Treatment of acute decompensated heart failure: Components of therapy

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**INTRODUCTION** — Acute decompensated heart failure (ADHF) is a common and potentially fatal cause of acute respiratory distress. The clinical syndrome is characterized by the development of dyspnea, generally associated with rapid accumulation of fluid within the lung's interstitial and alveolar spaces, which is the result of acutely elevated cardiac filling pressures (cardiogenic pulmonary edema) [1]. ADHF can also present as elevated left ventricular filling pressures and dyspnea without pulmonary edema.

ADHF is most commonly due to left ventricular (LV) systolic or diastolic dysfunction, with or without additional cardiac pathology, such as coronary artery disease or valve abnormalities. However, a variety of conditions or events can cause cardiogenic pulmonary edema due to an elevated pulmonary capillary wedge pressure in the absence of heart disease, including primary fluid overload (eg, due to blood transfusion), severe hypertension, particularly renovascular hypertension, and severe renal disease.

The components of therapy of ADHF in patients with and without acute myocardial infarction (MI) will be reviewed here. A table to assist with emergency management of ADHF is provided (table 1). General considerations for treatment of ADHF and the pathophysiology and evaluation of patients with ADHF are presented separately. (See "Treatment of acute decompensated heart failure: General considerations" and "Evaluation of acute decompensated heart failure".)

Treatment of ADHF and cardiogenic shock in the setting of acute coronary syndrome is discussed separately. Management of right ventricular MI, which typically presents with hypotension and clear lungs, is also discussed separately. (See "Treatment of acute decompensated heart failure in acute coronary syndromes" and "Prognosis and treatment of cardiogenic shock complicating acute myocardial infarction" and "Right ventricular myocardial infarction".)

**INITIAL STABILIZATION** — Patients presenting with acute dyspnea from ADHF should be rapidly assessed and stabilized. A table to assist with emergency management of ADHF is provided (table 1). Stabilization measures include:

- Airway assessment to assure adequate oxygenation and ventilation, including continuous pulse oximetry
- Vital signs assessment with attention to hypotension or hypertension
- Continuous cardiac monitoring
- Intravenous access
- Seated posture
- Diuretic therapy
- Vasodilator therapy
Urine output monitoring (perhaps with urethral catheter placement)

Following airway and oxygenation assessment, initial stabilization includes the initiation of therapies aimed at the rapid correction of hemodynamic and intravascular volume abnormalities. The mainstay of therapy for these abnormalities in the acute setting is vasodilator and diuretic therapy. The aggressiveness of each depends on the patient's hemodynamic and volume status. Patients with flash pulmonary edema due to hypertension, for instance, require aggressive vasodilatory therapy. Patients with normotension and volume overload best respond to a combination of diuretic therapy and vasodilators. Patients with hypotension and intravascular overload cannot tolerate vasodilators, and may respond either to diuretics alone or in combination with inotropes. It is important to tailor the therapy to the individual patient. (See 'Inotropic agents' below and 'Mechanical cardiac assistance' below and "Prognosis and treatment of cardiogenic shock complicating acute myocardial infarction" and "Overview of mechanical ventilation").

**Supplemental oxygen and assisted ventilation** — Supplemental oxygen therapy and assisted ventilation should be provided as needed. The 2009 focused update of the 2005 ACC/AHA guidelines recommend oxygen therapy to relieve symptoms related to hypoxemia. The 2010 HFSA guidelines note that routine administration of supplemental oxygen in the absence of hypoxia is NOT recommended [2].

For patients requiring supplemental oxygen, we suggest initial therapies in the following order:

- Non-rebreather face mask delivering high-flow percent oxygen.
- If respiratory distress, respiratory acidosis, and/or hypoxia persist, we suggest noninvasive positive pressure ventilation (NPPV) as the preferred initial modality of assisted ventilation as long as the patient does not have a contraindication (table 2).

This approach is supported by evidence from meta-analyses and randomized trials in patients with cardiogenic pulmonary edema indicating that NPPV decreases the need for intubation and improves respiratory parameters, such as dyspnea, hypercapnia, acidosis, and heart rate. NPPV may be particularly beneficial in patients with hypercapnia. These issues and conflicting data on a possible impact on mortality are discussed in detail separately. (See "Noninvasive positive pressure ventilation in acute respiratory failure in adults", section on 'Cardiogenic pulmonary edema'.)

- Patients with respiratory failure who fail NPPV, or do not tolerate or have contraindications to NPPV (table 2) should be intubated for conventional mechanical ventilation. In such patients, positive end-expiratory pressure is often useful to improve oxygenation. (See "Overview of mechanical ventilation" and "Positive end-expiratory pressure (PEEP)").

Once initial therapy has begun, oxygen supplementation can be titrated in order to keep the patient comfortable and arterial oxygen saturation above 90 percent.

**Diuretics** — Patients with ADHF are usually volume overloaded. Even in the less common situation in which cardiogenic pulmonary edema develops without significant volume overload (eg, with hypertensive emergency, acute aortic or mitral valvular insufficiency), fluid removal with intravenous diuretics can relieve symptoms and improve oxygenation.

Limited clinical trial data have shown a mortality benefit from diuretic therapy in patients with chronic HF. (See "Use of diuretics in patients with heart failure", section on 'Efficacy and safety'.) Although the safety and efficacy of diuretics to treat ADHF have not been established in randomized trials, extensive observational experience has demonstrated that they effectively relieve congestive symptoms [3].

Patients with ADHF and evidence of volume overload, regardless of etiology, should be treated
with intravenous diuretics as part of their initial therapy [2,4,5]. Rare exceptions include patients with severe hypotension or cardiogenic shock. In such cases, the underlying cause for hemodynamic instability should be sought and the patient may require hemodynamic and mechanical ventilatory support. Patients with aortic stenosis with volume overload should be diuresed with caution. As noted in the 2009 focused update of the 2005 ACC/AHA HF guidelines, patients admitted with significant fluid overload should receive diuretic therapy without delay in the emergency department or outpatient clinic as early intervention may produce better outcomes [4].

Intravenous rather than oral administration is recommended because of greater and more consistent drug bioavailability.

**Diuretic dosing** — Common initial intravenous doses of loop diuretics in patients with normal renal function include the following:

- **Furosemide** — 40 mg intravenously
- **Bumetanide** — 1 mg intravenously
- **Torsemide** — 10 to 20 mg intravenously

Diuretic dosing should be individualized and titrated according to response and patient status. Patients who are treated with loop diuretics chronically are usually treated with a higher dose in the acute setting; the intravenous dose should be equal to or greater than (eq, 2.5 times) their maintenance oral dose (eg, an intravenous furosemide dose of 40 to 100 mg for a patient who had been taking 40 mg orally per day) [4]. In the DOSE trial of intravenous furosemide in patients with ADHF, there was an almost significant trend toward greater improvement in patients’ global assessment of symptoms in the high dose (2.5 times the patients’ prior dose) group compared to the low dose (equal the prior dose) group as discussed below [6].

