patients without contraindications**, including reinitiation of therapies withheld earlier in the admission.

Reference

Joseph T. DiPiro, Robert L. Pharmacotherapy: A Pathophysiologic Approach, 11th Edition. 2021.