Heart Failure

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Christopher J. Hogan

Acute Heart Failure

Critical Points

- Assess if preserved versus reduced ejection fraction heart failure: old records, echocardiography.
- Evaluate early for myocardial infarction or acute ischemia: ECG, serial cardiac enzymes.
- Use noninvasive pressure support ventilation often and early.
- Hypotension (do not overlook *relative* hypotension) is ominous and should be corrected early and aggressively (fluids, dobutamine).
- N-terminal brain natriuretic peptide (NT-proBNP) or B-type natriuretic peptide (BNP) measurements are of limited use in renal failure patients.
- If using nitrates, higher doses may be more beneficial, but may be of less value in patients who are on chronic nitrate therapy.
- If the initial dose of loop diuretics fails to be effective, consider adding a low-dose second agent such as thiazides or spironolactone.

Introduction

Acute heart failure (AHF) affects approximately 5.7 million Americans, with 87,000 new AHF cases annually [1]. For every large myocardial infarction saved by an intervention, another heart failure patient is created. Projections suggest that the prevalence of AHF will increase 46% from 2012 to 2030, resulting in over 8 million people with the disease [2, 3]. A disease of the elderly [4], up to 75% of AHF patients also have preceding hypertension, another reason why emphasizing follow-up for uncontrolled hypertension in emergency department (ED) patients presenting with other complaints is important. Because AHF disproportionally affects minorities, urban medical centers evaluate and treat AHF-related problems more frequently.

AHF is particularly germane to emergency physicians because 80% of patients hospitalized with the disease are admitted through the ED [5], accounting

C. J. Hogan (✉)
Department of Emergency Medicine, Department of Surgery, Division of Trauma/Critical Care, VCU Medical Center, Medical College of Virginia Campus, Richmond, VA, USA
e-mail: chogan@mcvh-vcu.edu

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for almost a million ED visits annually in the United States. Once admitted, patients stay for a median of 3.4 days, a duration that has not changed in a decade [4]. While most of the cost of AHF is from post-discharge care [6–8], the cost of ED evaluation and subsequent admission are expensive as well [4]. The treatment rendered by ED physicians impacts patient outcome and cost [9], not only in those patients discharged from the ED [10], but those who are admitted as outpatients as well [11, 12].

Pathophysiology

The nomenclature of AHF has undergone several iterations. The classic concept of "heart failure" has a reduced ejection fraction in which the left ventricle is dilated with reduced systolic function (defined as an ejection fraction less than 40%). This occurs in ~50% of AHF patients. While in the United States the leading cause is uncontrolled hypertension and post-myocardial infarction loss of myocardium, the worldwide cause is Chagas disease. To offset falling cardiac output and perfusion, vasoconstriction is enhanced by upgrading the renin–angiotensin axis. Unfortunately, this further taxes a failing heart, exacerbating the diminished forward flow.

The other half of HF patients has a normal ejection fraction, defined as an EF equal to or greater than 50% [13]. Previously, this was referred to as diastolic AHF because it was thought that most patients with the symptoms of AHF and a normal EF had diastolic dysfunction, but this has been found to not be the case. The current prevailing theory is that prolonged hypertension causes left ventricular hypertrophy, decreased renal function, and vascular changes, all of which impair microvascular perfusion and cause local ischemia. This disrupts the balance of autoregulation and vasodilation, causing organ remodeling, myocardial fibrosis, hypertrophy, and necrosis. Additionally, pulmonary hypertension occurs in about 80% [14] of patients with preserved EF AHF. One potential clue of the presence of preserved EF AHF is decreased exercise tolerance – as stroke volume fails to rise, patients develop dyspnea and fatigue.

Although the initial evaluation and treatment of preserved EF AHF is not drastically different from classic AHF, the overall behavior of the disease differs. Secondary analyses of the Irbesartan in Heart Failure with Preserved Ejection Fraction (I-PRESERVE) trial reported an annual death rate of 5.2%, 26% of which was due to sudden death, 14% AHF, 5% myocardial infarction, and 9% from stroke death [5]. Most of these presentations will be to the ED.

Classic teaching has centered around two main components of heart failure: The degree of fluid overload (wet vs. dry) and the perfusion from diminished cardiac output (warm vs. cold) [15, 16]. While most presentations are warm and wet, patients can be hypovolemic from over-diuresis and can demonstrate a low perfusion state (cold) that will initially require resuscitation. Cardiogenic shock is caused by fluid overload and diminished perfusion (cold and wet) and is difficult to treat because it requires resuscitation despite fluid overloaded patients.

Patient Presentation

The traditional evaluation for acute AHF relies on qualitative measures and clinical gestalt based on physical examination findings, patient symptoms, and chest radiograph findings [17]. ED physicians in particular are not good at estimating the perfusion and fluid status, as one study found that one in five patients thought to have AHF in the ED did not have that as a final diagnosis [18]. This is echoed by an older study suggesting AHF patients admitted with an AHF diagnosis were misdiagnosed in approximately 10% of hospital admissions [19].