Peak diuresis typically occurs 30 minutes after administration. Most patients will require additional diuresis through the course of their care. Diuretic administration two or more times per day may be necessary.

No single intravenous dosing regimen (bolus versus continuous infusion; high dose versus lower dose) has been shown to be superior to others as illustrated by the following observations:

- A meta-analysis of seven trials with a total of 221 patients with ADHF suggested that continuous infusion of a loop diuretic slightly increased the urine output (by a mean of 271 mL/day) compared to intermittent bolus injections [7]. Less tinnitus and hearing loss occurred with continuous infusion. However, the studies were small and heterogeneous and the results were largely driven by the largest trial (107 patients) in which hypertonic saline was administered only to the patients receiving continuous infusion of diuretic.

- The best data come from the DOSE trial, published after the meta-analysis [6]. The trial randomly assigned 308 patients to receive furosemide administered intravenously via either a bolus every 12 hours or continuous infusion and at either a low dose (equivalent to the patient’s previous oral dose) or a high dose (2.5 times the previous oral dose). The efficacy endpoint was the patients’ global assessment of symptoms over the course of 72 hours and the safety endpoint was change in serum creatinine from baseline to 72 hours. Worsening renal function was defined as increase in the serum creatinine >0.3 mg/dL [>26.5 micromol/L] at any time during the 72 hours after randomization.

The following findings were noted:

There was no significant difference in efficacy or safety endpoints for bolus versus continuous infusion. Patients assigned to intravenous bolus therapy were more likely to require a dose increase at 48 hours; as a result, the total dose of furosemide over 72 hours was higher in the bolus group compared with the continuous infusion group, a
difference that was almost statistically different (592 versus 480 mg, \( p = 0.06 \)).

High-dose \textit{furosemide}, compared with low-dose furosemide, produced greater net fluid loss, weight loss, and relief from dyspnea but also more frequent transient worsening of renal function (23 versus 14 percent). There was an almost significant trend toward greater improvement in patients’ global assessment of symptoms in the high-dose group (\( p = 0.06 \)); the mean change in the serum creatinine was less than 0.1 mg/dL (9 micromol/L) in both groups.

In summary, the available data suggest that intravenous continuous infusion and bolus loop diuretic therapy have similar efficacy in patients with ADHF.

Later transition from intravenous to oral diuretics should be made with careful attention to HF status, supine and upright hypotension, renal function and electrolytes [4].

**Monitoring** — Volume status, evidence of congestion, daily weights, intake, and output should be continually reassessed. Monitoring should also include watching for and guarding against side effects (including worsening renal function, electrolyte abnormalities (with associated arrhythmia risk), and symptomatic hypotension). Diuretic therapy can also precipitate attacks of gout. (See "Loop diuretics: Maximum effective dose and major side effects" and "Diuretic-induced hyperuricemia and gout".)

Serum potassium and magnesium levels should be monitored at least daily, and more frequent monitoring is indicated when diuresis is rapid. Severe muscle cramps may occur with overly rapid diuresis and should be treated with potassium repletion if indicated [2].

**Hemodynamic effects** — By reducing intravascular volume, diuresis will eventually lower central venous and pulmonary capillary wedge pressures. In addition, \textit{furosemide} and possibly other loop diuretics also have an initial \textit{morphine}-like effect in acute pulmonary edema, causing venodilation that can decrease pulmonary congestion prior to the onset of diuresis [8]. This effect appears to be mediated by enhanced release of prostaglandins. (See "Use of diuretics in patients with heart failure", section on 'Venodilatory effect in acute pulmonary edema'.)

Reductions in right and left heart filling pressures with diuresis are frequently associated with augmented forward stroke volume and cardiac output related to decreases in functional tricuspid and mitral regurgitation and reduction in right ventricular volume with relief of left ventricular compression and improved left ventricular distensibility [2].

However, during diuresis some patients experience symptomatic hypotension with decreasing cardiac output and systemic blood pressure due to a lag in reequilibration of intravascular volume via movement of fluid from the interstitial space. Patients with HF with preserved LV ejection fraction (LVEF) or restrictive physiology may be more sensitive to diuresis-induced reductions in preload. Diuretics may enhance the hypotensive effects of ACE inhibitor or angiotensin receptor blocker (ARB) therapy even when volume overload persists. Careful monitoring during diuresis is required to prevent adverse hemodynamic effects.

**Effects on renal function** — The blood urea nitrogen (BUN) and serum creatinine often rise during diuretic treatment of ADHF and careful monitoring is recommended. In the absence of other causes for an elevated BUN, a disproportionate rise in BUN relative to serum creatinine (BUN/serum creatinine ratio >20:1) suggests a prerenal state with increased passive reabsorption of urea. An initial rise in BUN may be accompanied by a stable serum creatinine, reflecting preserved glomerular filtration rate (GFR). Further elevations in BUN along with a rise in serum creatinine are likely if diuresis is continued in such patients. (See "Etiology and diagnosis of acute tubular necrosis and prerenal disease", section on 'BUN/plasma creatinine ratio'.)

An otherwise unexplained rise in serum creatinine, which reflects a reduction in GFR, may be a marker of reduced perfusion to the kidney and other organs. Patients in whom this occurs before euvoletic status is achieved have a worse prognosis. Nevertheless, fluid removal may still be required to treat signs and symptoms of congestion, particularly pulmonary edema. On the other
hand, a stable serum creatinine suggests that perfusion to the kidneys (and therefore to other organs) is being well maintained and that the diuresis can be continued if the patient is still edematous. (See "Cardiorenal syndrome: Definition, prevalence, diagnosis, and pathophysiology", section on 'Reduced renal perfusion' and "Cardiorenal syndrome: Prognosis and treatment", section on 'Change in GFR during therapy for HF'.) Changes in cardiac output and the consequent changes in renal perfusion is not the only determinant of changes in GFR in patients with HF. Among patients with an elevated central venous pressure, the associated increase in renal venous pressure can reduce the GFR, while lowering venous pressure with diuretics and other therapies might therefore increase the GFR. (See "Cardiorenal syndrome: Definition, prevalence, diagnosis, and pathophysiology".)

Guidelines for management of patients with ADHF with elevated or rising BUN and/or serum creatinine include the following [2]:

- Other potential causes of kidney injury (eg, use of nephrotoxic medications, urinary obstruction) should be evaluated and addressed.

- Patients with severe symptoms or signs of congestion, particularly pulmonary edema, require continued fluid removal independent of changes in GFR. In the presence of elevated central venous pressure, renal function may improve with diuresis. (See "Cardiorenal syndrome: Definition, prevalence, diagnosis, and pathophysiology", section on 'Increased renal venous pressure'.)

- If the BUN rises and the serum creatinine is stable or increases minimally, and the patient is still fluid overloaded, the diuresis can be continued to achieve the goal of eliminating clinical evidence of fluid retention with careful monitoring of renal function. (See "Use of diuretics in patients with heart failure", section on 'Goals of therapy'.)