In patients presenting with what appears to be AHF, but who do not carry the diagnosis, a further evaluation in necessary. In patients from South or Central America, the presence of a systolic murmur may be an indication of valvular damage from Chagas disease. In patients with a drug abuse history, valvular disease should also be considered, necessitating a formal echocardiogram. All patients need an ECG to evaluate for

acute or recent infarct as well as left ventricular hypertrophy or pulmonary hypertension.

Although the Forrester AHF classification was developed in AMI patients, it lends itself well to the acutely decompensated reduced EF AHF population [16]. Patients are classified clinically on the basis of peripheral perfusion (cool/clammy skin, cyanosis, altered mental status, or oliguria) and pulmonary congestion (rales, abnormal chest X-ray). If the hemodynamic component of the classification is not readily available in the ED (cardiac index $\leq$2.2 L/min/m^2 or pulmonary capillary pressure >18 mmHg), they may be found in old records. Treatment strategy is based according to the clinical and hemodynamic status and its approach is still valuable when assessing AHF patients. For instance, even though a patient may be grossly fluid overloaded, she may still need intravascular volume if hypoperfusion is present [16]. Mortality was 2.2% in group I, 10.1% in group II, 22.4% in group III, and 55.5% in group IV – not too different from the current cardiogenic shock population [20].

The one universal finding in compensated AHF, regardless of its etiology, is hypertension. This is from a combination of the worsening renin–angiotensin feedback loop and anxiety. It also enables the use of afterload reduction and diuresis, giving a buffer to the treating physician.

Physical examination findings, review of systems, and the elements of the history are by themselves limited in attempting to determine the presence of AHF, but the lack of these findings does not mean it is not present. While the specificity of physical examination findings such as a cardiac third heart sound (S3) (99%), rales (78%), or JVD (92%) are reasonable, the respective sensitivities are poor (13%, 60%, and 39%) for evaluating for AHF [21, 22] as are the likelihood ratios. In one study, rales on lung examination were absent in 80% of patients who were found by pulmonary artery catheter pressure monitoring to have elevated filling pressures [23]. Wang et al. published a thorough analysis of physical examination and chest radiographs findings in acutely decompensated AHF, concluding that the most useful piece of history is preexisting AHF and the presence of paroxysmal nocturnal dyspnea, orthopnea, and peripheral edema on physical examination have an acceptable positive likelihood ratios for the presence of acute decompensated systolic AHF [22].

In patients with preserved EF AHF, decreased ventricular compliance predisposes them to pulmonary edema because small changes in volume can lead to large changes in left ventricular diastolic pressure. The ventricle is unable to tolerate venous return without elevated diastolic pressures, so small changes in fluid balance will manifest clinically, such as hypertension and dyspnea. This makes patients very sensitive to vasodilation and vasoconstriction, and they can also develop hypotension with aggressive diuresis or vasodilation [14].

Cardiogenic shock is usually obvious and ominous, as patients have hypotension and other indicators of poor perfusion, coupled with dyspnea and lung rales usually associated with classic AHF. Although there is usually a component of dyspnea with cardiogenic shock, poor perfusion can also manifest itself in other ways, such as altered mental status or worsening renal failure. These presentations can be more subtle than straightforward acute AHF decompensation.

Diagnostics

Traditionally, chest radiographs (CXR) are the mainstay of AHF evaluation, looking for pulmonary edema or other causes of dyspnea (Table 12.1). But pulmonary edema or increased vascular markings [24, 25] found on CXR are poor indicators of the degree of AHF present [22, 25], and chronic heart failure can also account for findings that can be confused with acute disease [24, 25]. While pulmonary venous congestion, cardiomegaly, and interstitial edema are the most specific test findings for AHF, their absence will not rule it out [22]. Twenty percent of AHF ED patients can demonstrate no evidence of congestion on CXR [26].

Surrogate markers have had limited success in guiding treatment for AHF [27], and risk stratification models have yet to prove long-term accu-

Table 12.1 Summary of diagnostic accuracy of findings on chest radiography and electrocardiography for acute heart failure in emergency department patients presenting with dyspnea

	Pooled		Summary LR (95% CI)	
Finding	Sensitivity	Specificity	Positive	Negative
Chest radiography				
Pulmonary venous congestion	0.54	0.96	12.0 (6.8–21.0)	0.48 (0.28–0.83)
Interstitial edema	0.34	0.97	12.0 (5.2–27.0)	0.68 (0.54–0.85)
Alveolar edema	0.06	0.99	6.0 (2.2–16.0)	0.95 (0.93–0.97)
Cardiomegaly	0.74	0.78	3.3 (2.4–4.7)	0.33 (0.23–0.48)
Pleural effusion	0.26	0.92	3.2 (2.4–4.3)	0.81 (0.77–0.85)
Any edema	0.70	0.77	3.1 (0.60–16.0)	0.38 (0.11–1.3)
Pneumonia	0.04	0.92	0.50 (0.29–0.87)	1.0 (1.0–1.1)
Hyperinflation	0.03	0.92	0.38 (0.20–0.69)	1.1 (1.0–1.1)
Electrocardiography				
Atrial fibrillation	0.26	0.93	3.8 (1.7–8.8)	0.79 (0.65–0.96)
New T-wave changes	0.24	0.92	3.0 (1.7–5.3)	0.83 (0.74–0.92)
Any abnormal finding	0.50	0.78	2.2 (1.6–3.1)	0.64 (0.47–0.88)
ST-segment elevation	0.05	0.97	1.8 (0.80–4.0)	0.96 (0.95–1.0)
ST-segment depression	0.11	0.94	1.7 (0.97–2.9)	0.95 (0.90–1.0)

LR likelihood ratio, *CI* confidence interval
Used with permission from Collins et al. [35]

racy in long-term outpatients. However, they are of good value in the ED setting. The mainstay of the suspected AHF diagnostic armamentarium are N-terminal brain natriuretic peptide (NT-proBNP) and B-type natriuretic peptide (BNP). Serum natriuretic testing is supported as a Level B guideline in the ACEP Clinical Guidelines for heart failure [17] and is highly recommended by the American College of Cardiology Foundation (ACCF)/American Heart Association [28]. The ACEP Guidelines for AHF specifically stating that a single BNP or NT-proBNP level can improve the diagnostic accuracy for the presence of AHF when compared to standard clinical judgment alone. When ruling out AHF in the acutely dyspneic patient, a BNP < 100 pg/dL or NT-proBNP < 300 pg/dL makes AHF less likely (negative LR = 0.1). When trying to rule in ADHF, a BNP > 500 pg/dL or NT-proBNP > 1000 pg/dL is present (positive LR = 6) [17].

Natriuretic peptide measurement is most useful when trying to rule out the presence of AHF in patients presenting with dyspnea [29, 30]. Specifically, a value <100 pg/mL yields a negative LR = 0.11 (95% CI, 0.07–0.16) [22, 31]. In one study, BNP had greater utility than CXR for diagnosing AHF [29]. There are limitations to the usefulness of BNP, namely that it increases with age and are affected by weight and ethnicity [31]. Since BNP is released from atrial stretching, conditions that cause distention can also cause false elevated levels, such as pulmonary embolism, pulmonary hypertension, and hemodialysis. Since it is cleared renally, chronic or acute kidney disease will also cause elevated levels. Finally, genetic variation can alter BNP levels and obesity can cause falsely low BNP values [32].

BNP levels can also help guide initial treatment. If a prior BNP level is known, a level greater than 50% suggests volume overload, as does a dyspneic patient with a history of AHF found with a BNP level >600 pg/ml for BNP or >6000 pg/ml for proBNP. If being discharged from the ED, remember a decrease in BNP in response to treatment is important, as the final BNP level seems to be the most accurate predictor of death or readmission. A BNP in the 350–400 pg/ml or NT-proBNP in the 4000 pg/ml range at the time of discharge predicts a stable posthospital course [33].

Bedside cardiac ultrasonography is a more recent addition to diagnostics that holds promise for determining the etiology of dyspnea. It provides a real-time assessment of left ventricular function and volume status, and can be repeated

as treatment is rendered. ED physicians can estimate ejection fraction with good interrater reliability [34], and volume status can be estimated by inferior vena cava (IVC) diameter and its degree of change with respiratory variation, specifically looking for dilation without any respiratory variation, consistent with fluid overload [35]. Pulmonary edema may be evident on pulmonary ultrasound (US) by looking for sonographic B lines, which occur most commonly in patients with AHF and correlate with elevated PCWP and pulmonary edema [36]. When used in conjunction with serum markers, US accuracy improves [37]. For further discussion on US, see Chap. 35.

More recently, bedside ultrasound has been used to augment the diagnosis of AHF, particularly when there are other potential causes of dyspnea, such as COPD or end-stage renal disease. One study (n = 130) prospectively examined patients presenting with dyspnea and for the diagnosis of reduced EF AHF and found cardiopulmonary ultrasound had an accuracy of 90% (95% CI: 84–95) versus 81% (95% CI: 72–88) for the combination clinical examination, NT-proBNP and CXR. In addition to evaluating AHF in the setting of dyspnea, cardiopulmonary ultrasound can also shed light into the presence of pneumonia or pleural effusion with an accuracy of 86% (95% CI, 80–92) and decompensated chronic obstructive pulmonary disease or asthma with an accuracy of 95% (95% CI, 92–99) [38].