- If increases in serum creatinine appear to reflect intravascular volume depletion, then reduction in or temporary discontinuation of diuretic and/or ACE inhibitor/ARB therapy should be considered. Adjunctive inotropic therapy may be required. (See 'Inotropic agents' below.)

- If substantial congestion persists and adequate diuresis cannot be achieved, then ultrafiltration or dialysis should be considered. (See 'Ultrafiltration' below and 'Renal replacement therapy (dialysis) in acute kidney injury (acute renal failure) in adults: Indications, timing, and dialysis dose", section on 'Indications for and timing of initiation of dialysis'.)

  **Inadequate response to diuretic therapy** — Some patients with ADHF do not respond adequately to initial loop diuretic therapy [2,4]. These patients should be re-evaluated for congestion. The approach to patients with refractory edema is discussed in detail elsewhere. (See "Treatment of refractory edema in adults".)

  Summarized briefly:

- Sodium intake should be restricted to a limit of <2 g daily [2]. Water restriction is also warranted in patients with hyponatremia. (See 'Sodium and fluid restriction' below.)

- Doubling the diuretic dose until diuresis ensues or the maximum recommended dose is reached. (See "Loop diuretics: Maximum effective dose and major side effects", section on 'Maximum effective dose'.)

- Addition of a second diuretic to potentiate the effects of the loop diuretic. The HFSA and ACC/AHA guidelines recommend oral metolazone or spironolactone or intravenous chlorothiazide as the second diuretic agent to add when diuretic response is inadequate [2,4].
Chlorothiazide is the only thiazide diuretic that can be given intravenously (500 to 1000 mg/day). However, the availability of this preparation may be limited. An oral thiazide, such as hydrochlorothiazide (25 to 50 mg twice daily) or metolazone (which has the advantage of once daily dosing) is an alternative for acute therapy and can be given chronically. Although it has been suggested that metolazone is the thiazide of choice in refractory patients with advanced renal failure (GFR below 20 mL/min), there is at present no convincing evidence that metolazone has unique efficacy among the thiazides when comparable doses are given. (See "Treatment of refractory edema in adults", section on 'Enhanced tubular sodium reabsorption'.)

Addition of an aldosterone antagonist (spironolactone or eplerenone) is recommended in selected patients with systolic HF to improve survival. In addition, the associated reduction in collecting tubule sodium reabsorption and potassium secretion can both enhance the diuresis and minimize the degree of potassium wasting. Thus, if not already being given, it is reasonable to initiate aldosterone antagonist therapy prior to the addition of a thiazide diuretic in patients with a low or low-normal serum potassium on loop diuretic therapy alone. Aldosterone antagonist therapy should be continued following hospital discharge only in patients who can be carefully monitored for hyperkalemia. When given for diuresis or potassium sparing effects, a higher dose (up to 100 mg daily) than the usual heart failure dose may be needed. (See "Treatment of refractory edema in adults", section on 'Enhanced tubular sodium reabsorption' and 'Aldosterone antagonist therapy' below.)

If these modalities are not sufficiently effective, ultrafiltration may be considered. (See 'Ultrafiltration' below.)

Sodium and fluid restriction — Dietary sodium restriction is an important component of therapy to restore euvolemia, and greater restriction may be feasible in hospital than in the outpatient setting. The Heart Failure Society of America (HFSA) guidelines on acute decompensated heart failure (ADHF) recommend a low-sodium diet (2 g daily) and consideration of stricter sodium restriction in patients with recurrent or refractory volume overload [2].

Hyponatremia is common among HF patients and the degree of reduction in serum sodium parallels the severity of the heart failure. As a result, a low serum sodium is an adverse prognostic indicator. (See "Hyponatremia in patients with heart failure", section on 'Predictor of adverse prognosis'.)

Most HF patients with hyponatremia have volume overload, rather than volume depletion. The HFSA guidelines recommend fluid restriction (<2 L/day) in HF patients with moderate hyponatremia (serum sodium <130 meq/L) and volume overload and suggest that fluid restriction should be considered to assist in treatment of fluid overload in other patients [2]. Stricter fluid restriction may be considered in patients with severe (serum sodium <125 meq/L) or worsening hyponatremia, although patient tolerance of strict fluid restriction may be limited. (See "Hyponatremia in patients with heart failure", section on 'Treatment'.)

Vasodilator therapy — In patients without hypotension with severely symptomatic fluid overload, vasodilators such as intravenous nitroglycerin, nitroprusside, or nesiritide can be beneficial when added to diuretics or in those who do not respond to diuretics alone [4]. Patients with systemic hypertension may require more aggressive vasodilator therapy (eg, up-titration of nitroglycerin) to assure more rapid reversal of dyspnea.

The 2010 HFSA guidelines provide the following recommendations for use of vasodilators [2]:

- Intravenous vasodilators (nitroglycerin or nitroprusside) and diuretics are recommended for rapid symptom relief in patients with acute pulmonary edema or severe hypertension.
In the absence of symptomatic hypotension, intravenous nitroglycerin, nitroprusside or nesiritide may be considered as an addition to diuretic therapy for rapid improvement of congestive symptoms in patients admitted with ADHF.

Frequent blood pressure monitoring is recommended with vasodilator agents. Dosage of these agents should be decreased if symptomatic hypotension develops. Once symptomatic hypotension is resolved, reintroduction and titration may be considered.

Intravenous nitroprusside, nitroglycerin or nesiritide may be considered in patients with ADHF and advanced HF who have persistent severe HF despite aggressive treatment with diuretics and standard oral therapies.

**Nitroglycerin** — Nitrates are the most commonly used vasodilators. In patients without symptomatic hypotension, intravenous nitroglycerin added to diuretic therapy may contribute to rapid improvement in congestive symptoms [2,4]. Nitroglycerin reduces LV filling pressure primarily via venodilation. At higher doses the drug variably lowers systemic afterload and increases stroke volume and cardiac output.

The benefit of nitrate therapy was illustrated by a study in which 110 patients were randomly assigned to a combination of either high dose intravenous isosorbide dinitrate plus low dose intravenous furosemide or low dose isosorbide dinitrate plus high dose furosemide [9]. Patients receiving the high dose isosorbide dinitrate and low dose furosemide combination had a significantly lower combined risk of myocardial infarction, requirement for mechanical ventilation or death than those treated with the high dose diuretic and low dose isosorbide regimen.

Tachyphylaxis can occur within hours with administration of high doses of nitroglycerin and the strategy of nitrate-free interval used to reduce tolerance during chronic therapy could result in adverse hemodynamic effects in patients with ADHF. Potential adverse effects of nitroglycerin include hypotension and headache. Nitrate administration is contraindicated after use of PDE-5 inhibitors such as sildenafil. (See “Sexual activity in patients with heart disease”, section on ‘Adverse interaction with nitrates’.)

In patients with ADHF, we recommend intravenous rather than transdermal (ointment or patch) or oral nitrate administration for greater speed and reliability of delivery and ease of titration. An initial dose of 5 to 10 mcg/min of intravenous nitroglycerin is recommended with the dose increased in increments of 5 to 10 mcg/min every 3 to 5 minutes as required and tolerated (dose range 10 to 200 mcg/min).

Similar benefits have been described with high-dose intravenous isosorbide dinitrate, where available [9,10]. However, if hypotension occurs, the longer half-life of isosorbide dinitrate compared to intravenous nitroglycerin (four hours versus three to five minutes) is a major disadvantage.

**Nitroprusside** — Nitroprusside is a potent vasodilator with balanced venous and arteriolar effects producing rapid reduction in pulmonary capillary wedge pressure and increase in cardiac output. A need for pronounced afterload reduction is an indication for nitroprusside (initial dose 5 to 10 mcg/min, dose titrated up to every 5 minutes, dose range 5 to 400 mcg/min) as opposed to nitroglycerin [11]. Examples of such settings include hypertensive emergency, acute aortic regurgitation, acute mitral regurgitation, or acute ventricular septal rupture. The dose is generally titrated to maintain a systolic blood pressure >90 mmHg or mean arterial pressure > 65 mmHg. (See "Drug treatment of hypertensive emergencies", section on 'Nitroprusside'.)

The major limitation to the use of nitroprusside is its metabolism to cyanide. The accumulation of nitroprusside metabolites can lead to the development of cyanide, or rarely thiocyanate, toxicity which may be fatal. Doses above 400 mcg/min generally do not provide greater benefit and may increase the risk of thiocyanate toxicity. Nitroprusside administration requires close and continuous blood pressure monitoring, and may cause reflex tachycardia. Another potential risk is...
Nesiritide — The largest randomized trial of nesiritide in patients with acute HF, ASCEND-HF, found that nesiritide increased rates of hypotension, did not alter rates of death or rehospitalization at 30 days, and showed a borderline significant trend toward reducing dyspnea. There was no change in risk of worsening renal function [13]. (See "Nesiritide in the treatment of acute decompensated heart failure").

For most patients hospitalized with acute heart failure (HF), we recommend not treating with nesiritide. In carefully selected patients with appropriate hemodynamics (without hypotension or cardiogenic shock) who remain symptomatic despite routine therapy, a trial of nesiritide may be helpful as an alternative to other vasodilator therapy (nitroglycerin or nitroprusside). Nesiritide has a longer effective half-life than nitroglycerin or nitroprusside, so side effects such as hypotension may persist longer. (See "Nesiritide in the treatment of acute decompensated heart failure", section on 'Use'.)

Nesiritide is typically given as an initial intravenous bolus of 2 mcg/kg, followed by a continuous infusion of 0.01 mcg/kg per minute, with subsequent dose adjustment as necessary. Close monitoring of hemodynamics, urine output, and renal function are necessary for effective clinical use and safety.

ADDITIONAL THERAPY

ACE inhibitors and ARBs — For patients with HF due to systolic dysfunction, ACE inhibitors or angiotensin receptor blockers (ARBs) are a mainstay of chronic therapy. (See "ACE inhibitors in heart failure due to systolic dysfunction: Therapeutic use" and "Angiotensin II receptor blockers in heart failure due to systolic dysfunction: Therapeutic use".)

Among patients with ADHF, the role of angiotensin inhibition depends upon whether the patient is already receiving such therapy.

Continued therapy — For the majority of patients with systolic dysfunction who have been treated with chronic ACE inhibitor or ARB therapy, maintenance oral therapy can be cautiously continued during an episode of ADHF in the absence of hemodynamic instability or contraindications [4]. These medications should be decreased or discontinued in the following settings:

- Hypotension
- Acute renal failure
- Hyperkalemia

With regard to hypotension, two additional points should be considered:

- Some patients with chronic HF and severe left ventricular systolic dysfunction tolerate relatively low blood pressures (eg, systolic blood pressure 90 to 100 mmHg). Such patients often tolerate chronic ACE inhibitor or ARB therapy and may tolerate these drugs in the acute setting as well.

- Patients with acute pulmonary edema may initially be hypertensive due to high catecholamine levels during the early period of distress. With initial therapy, blood pressure may fall rapidly and patients may become relatively hypotensive, particularly if they are aggressively diuresed. Thus, long-acting drugs, such as ACE inhibitors and ARBs, should be administered with caution the first few hours of hospitalization.

Initiation of therapy — Although some have advocated early use of ACE inhibitor in patients with acute decompensated heart failure, we do not recommend this approach. There are limited data on the safety and efficacy of initiating new ACE inhibitor or ARB therapy in the early phase of therapy of ADHF (ie, the first 12 to 24 hours) [14].
Major concerns with early therapy include:

- Patients with ADHF may develop hypotension and/or worsening renal function during initial therapy. Determining the pathogenesis of such complications is more difficult if an ACE inhibitor or ARB has been given. Hypotension following administration of these agents may be prolonged given the long effective half-lives of these agents.

- The intravenous ACE inhibitor enalaprilat may have deleterious effects in patients with an acute myocardial infarction, especially when complicated by HF or aggressive diuresis [15,16].

Thus, intravenous enalaprilat should be avoided in patients with an acute myocardial infarction and probably in all patients with HF [14,16]. Early initiation of oral ACE inhibitor therapy is also not recommended (except for those with acute infarction), and should be avoided in patients at high risk for hypotension (eg, low baseline blood pressure or hyponatremia, which is a marker for increased activation of the renin-angiotensin system and therefore increased dependence upon angiotensin II for blood pressure maintenance). In addition, the aggressive diuretic therapy typically given for acute pulmonary edema may increase sensitivity to ACE inhibition or angiotensin blockade, including risks of hypotension and renal dysfunction. (See "Angiotensin converting enzyme inhibitors and receptor blockers in acute myocardial infarction: Recommendations for use" and "Pathophysiology of heart failure: Neurohumoral adaptations" and "Hyponatremia in patients with heart failure".)

Once the patient is stable, chronic oral therapy with ACE inhibitor or ARB can be started. Initiation of these therapies known to improve outcomes is recommended in stable patients with systolic dysfunction prior to hospital discharge [4]. (See "ACE inhibitors in heart failure due to systolic dysfunction: Therapeutic use" and "Angiotensin II receptor blockers in heart failure due to systolic dysfunction: Therapeutic use".)

**Inotropic agents** — The intravenous inotropic agents such as dobutamine and/or milrinone may be helpful in selected patients with severe LV systolic dysfunction and low output syndrome (diminished peripheral perfusion and end-organ dysfunction) for whom treatment may be limited by marginal systemic blood pressure or inadequate response to vasodilator and diuretic therapy [17,18].