Previously stable AHF often is exacerbated by other comorbidities. Considerations include:

- Unstable angina/myocardial infarction (particularly involving right ventricle)
- Myocarditis
- Poor dietary or medication compliance (NSAID use)
- Arrhythmias +/− electrolyte abnormalities
- Hypertensive crisis
- Chordae tendineae rupture or other valvular regurgitation
- Acute kidney injury/failure
- Aortic valve stenosis
- Sympathomimetic (cocaine) abuse
- High-output syndromes (wet beriberi)
- Sepsis/SIRS
- Cardiac tamponade
- Aortic dissection
- Postpartum cardiomyopathy
- Pulmonary hypertension/asthma/COPD
- Pheochromocytoma or thyrotoxicosis crisis
- Critical anemia

Initial Stabilization

Acute HF patients typically present with dyspnea, ranging from wheezing to complete respiratory failure. Often, comorbidities such as COPD or asthma may accompany AHF, and preserved EF AHF patients often have a component of pulmonary hypertension that can complicate presentation and management. The majority of AHF patients are hypertensive upon presentation, as this is part of the AHF pathophysiology. Hypotension in the AHF population is ominous and makes the usual management (diuresis, afterload reduction) more challenging. Resuscitation with small volume of intravenous fluids or initiation of an inotropic agent is reasonable first moves.

An ECG early in the presentation is important to evaluate for an acute myocardial infarction or cardiac ischemia (particularly in hypotensive patients), which may alter the trajectory of the patient's care (Table 12.2). A CXR will also allow a more thorough differential diagnosis, including pneumonia, pleural effusion, or the presence of chronic pulmonary disease, in addition to serum lab work.

Patients with underlying AHF are at risk for a variety of cardiac arrhythmias, sometimes from ischemic myocardium or hypokalemia. For ventricular fibrillation or tachycardia, the usual ACLS guidelines apply. Low doses of beta blockade (metoprolol or esmolol) can be used to treat sinus or supraventricular tachycardias. Atrial fibrillation or flutters are occasional arrhythmias that require cardioversion (if unstable), β blockade, or amiodarone to slow AV conduction without compromising left ventricular function. Rarely, theophylline is required in AMI patients with atropine-resistant bradycardia [15]. If the bradycardia is nonresponsive to medications,

Table 12.2 Suggested workup in patients with acute heart failure

Complete blood count	Always
Electrocardiogram	Always
PT/PTT/INR	If patient anticoagulated or may need anticoagulation
Basic metabolic panel	Always
Cardiac enzymes (troponin)	Always
BNP or NT-proBNP	Always except in renal failure patients
Echocardiography	If no recent one available or if new issue suspected
Arterial blood gas	If acidosis or hypoxia suspected
Serum lactate	Always
Liver function tests	If hepatic dysfunction suspected or AMS
Urinalysis	If infection suspected
Chest radiograph	Always
Chest radiograph	Always

consider temporary transcutaneous or transvenous pacing.

Noninvasive Pressure Support Ventilation

The urgency to treat AHF and cardiogenic shock is dictated primarily by the pulmonary status of the patient. Dyspnea and impending respiratory failure from fluid overload are often the presenting complaint and main issue to address. Patients with chronic AHF, regardless of whether it is preserved versus reduced EF, know their disease, and often before ED presentation, will increase their diuretic dose as previously instructed by their cardiologist based on their daily weight in an attempt to mobilize excess fluid.

Noninvasive pressure support ventilation (NIPSV), either bilevel positive airway pressure support or continuous positive pressure airway support, is the greatest innovation available for AHF. It improves respiratory distress from cardiogenic pulmonary edema by preventing alveolar collapse and, to a small extent, helps to redistribute intra-alveolar fluid that improves pulmonary compliance. These reduce the work of breathing that has translated into clinical studies, as a recently updated Cochrane Review concluded that when compared to standard care without NIPSV, its use significantly reduced hospital mortality (relative risk reduction of 0.66) and endotracheal intubation (relative risk reduction of 0.52). While this did not translate into decreases in hospital length of stay, intensive care unit stay was reduced by 1 day. NPPV is an effective and safe intervention for the treatment of adult patients with acute cardiogenic pulmonary edema based on several small trials [39].

Although only a temporary measure, NIPSV can buy time while diuresis and afterload reduction therapy offload excess fluid [17]. It also frequently avoids endotracheal intubation in a subset of patients who are at a high likelihood of prolonged intubation because of their comorbidities. Altered mental status can sometimes cause NIPSV to fail because of an uncooperative patient, and it should also be avoided in patients at risk for vomiting or aspiration. NPPV, particularly the EPAP (or CPAP), reduces preload as well as afterload and acts as a mild LV assist device.

Definitive Treatment

Before initiating treatment, get a sense of the cardiac function, specifically the degree of preload, afterload, and contractility. This can be done with a chart review for the patient's most recent echocardiography or catheterization report. Not only is systolic function important, but particular consideration should be given to the patient's diastolic function.