As recommended in the 2009 ACC/AHA focused update, for patients with evidence of hypotension associated with hypoperfusion AND obvious evidence of elevated cardiac filling pressures (eg, elevated jugular venous pressure or elevated pulmonary artery wedge pressure), intravenous inotropic or vasopressor drugs are recommended to maintain systemic perfusion and preserve end-organ function while more definitive treatment is considered [4]. However, the usefulness of intravenous inotropic drugs to maintain systemic perfusion and preserve end-organ performance is uncertain for patients with severe systolic dysfunction, low blood pressure and evidence of low cardiac output.

Similarly, the 2010 HFSA guidelines for ADHF include the following recommendations for use of inotropes [2]:

- Intravenous inotropes (milrinone or dobutamine) may be considered to relieve symptoms and improve end-organ function in patients with advanced HF characterized by LV dilation, reduced LVEF, and diminished peripheral perfusion or end-organ dysfunction (low output syndrome), particularly if these patients have marginal systolic blood pressure (<90 mmHg), have symptomatic hypotension despite adequate filling pressure, or are unresponsive to, or intolerant of, intravenous vasodilators.

- Intravenous inotropes may be considered in similar patients (ie, patients with depressed systolic function and marginal cardiac output) with evidence of fluid overload if they...
When adjunctive therapy is needed in other patients with ADHF (eg, patients with preserved cardiac output), administration of vasodilators should be considered instead of intravenous inotropes.

Intravenous inotropes are not recommended unless left heart filling pressures are known to be elevated or cardiac index is severely impaired based on direct measurement or clear clinical signs.

Administration of intravenous inotropes (milrinone or dobutamine) in the setting of ADHF should be accompanied by continuous or frequent blood pressure monitoring and continuous monitoring of cardiac rhythm.

If symptomatic hypotension or worsening tachyarrhythmias develop during administration of these agents, discontinuation or dose reduction should be considered.

Inotropes are not indicated for treatment of ADHF in the setting of preserved systolic function.

**Adverse effects** — There is concern that inotropic agents may adversely impact outcomes in patients with ADHF with congestion without a low output state [19,20]. Inotropic agents may increase heart rate and myocardial oxygen consumption and thus provoke ischemia and potentially damage hibernating but viable myocardium, particularly in patients with ischemic heart disease. In addition, inotropic agents can increase atrial [19] and ventricular [21] arrhythmias. Given these concerns, careful patient selection is required for inotrope use. (See "Inotropic agents in heart failure due to systolic dysfunction", section on 'Intravenous therapy' and "Use of vasopressors and inotropes").

Routine use of inotropes in patients hospitalized for heart failure was found to be harmful in the OPTIME-CHF trial [19]. In this trial, 949 patients admitted to the hospital with an acute exacerbation of chronic HF were randomly assigned to a 48 to 72 hour infusion of milrinone or placebo. Milrinone therapy was associated with significant increases in hypotension requiring intervention and atrial arrhythmias, and with nonsignificant increases in mortality in-hospital (3.8 versus 2.3 percent) and at 60 days (10.3 versus 8.9 percent). This trial did not evaluate patients whose treating physicians felt could not be randomized, but demonstrates overall adverse effects in noncritical patients despite improved symptoms.

The general role of inotropic agents in patients with heart failure is discussed separately. (See "Inotropic agents in heart failure due to systolic dysfunction", section on 'Intravenous therapy'.)

**Specific agents** — The 2010 HFSA guidelines advised careful titration of either of the following inotropes when used in highly selected patients with ADHF [2]:

- **Milrinone** — Milrinone is a phosphodiesterase inhibitor that increases myocardial inotropy by inhibiting degradation of cyclic AMP. Other direct effects of milrinone include reducing systemic and pulmonary vascular resistance (via inhibition of peripheral phosphodiesterase) and improving left ventricular diastolic compliance [22,23]. These changes lead to an increase in cardiac index and decrease in left ventricular afterload and filling pressures. Patients should receive a loading dose of 50 mcg/kg over 10 minutes, followed by a maintenance dose of 0.375 to a maximum of 0.750 mcg/kg per min. Dose adjustment is required in the presence of renal insufficiency, hypotension, or arrhythmias.

- **Dobutamine** — Dobutamine acts primarily on beta-1 adrenergic receptors, with minimal effects on beta-2 and alpha-1 receptors. The hemodynamic effects of dobutamine include increase in stroke volume, and cardiac output, and modest decreases in systemic vascular resistance and pulmonary capillary wedge pressure [24,25]. The 2004 ACC/AHA STEMI guidelines suggest using dobutamine in patients with hypotension who do not have clinical evidence of shock [16]. It should be started at 2.5 mcg/kg per min and, if tolerated and
needed, can be gradually increased to 15 mcg/kg per min.

Since milrinone does not act via beta receptors, its effects are not as diminished as those of dobutamine by concomitant beta blocker therapy. (See "Use of beta blockers in heart failure due to systolic dysfunction", section on 'Combination with dobutamine'.)

Use of dopamine is discussed separately. (See "Treatment of acute decompensated heart failure in acute coronary syndromes", section on 'Inotropic agents'.)

**Beta blockers** — Beta blockers reduce mortality when used in the long-term management of such patients, but must be used cautiously in patients with decompensated HF with systolic dysfunction because of the potential to worsen acute HF due to systolic dysfunction. (See "Use of beta blockers in heart failure due to systolic dysfunction").

Thus, in patients with systolic dysfunction and ADHF, we approach the use of beta blockers in the following manner:

- For patients on chronic beta blocker therapy, if the degree of decompensation is mild without hypotension or evidence of hypoperfusion, continuation of beta blocker as tolerated is recommended [4]. Support for continuation of beta blocker therapy in this setting comes from retrospective analyses of patients enrolled in randomized trials [26,27] and reports from the OPTIMIZE-HF program and the Italian Survey on Acute Heart Failure [28,29]. Withdrawal of beta blocker therapy was associated with increased mortality as compared to continuation of such therapy. However, these retrospective analyses cannot definitively determine whether the discontinuation was the cause of the worse outcome. While the increase in mortality was only partially explained by greater clinical risk factors in the patients withdrawn from beta blocker therapy, such analyses cannot account for all factors. For more severely ill patients, halving of the dose of beta blockers or discontinuation may be necessary.

- For patients on chronic beta blocker therapy with moderate-to-severe decompensation or hypotension, we decrease or withhold beta blocker therapy during the early phase of treatment. In patients requiring inotropic support or those with severe volume overload, we withhold therapy [30].

- For patients who are not treated with beta blocker therapy chronically, we do not initiate a beta blocker in the early management of acute HF. However, a small randomized trial and a larger observational study found that initiation of therapy prior to hospital discharge in stable patients improves long-term beta blocker compliance without an increase in side effects or drug discontinuation, so initiation prior to discharge is recommended in stable patients. Prior to initiation of therapy, the patient should have no or minimal evidence of fluid retention and should not have required recent intravenous inotropic therapy. Beta blocker therapy should start with low doses. Particular caution is indicated in patients who have required inotropes during their hospitalization. (See "Use of beta blockers in heart failure due to systolic dysfunction", section on 'Initiation of therapy'.)

**Aldosterone antagonist therapy** — Randomized trials have demonstrated that aldosterone antagonist therapy (spironolactone or eplerenone) reduces mortality when included in long-term management of selected patients with systolic heart failure who can be carefully monitored for serum potassium and renal function. These include patients who have NYHA functional class II HF and an LVEF ≤30 percent; or NYHA functional class III to IV HF and an LVEF ≤35 percent; and patients post ST elevation MI who are already receiving therapeutic doses of ACE inhibitor, have an LVEF ≤40 percent, and have either symptomatic heart failure or diabetes mellitus. The serum potassium should be <5.0 meq/L and eGFR should be ≥30 mL/min per 1.73 m². (See "Use of aldosterone antagonists in heart failure", section on 'Our approach'.)

In patients already taking an aldosterone antagonist, such therapy can generally be continued...
during an episode of acute decompensation, with appropriate monitoring of blood pressure, renal function, and electrolytes. For patients not taking an aldosterone antagonist who have an indication for therapy, we favor initiation prior to discharge.

**Venous thromboembolism prophylaxis** — Prophylaxis against venous thromboembolism (deep vein thrombosis and pulmonary embolism) with low-dose unfractionated heparin or low molecular weight heparin, or fondaparinux is indicated in patients admitted with ADHF who are not already anticoagulated and have no contraindication to anticoagulation. In patients admitted with ADHF who have a contraindication to anticoagulation, venous thromboembolism prophylaxis with a mechanical device (eg, intermittent pneumatic compression device) is suggested [2]. These issues are discussed in detail separately. (See "Prevention of venous thromboembolic disease in medical patients").

**Morphine sulfate** — Data are limited on the efficacy and safety of morphine therapy in ADHF. Morphine reduces patient anxiety and decreases the work of breathing. These effects diminish central sympathetic outflow, leading to arteriolar and venous dilatation with a resultant fall in cardiac filling pressures [31,32].

However, retrospective studies have found that morphine administration for ADHF is associated with increased frequency of mechanical ventilation and in-hospital mortality [33,34], although a causal relationship has not been established. In one retrospective analysis, morphine was administered in 14 percent of 150000 ADHF hospitalizations [34]. Morphine use was associated with more frequent mechanical ventilation, longer hospitalizations, more intensive care unit admissions, and greater mortality. After risk adjustment and exclusion of ventilated patients, morphine remained an independent predictor of mortality (OR 4.8, 95% CI 4.52 to 5.18, p <0.001). Although risk adjustment in this study may not have been adequate, these results raise concern about the safety of morphine in this population.

The 2008 ESC guidelines for the treatment of acute heart failure include consideration of morphine as an ungraded recommendation noting that supporting data are limited [35]. Morphine therapy is not mentioned in the 2010 HFSA guidelines on management of ADHF or in the 2009 ACC/AHA focused update.

Given the limited evidence of benefits and potential risks of morphine, we suggest generally avoiding morphine therapy in the treatment of ADHF without acute MI.

The role of morphine sulfate in patients with ADHF who have an acute MI is discussed separately. (See "Treatment of acute decompensated heart failure in acute coronary syndromes", section on 'Morphine sulfate'.)

**ADDITIONAL CONSIDERATIONS** — In addition to the above treatments, several additional options and considerations may be relevant to selected patients. Management of refractory heart failure is discussed in detail separately. (See "Management of refractory heart failure".)

**Mechanical cardiac assistance** — Patients with cardiogenic pulmonary edema who are also in cardiogenic shock should be considered candidates for mechanical circulatory support. These patients usually have a cardiac index less than 2.0 L/min per m2, a systolic arterial pressure below 90 mmHg, and a pulmonary capillary wedge pressure above 18 mmHg, despite adequate pharmacologic therapy.

The two major mechanical modalities used in this setting are intraaortic balloon counterpulsation and an internally implanted left ventricular assist device. (See "Intraaortic balloon pump counterpulsation" and "Circulatory assist devices: Cardiopulmonary assist device and short-term left ventricular assist devices".)

**Ultrafiltration** — Ultrafiltration is an effective method of fluid removal with advantages that include adjustable fluid removal volumes and rates, no effect on serum electrolytes, and decreased neurohormonal activity. (See "Continuous renal replacement therapies: Overview").
Patients with ADHF accompanied by renal insufficiency or diuretic resistance may benefit from ultrafiltration. Most studies have used a peripherally inserted ultrafiltration device that does not require central access, specialized nursing, or ICU admission [4,36].

The efficacy of ultrafiltration in patients with ADHF has been evaluated in several randomized trials. In the RAPID-CHF trial, 40 patients with ADHF and renal insufficiency (serum creatinine ≥1.5 mg/dL [133 µmol/L]) and/or anticipated diuretic resistance (high daily oral diuretic doses) were randomly assigned to receive usual care with or without ultrafiltration [37]. Ultrafiltration was associated with significant increases in fluid removal after 24 hours (4650 versus 2838 mL without ultrafiltration) and weight loss (2.5 versus 1.9 kg) without a difference in serum creatinine.

In the larger UNLOAD trial, 200 patients hospitalized for ADHF were randomly assigned to ultrafiltration or to standard care including intravenous diuretics during the admission [30]. Renal dysfunction and/or anticipated diuretic resistance were not entry criteria. Thus, this study included a less selected group of HF patients. The following findings were noted:

- At 48 hours, patients assigned to ultrafiltration had a significantly greater fluid loss (4.6 versus 3.3 liters with standard care). This difference may in part reflect the relatively modest level of diuretic therapy used in the standard care arm.
- At 90 days, patients assigned to ultrafiltration had significantly fewer HF rehospitalizations than patients assigned to standard care (0.22 versus 0.46 admissions per patient) and fewer unscheduled clinic visits (21 versus 44 percent with standard care).
- The rates of adverse events were similar in the two groups, although there was a higher incidence of bleeding in the standard care arm. There was no difference in serum creatinine, as was also found in a smaller trial with detailed assessment of renal hemodynamics [38].

While these data suggest that ultrafiltration is an effective method for fluid volume removal, it is not clear if it provides an advantage in patients who respond adequately to standard intravenous diuretics or those who require more aggressive diuresis. In addition, given the relatively small body of data, it is not possible to assess the safety of ultrafiltration.

Ultrafiltration is reserved for patients who do not achieve an adequate response to an aggressive diuretic regimen. This recommendation is consistent with the 2005 (with 2009 update) ACC/AHA, 2008 ESC and 2010 HFSA heart failure guidelines [2,4,35]. Consultation with a kidney specialist may be appropriate prior to opting for a mechanical strategy of fluid removal [4].