If a recent cardiac assessment is unavailable, a bedside-limited transthoracic echocardiography (LTTE) examination can be done to get a rough idea of fluid status and contractility, as well as determine the presence of a pleural or cardiac effusion. Collins et al. [35] suggest an approach based on presenting blood pressure that is helpful (Table 12.3). Therapy can be guided based on patient blood pressure: hypertensive (SBP > 140 mm Hg), normotensive (SBP 100–140 mm Hg), or hypotensive (SBP < 100 mm Hg) [40, 41]. Hypertension is an important target

Table 12.3 Associated clinical characteristics and treatment approaches based on emergency department presentation phenotype

ED presentation phenotype	Clinical characteristics	Treatment
Low BP (SBP < 100 mm Hg)	Known/suspected low LVEF Likely CAD and CRI	Diuretics (+++) Inotropes/vasopressors (++) Mechanical support (+)
Normal BP (SBP 100–140 mm Hg)	Subacute symptoms Preserved or reduced LVEF Dietary/medical indiscretion	Diuretics (++) IV vasodilators (+) Topical nitrates (++)
High BP (SBP > 140 mm Hg)	History of HTN Abrupt symptom onset Flash pulmonary edema Multiple non-CV comorbidities	Topical/SL nitrates (++) Diuretics (+) IV vasodilators (+++) NIV

Adapted from and used with permission from Collins et al. [35]
+ relative intensity of use, *BP* blood pressure, *SBP* systolic blood pressure, *LVEF* left ventricular ejection fraction, *CAD* coronary artery disease, *CRI* chronic renal insufficiency, *IV* intravenous, *HTN* hypertension, *SL* sublingual, *NIV* noninvasive ventilation

because AHF patients may present with volume redistribution rather than volume overload, in which congestion is due to increased afterload rather than excess fluid. This is also important in diastolic AHF patients, who are known to present with a rapid onset of dyspnea and flash pulmonary edema. While for volume overloaded patients, intravenous loop diuretics remain the primary ED pharmacologic therapy, patients with volume redistribution may respond better to vasodilation therapy [42].

There are specific instances when emergent surgery is required in patients presenting with new or suddenly worsening AHF (of note, a bedside echocardiogram will help diagnose a majority of the following):

- Cardiogenic shock after AMI
- Postinfarction ventricular septal defect or free wall rupture
- Prosthetic valve failure or thrombosis
- Aortic aneurysm or aortic dissection rupture into the pericardial sac
- Acute mitral regurgitation from infection, ischemia or trauma
- Acute aortic regurgitation from infection, ischemia, dissection
- Mechanical assist device failure

The classic medication class used as an initial intervention for AHF for both EMS [43] and ED physicians [35] is loop diuretics, most commonly furosemide (Table 12.4). Despite its widespread usage (88% of the patients in on large database received IV diuretics during their admission) [44], there have been limited studies evaluating this drug class. Diuretics cause a decrease in plasma and extracellular fluid volume, leading to reduced ventricular filling pressures, peripheral congestion, and pulmonary edema. They also cause an early but temporary vasodilation effect with the first dose, as well as a reduction in neurohormonal activation [45]. Failure to respond to diuretics may be caused by intravascular volume depletion, rebound sodium uptake after volume loss, decreased tubular secretion from renal failure or nonsteroidal drug use (NSAIDs), and decreased renal or gut perfusion (not absorbing oral diuretics) from low cardiac output.

If the patient fails to respond to the initial dose of loop diuretics, consider adding a thiazide, as low-dose combinations can be more effective with fewer secondary effects than the use of higher doses of a single drug. Similarly, using diuretics in conjunction with dobutamine, dopamine, or nitrates can be effective and produce fewer secondary effects than increasing the dose of the diuretic [15]. The use of diuretics alone is further discouraged by the ACEP guidelines that caution against "aggressive" diuretic monotherapy, as it is unlikely to prevent the need for endotracheal intubation compared with aggressive nitrate monotherapy. These guidelines further recommend if diuretics are used,

Table 12.4 Medications commonly used in acute decompensated heart failure

Medication	Indication	Dosing	Side effect	Miscellaneous
Vasodilators				
Nitroglycerin	Afterload reduction, blood pressure control	Start 10 μg/min, increase by 10, Max 200 μg/min	Hypotension, headache	Decreased efficacy with chronic use
Isosorbide dinitrate	Afterload reduction, blood pressure control	Start 1 mg/h, Max 10 mg/h	"	Decreased efficacy with chronic use
Nitroprusside	Hypertensive urgency or emergency	0.3–5 μg/kg/min	Hypotension, CN toxicity	Watch for cyanide toxicity in renal failure
Natriuretic peptides				
Nesiritide[a]	Acute HF, failed other measures	2 μg/kg IV bolus, then 0.01–0.03 μg/kg/min	Hypotension, atrial fibrillation	Infusion only if hypotension a concern
Loop diuretics				
Furosemide	Afterload reduction, diuresis	Mild to moderate: 40 mg PO/IV Severe: 80 mg IV	Dehydration, ototoxicity renal injury	If first dose fails, consider adding another agent below
Bumetanide	Prior patient use, diuresis	0.5–4 mg PO or IV	"	Monitor Na, K, and creatinine closely
Torasemide	Prior patient use, diuresis	10–20 mg PO or IV	"	Monitor Na, K, and creatinine closely
Thiazide diuretics				
Metalozone	Augment loop diuresis	2.5–5.0 mg PO	Worsening renal failure	Use in renal insufficiency
Hydrochlorothiazide	↓ sodium reabsorption in distal tubule	25–50 mg PO	"	"
Inotropes				
Dobutamine	Enhances cardiac contractility and diuresis if used with diuretics	2–20 μg/kg/min IV infusion, no bolus	Tachycardia (try fluid bolus), hypotension	Insert arterial and central catheters
Milrinone	Enhances cardiac contractility	50 μg/kg bolus, then 0.3–0.7 μg/kg/min	Arrhythmias, hypotension tachycardia	Insert arterial and central catheters