**Vasopressin receptor antagonists** — Vasopressin receptor antagonists have been investigated as an adjunct to diuretics and other standard therapies in patients with ADHF as a means of countering arterial vasoconstriction, hyponatremia, and water retention. However, such treatment is controversial and not included in the HFSA guidelines. The 2008 ESC guidelines suggest consideration of tolvaptan for HF patients with hyponatremia in an ungraded recommendation [35]. Tolvaptan is the most studied agent in this setting. (See "Possibly effective emerging therapies for heart failure" and "Hyponatremia in patients with heart failure", section on 'Vasopressin receptor antagonists'.)

**SUMMARY AND RECOMMENDATIONS** — The following summary and recommendations apply to the management of patients with ADHF. They are generally in agreement with those published in the 2005 ACC/AHA HF guidelines with 2009 focused update, the 2010 HFSA ADHF guidelines [2] and the 2004 ACC/AHA STEMI guidelines with 2007 focused update and the 2002 ACC/AHA NSTEMI guidelines [4,16,39,40]. A table to assist with emergency management of ADHF is provided (table 1).

Initial therapy includes the following:
- Supplemental oxygen and assisted ventilation if necessary
- Diuresis with an intravenous loop diuretic
- Vasodilator therapy in patients without hypotension (e.g., intravenous nitroglycerin)

In selected patients with severe or refractory symptoms, the following additional therapies may be indicated:

- Intravenous positive inotropic agents
- Mechanical cardiac assistance
- Ultrafiltration

**Oxygen and ventilatory support** — Patients with ADHF and a decreased oxygen saturation should be treated with supplemental oxygen.

- Patients with significant hypoxia or respiratory distress are generally treated with high flow oxygen via a nonrebreather facemask; later oxygen is titrated to patient comfort and an oxygen saturation of at least 90 percent.

- For patients with ADHF and respiratory failure, we recommend a trial of noninvasive positive pressure ventilation (NPPV) if emergent intubation is not indicated, no contraindications to NPPV exist (table 2), and personnel with experience in NPPV are available (Grade 1A). (See 'Supplemental oxygen and assisted ventilation' above and "Noninvasive positive pressure ventilation in acute respiratory failure in adults", section on 'Cardiogenic pulmonary edema'.)

- Patients with respiratory failure due to ADHF who fail NPPV, do not tolerate NPPV, or have contraindications to NPPV (table 2) require endotracheal intubation for conventional mechanical ventilation. (See "Overview of mechanical ventilation".)

**Fluid removal** — Patients with ADHF and pulmonary edema have symptomatic relief and improved oxygenation with fluid removal. Diuretics are recommended except in patients with severe hypotension or cardiogenic shock.

- In patients with ADHF and fluid overload, we recommend that initial therapy include an intravenous loop diuretic (Grade 1B). (See 'Diuretics' above.) Dosing is individualized, determined largely by the patient's renal function and prior diuretic exposure. (See 'Diuretic dosing' above and 'Effects on renal function' above.)

Bolus dosing with intravenous loop diuretics achieves adequate diuresis in most patients. Determination of effective diuretic dosing should be confirmed by demonstration of a negative fluid balance. For patients who do not have adequate fluid removal with this approach, options include:

- Continuous infusion of loop diuretic
- Addition of a thiazide diuretic

Use of aldosterone antagonists is discussed below. (See 'Systolic dysfunction' below.)

Ultrafiltration is an option for patients refractory to diuretic therapy. (See 'Ultrafiltration' above.)

**Vasodilators** — Vasodilators, including nesiritide, nitroglycerin, and nitroprusside, can reduce filling pressures, improve symptoms, and facilitate diuresis. (See 'Vasodilator therapy' above.)

- In patients with acute decompensated heart failure who are not hypotensive, we suggest...
the use of a vasodilator in addition to diuretic therapy with close hemodynamic monitoring (Grade 2C). (See 'Vasodilator therapy' above.) When using vasodilators in patients with ADHF, we favor the following approach:

Intravenous nitroglycerin is generally recommended. Nitrate administration is contraindicated after use of PDE-5 inhibitors such as sildenafil.

In selected cases when there is a need for significant afterload reduction (eg, hypertensive emergency, acute aortic or mitral regurgitation), we recommend nitroprusside, although the risk of cyanide or thiocyanate toxicity limit its use.

For most patients hospitalized with acute heart failure (HF), we recommend not treating with nesiritide (Grade 1A). In carefully selected patients with appropriate hemodynamics (without hypotension or cardiogenic shock) who remain symptomatic despite routine therapy, a trial of nesiritide may be helpful as an alternative to other vasodilator therapy (nitroglycerin or nitroprusside). Nesiritide has a longer effective half-life than nitroglycerin or nitroprusside, so side effects such as hypotension may persist longer. (See "Nesiritide in the treatment of acute decompensated heart failure", section on 'Use' and 'Vasodilator therapy' above.)

Inotropes and mechanical cardiac support — Patients with ADHF and systolic dysfunction who are hypotensive or who remain in pulmonary edema despite oxygen, diuresis, and, if tolerated, vasodilators, may benefit from intravenous inotropic support and may require mechanical cardiac support. (See 'Inotropic agents' above and "Inotropic agents in heart failure due to systolic dysfunction" and 'Mechanical cardiac assistance' above.)

ACE inhibitors/ARBs and beta blockers — ACE inhibitors, ARBs, and beta blockers require special consideration in patients with decompensated heart failure. The approach to their use depends upon whether the patient has primarily systolic or diastolic dysfunction. (See 'Systolic dysfunction' below and 'Diastolic dysfunction' below.)

Systolic dysfunction — In patients with chronic HF due to systolic dysfunction the long-term use ACE inhibitors/ARBs and beta blockers reduces mortality, but there are short-term risks to the use of these medications in the setting of acute HF. (See 'ACE inhibitors and ARBs' above and 'Beta blockers' above.)

We approach the use of these medications in this setting in the following manner:

- For patients who are not already taking an ACE inhibitor or ARB, we suggest that they NOT be initiated at the time of presentation with an episode of ADHF (Grade 2C). An oral ACE inhibitor or ARB can usually be started within 24 to 48 hours, once the patient is hemodynamically stable.

- For patients who are not already taking a beta blocker, we suggest that they NOT be initiated at the time of presentation with an episode of ADHF (Grade 2B). Beta blockers are generally started later than ACE inhibitors or ARBs, when the patient is euvolemic, usually shortly before discharge.

A detailed discussion of the initiation of these medications, including dosing and sequence of initiation, is presented separately. (See "Overview of the therapy of heart failure due to systolic dysfunction", section on 'Pharmacologic therapy of HF'.)

- For patients who are already taking an ACE inhibitor or ARB, we suggest that maintenance of oral therapy be cautiously continued (Grade 2C). However, the dose should be decreased or the drug discontinued if hypotension, acute renal failure, or hyperkalemia is present. (See 'Continued therapy' above.)

- For patients who are already taking a beta blocker, management depends upon the
severity of HF decompensation and hemodynamic instability (see 'Beta blockers' above):

For patients with severe decompensation (eg, severe volume overload and/or requiring inotropic support), we suggest withholding beta blockers (Grade 2C).

For patients with moderate-to-severe decompensation, we suggest decreasing or withholding beta blocker therapy (Grade 2C).

For patients with mild decompensation without hypotension or evidence of hypoperfusion, we suggest continuation of beta blocker as tolerated (Grade 2C).

Aldosterone antagonist therapy (spironolactone or eplerenone) reduces mortality when included in long-term management of selected patients with systolic HF who can be carefully monitored for serum potassium and renal function. In patients already taking an aldosterone antagonist, such therapy can generally be continued during an episode of acute decompensation, with appropriate monitoring of blood pressure, renal function, and electrolytes. For patients not taking an aldosterone antagonist who have an indication for therapy, we favor initiation prior to discharge. (See 'Aldosterone antagonist therapy' above.)

Diastolic dysfunction — As noted above, patients with ADHF are treated similarly whether they have primarily systolic or diastolic dysfunction. However, in patients with diastolic dysfunction, long-term use of ACE inhibitors/ARBs and beta blockers does not provide the same benefit as in patients with HF due to systolic dysfunction. The efficacy of aldosterone antagonist therapy in this population is under investigation. On the other hand, the short term risks of beta blockers are less concerning and treatment of hypertension and tachycardia are particularly important. Thus, antihypertensive agents and beta blockers may be useful in acute as well as chronic HF in patients with primarily diastolic dysfunction. (See "Treatment and prognosis of diastolic heart failure".)

Venous thromboembolism prophylaxis — Venous thromboembolism prophylaxis is indicated in patients hospitalized with ADHF. (See 'Venous thromboembolism prophylaxis' above.)

Morphine — There is limited evidence of benefit (eg, reduced patient anxiety and decreased worked of breathing) from morphine sulfate and there is potential risk (eg, increased need for ventilatory support), so we suggest avoiding morphine therapy in patients with ADHF without acute myocardial infarction. (See 'Morphine sulfate' above.)

Management of ADHF in MI — Specific considerations apply to treatment of ADHF during acute MI, particularly the importance of revascularization. (See "Treatment of acute decompensated heart failure in acute coronary syndromes".)

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35. Dickstein K, Cohen-Solal A, Filippatos G, et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). Eur Heart J 2008; 29:2388.


Topic 3450 Version 19.0
### Differential diagnosis: Pulmonary embolism, acute asthma, pneumonia, noncardiogenic pulmonary edema (eg, ARDS), pericardial tamponade or constriction

### Symptoms and signs

- **Acute dyspnea, orthopnea, tachypnea, tachycardia, and hypertension are common**
- **Hypotension reflects severe disease and arrest may be imminent; assess for inadequate peripheral or end-organ perfusion**
- **Accessory muscles are often used to breathe**
- **Diffuse pulmonary crackles are common; wheezing (cardiac asthma) may be present**
- **S3 is a specific sign but may not be audible; elevated jugular venous pressure and/or peripheral edema may be present**

### Diagnostic studies

- **Obtain ECG: Look for evidence of ischemia, infarction, arrhythmia (eg, atrial fibrillation), and left ventricular hypertrophy**
- **Obtain portable chest x-ray: Look for signs of pulmonary edema, cardiomegaly, alternative diagnoses (eg, pneumonia); Normal radiograph does not rule out ADHF**
- **Obtain: Blood counts; cardiac troponin; electrolytes (Na+, K+, Cl-, HCO3-); BUN and creatinine; arterial blood gas; BNP or NT-proBNP if diagnosis is uncertain.**
- **Perform bedside echocardiography if available**

### Treatment

- **Monitor oxygen saturation, vital signs, and cardiac rhythm**
- **Provide supplemental oxygen, place two IV catheters, and position patient upright**
- **Provide noninvasive positive pressure ventilation (NIPPV), unless immediate intubation is needed or NIPPV is otherwise contraindicated; have airway management equipment readily available; etomidate is a good induction agent for rapid sequence intubation in ADHF**
- **Search for cause of ADHF (including: acute coronary syndrome, hypertension, arrhythmia, acute aortic or mitral regurgitation, aortic dissection, sepsis, renal failure, or anemia) and treat appropriately**
- **Patients with ADHF and atrial fibrillation (AF) often require medication (eg, esmolol) to slow their heart rate**
- **Direct current cardioversion is indicated for patients with new onset AF and hemodynamic instability or refractory symptoms despite rate control**
- **Obtain immediate cardiac surgery consultation for acute aortic or mitral regurgitation or ascending aortic dissection**
- **For patients with adequate end-organ perfusion (eg, normal or elevated blood pressure) and signs of ADHF:**
  - **Give an IV vasodilator (nitroglycerin or nitroprusside); titrate rapidly to effect (eg, start nitroglycerin at 20 mcg/minute and increase dose by 40 to 50 mcg every 3 to 5 minutes as needed); nitrates are contraindicated after use of PDE-5 inhibitors (eg, sildenafil)**
  - **Give an IV loop diuretic (eg, furosemide 40 mg IV; bumetanide 1 mg IV); higher doses are needed for patients taking diuretics chronically (give an IV dose at least equal to the chronic oral dose) and patients with renal dysfunction.**
- **For patients with known systolic heart failure (eg, documented low ejection fraction) presenting with signs of severe ADHF and hypotension or signs of shock:**
  - **Give an IV inotrope (eg, dobutamine or milrinone) and mechanical support (eg, intraaortic balloon counter pulsation)**
For patients with known diastolic heart failure (ie, preserved systolic function) presenting with signs of severe ADHF and hypotension or signs of shock:

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<thead>
<tr>
<th>Give an IV vasopressor (eg, phenylephrine); do not give an inotrope</th>
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<tbody>
<tr>
<td>Consider possibility of acute mitral or aortic regurgitation, or aortic dissection, and need for emergent surgical intervention. Obtain immediate echocardiography if available.</td>
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For patients whose cardiac status is unknown but present with signs of severe ADHF (ie, pulmonary edema) and hypotension or signs of shock:

<table>
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<tr>
<th>Give an IV inotrope (eg, dobutamine or milrinone), with or without an IV vasopressor (eg, norepinephrine) and mechanical support (eg, intraaortic balloon counter pulsation)</th>
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# Contraindications to NPPV

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<tr>
<td>Cardiac or respiratory arrest</td>
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<td>Nonrespiratory organ failure</td>
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<td>Severe encephalopathy (e.g., GCS &lt;10)</td>
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<td>Severe upper gastrointestinal bleeding</td>
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<td>Hemodynamic instability or unstable cardiac arrhythmia</td>
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<td>Facial or neurological surgery, trauma, or deformity</td>
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<td>Upper airway obstruction</td>
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<tr>
<td>Inability to cooperate/protect airway</td>
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<tr>
<td>Inability to clear secretions</td>
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<td>High risk for aspiration</td>
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