" "Same as Above

they should be administered judiciously, given the potential for worsening renal and long-term mortality [17].

Nitrates are another classic drug class that has been a mainstay for treatment of acute AHF with a paucity of convincing evidence. The mechanism of action addresses the arterial endothelial dysfunction and impaired endothelium-dependent dilation [46] known to occur in AHF, relieving pulmonary congestion without compromising stroke volume or increasing myocardial oxygen demand in AHF. While at low doses, nitrates should only induce venous dilation, and as the dose is gradually increased, arterial dilatation occurs as well. When titrated properly, nitrates can reduce left ventricular pre- and afterload without impairing tissue perfusion.

A recent Cochrane review [47] looked at four studies (634 participants) that met their inclusion criteria, with no significant difference in the rapidity of symptom relief between intravenous nitroglycerin and intravenous furosemide/morphine after 0.5, 3, or 24 hours, suggesting little evidence to support the use of intravenous nitrate vasodilator therapy in the AHF population. Other measures, such as the need for mechanical ventilation, change in blood pressure, and progression to myocardial infarction, suggest there was a significantly higher incidence of adverse events after 3 hours with nitroglycerin compared with placebo (odds ratio 2.29, 95% CI 1.26–4.16), but this was based on a single study. A more recent meta-analysis suggests intravenous vasodilators, when used in acute AHF in the ED, are safe and

improve short-term symptoms but have no impact on mortality [48].

The studies evaluating nitrates used relatively lower doses that may have a limited effect in improving clinical status, so consider higher doses with the understanding that it is also best to avoid nitrates in hypotensive and *relatively* hypotensive patients, meaning patients who on any given day are profoundly hypertensive, but have what would be considered a normal blood pressure when you are considering treatment. In patients who are chronically on nitrates, even higher doses may not work because of the rapid development (12–24 h) of tolerance (especially when given intravenously) [15].

Sodium nitroprusside is another short-acting vasodilator that can be considered in patients with severe heart failure, particularly those with predominantly increased afterload (hypertension or mitral regurgitation). It must be titrated cautiously and requires an arterial line. Also, prolonged administration can accumulate thiocyanide and cyanide, so should be used with caution in renal or hepatic failure patients. To further argue against its use, it may cause "coronary steal syndrome" in ischemic patients by shifting blood toward healthy myocardium whose coronaries dilate and away from those areas where the vessels are diseased or obstructed and cannot dilate [15].

Inotropes

Typically, the use of inotropic support has been a last resort in the ED, as using these medication means an ICU bed will be needed for admission, and patients need arterial and central lines (except for dobutamine or milrinone, since no alpha effects) to safety titrate these medications. Of all of the sympathomimetics used in the management of acute heart failure, dopamine and dobutamine are the most common. Both target beta-adrenergic receptors and have positive inotropic effects at lower doses. Dopamine, at higher doses, can increase systemic vascular resistance which may impact cardiac output, making dobutamine a better choice for patients with normal MAPs who need an inotropic agent. Dobutamine is not without its drawbacks, as the peripheral vasodilatory effects that make it useful in acute AHF can also cause tachyarrhythmias. For further discussion on vasopressors, see Chap. 32.

Although initiating vasopressors in the ED is time-consuming, earlier initiation of vasoactive therapy may impact outcomes based on the large Using the Acute Decompensated Heart Failure (ADHERE) registry [9]. Although this study was not prospective or randomized, the investigators evaluated if vasoactive agents were used early (defined as <6 hours) versus later impacted inpatient mortality and found in-hospital mortality was significantly lower in the early group (OR = 0.87; 95% CI: 0.79–0.96; P = .006). Furthermore, the adjusted odds of death increased 6.8% for every 6 hours of treatment delay (95% CI, 4.2–9.6; $p < .0001$). Thus, the therapy initiated in the ED may impact overall mortality and should be considered earlier rather than later.

Milrinone in one prospective study showed that there was no difference when compared against placebo in days of hospitalization, but there were significant occurrences of hypotension, ventricular fibrillation, and tachycardia. These results suggest that routine use of milrinone in most patients admitted with AHF is not indicated, but those select patients with low cardiac output (cold) and hypervolemia (wet) might benefit if other modalities are contraindicated or have failed [49].

Even in hypotensive patients, an assessment of volume is important because they may still be fluid overloaded. For such patients, inotropes should be used as a last resort or if there is clear evidence of shock or organ hypoperfusion [35].

ACE-I

ACE inhibitors work by interrupting the renin–angiotensin system that results in decreased preload and decreased afterload. To date, no controlled, randomized clinical trials exist that evaluate the use of ACE inhibitors in AHF, but they are well accepted in chronic management [28].

Beta Blockers

While beta-blocker therapy is commonly used in chronic AHF because they reverse cardiac remodeling, improve the quality of life, and reduce mortality [28], it has come under greater scrutiny in those patients with preserved EF [50]. Overall, there is no role of beta-blockers in the acute management of AHF. That being said, in patients with preserved EF, tachycardia can decrease preload and cardiac output, and a small dose of beta blocker (for instance, metoprolol 5 mg IV, slow push) that lowers the heart rate may paradoxically improve output.

Hydralazine

As a vasodilator primarily targeting arteries and arterioles, hydralazine decreases peripheral resistance and decreasing afterload and should be an ideal agent for acute AHF. However, for treatment of AHF, it has been poorly studied and data is limited [48]. Should urgent blood pressure reduction be needed in an AHF patient, hydralazine would be a prudent choice, but be aware of rebound hypertension once its effects wear off.

Calcium Sensitizers

Levosimendan is a newer drug class for the treatment of AHF currently available in Europe, but not in the United States. Its mechanism of action is increasing calcium activity inside the cardiac cell (therefore increasing contractility); and relaxation of smooth muscle (causing vasodilation) [51]. Currently, it is under consideration at the FDA for clinical use.

Ultrafiltration

In patients with chronic renal failure, removal of excess fluids is a prudent indication for those with respiratory failure or in embarrassment. In patients without chronic renal failure, continuous renal replacement therapy, specifically ultrafiltration, may be considered in refractory cases in which fluid overload and pulmonary congestion from a specific source (renal failure, acute myocardial infarction) is identified. Those patients with persistent congestion despite diuretic therapy, with or without impaired renal function, may be candidates for continuous venovenous ultrafiltration after discussion with cardiology and renal consultants [15].

Disposition

With aggressive treatment in the ED, impending respiratory failure can be reversed effectively, sometimes making disposition (ICU vs. floor) a challenge. A trial of time off NIPSV or follow-up ABG can assist in disposition. Positive cardiac markers or new/worsened renal failure can also help an ICU disposition occur.

Both fields of cardiology and emergency medicine struggle with how to disposition those patients with mild heart failure, as these patients often have subclinical inadequate perfusion whose symptoms are reversed but have not had the underlying pathophysiology addressed [52]. This accounts for the high readmission rate encountered with AHF. If close follow-up can be arranged or the patient is well known by their primary physician, discharge home is possible. Otherwise, an observation stay may be in order.

References

1. Ambrosy AP, Fonarow GC, Butler J, et al. The global health and economic burden of hospitalizations for heart failure: lessons learned from hospitalized heart failure registries. J Am Coll Cardiol. 2014;63(12):1123–33.
2. Bobrow BJ, Clark LL, Ewy GA, et al. Minimally interrupted cardiac resuscitation by emergency medical services for out-of-hospital cardiac arrest. JAMA. 2008;299(10):1158–65.
3. Heidenreich PA, Trogdon JG, Khavjou OA, et al. Forecasting the future of cardiovascular disease in the United States: a policy statement from the American Heart Association. Circulation. 2011;123(8):933–44.
4. Storrow AB, Jenkins CA, Self WH, et al. The burden of acute heart failure on U.S. emergency departments. JACC Heart Fail. 2014;2(3):269–77.

5. Zile MR, Gaasch WH, Anand IS, et al. Mode of death in patients with heart failure and a preserved ejection fraction: results from the Irbesartan in Heart Failure with Preserved Ejection Fraction study (I-PRESERVE) trial. Circulation. 2010;121(12):1393–405.
6. McDermott MM, Feinglass J, Lee P, et al. Heart failure between 1986 and 1994: temporal trends in drug-prescribing practices, hospital readmissions, and survival at an academic medical center. Am Heart J. 1997;134(5 Pt 1):901–9.
7. McCullough PA, Philbin EF, Spertus JA, Kaatz S, Sandberg KR, Weaver WD. Confirmation of a heart failure epidemic: findings from the resource utilization among congestive heart failure (REACH) study. J Am Coll Cardiol. 2002;39(1):60–9.
8. Haldeman GA, Croft JB, Giles WH, Rashidee A. Hospitalization of patients with heart failure: National hospital discharge survey, 1985 to 1995. Am Heart J. 1999;137(2):352–60.
9. Peacock WF, Emerman C, Costanzo MR, Diercks DB, Lopatin M, Fonarow GC. Early vasoactive drugs improve heart failure outcomes. Congest Heart Fail. 2009;15(6):256–64.
10. Rame JE, Sheffield MA, Dries DL, et al. Outcomes after emergency department discharge with a primary diagnosis of heart failure. Am Heart J. 2001;142(4):714–9.
11. Brar S, McAlister FA, Youngson E, Rowe BH. Do outcomes for patients with heart failure vary by emergency department volume? Circ Heart Fail. 2013;6(6):1147–54.
12. Singer AJ, Birkhahn RH, Guss D, et al. Rapid emergency department heart failure outpatients trial (REDHOT II): a randomized controlled trial of the effect of serial B-type natriuretic peptide testing on patient management. Circ Heart Fail. 2009;2(4):287–93.
13. Angeja BG, Grossman W. Evaluation and management of diastolic heart failure. Circulation. 2003;107(5):659–63.
14. Volpe M, McKelvie R, Drexler H. Hypertension as an underlying factor in heart failure with preserved ejection fraction. J Clin Hypertens (Greenwich). 2010;12(4):277–83.
15. Nieminen MS, Böhm M, Cowie MR, et al. Executive summary of the guidelines on the diagnosis and treatment of acute heart failure. Eur Heart J. 2005;26(4):384–416. https://doi.org/10.1093/eurheartj/ehi044.
16. Forrester JS, Diamond G, Chatterjee K, Swan HJ. Medical therapy of acute myocardial infarction by application of hemodynamic subsets (second of two parts). N Engl J Med. 1976;295(25):1404–13.
17. Silvers SM, Howell JM, Kosowsky JM, Rokos IC, Jagoda AS. American College of Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with acute heart failure syndromes. Ann Emerg Med. 2007;49(5):627–69.
18. Chaudhry A, Singer AJ, Chohan J, Russo V, Lee C. Interrater reliability of hemodynamic profiling of patients with heart failure in the ED. Am J Emerg Med. 2008;26(2):196–201.
19. Fonarow GC. The acute decompensated heart failure national registry (ADHERE): opportunities to improve care of patients hospitalized with acute decompensated heart failure. Rev Cardiovasc Med. 2003;4(Suppl 7):S21–30.
20. Mozaffarian D, Benjamin EJ, Go AS, et al. Executive summary: heart disease and stroke statistics-2015 update: a report from the American Heart Association. Circulation. 2015;131(4):434–41.
21. Lok CE, Morgan CD, Ranganathan N. The accuracy and interobserver agreement in detecting the "gallop sounds" by cardiac auscultation. Chest. 1998;114(5):1283–8.
22. Wang CS, FitzGerald JM, Schulzer M, Mak E, Ayas NT. Does this dyspneic patient in the emergency department have congestive heart failure? JAMA. 2005;294(15):1944–56.
23. Cody RJ. Clinical trials of diuretic therapy in heart failure: research directions and clinical considerations. J Am Coll Cardiol. 1993;22(4 Suppl A):165A–71A.
24. Chakko S, Woska D, Martinez H, et al. Clinical, radiographic, and hemodynamic correlations in chronic congestive heart failure: conflicting results may lead to inappropriate care. Am J Med. 1991;90(3):353–9.
25. Mahdyoon H, Klein R, Eyler W, Lakier JB, Chakko SC, Gheorghiade M. Radiographic pulmonary congestion in end-stage congestive heart failure. Am J Cardiol. 1989;63(9):625–7.
26. Collins SP, Lindsell CJ, Storrow AB, Abraham WT, ADHERE Scientific Advisory Committee, Investigators and Study Group. Prevalence of negative chest radiography results in the emergency department patient with decompensated heart failure. Ann Emerg Med. 2006;47(1):13–8.
27. Gheorghiade MF, Adams KF Jr, Gattis WA, Teerlink JR, Orlandi C, O'Connor CM. Surrogate end points in heart failure trials. Am Heart J. 2003;145(2 Suppl):S67–70.
28. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines. J Am Coll Cardiol. 2013;62(16):e147–239.
29. Maisel AS, Krishnaswamy P, Nowak RM, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. N Engl J Med. 2002;347(3):161–7.
30. McCullough PA, Nowak RM, McCord J, et al. B-type natriuretic peptide and clinical judgment in emergency diagnosis of heart failure: analysis from breathing not properly (BNP) multinational study. Circulation. 2002;106(4):416–22.
31. Maisel AS, Clopton P, Krishnaswamy P, et al. Impact of age, race, and sex on the ability of B-type natriuretic peptide to aid in the emergency diagno-

sis of heart failure: results from the breathing not properly (BNP) multinational study. Am Heart J. 2004;147(6):1078–84.
32. Wang TJ, Larson MG, Levy D, et al. Heritability and genetic linkage of plasma natriuretic peptide levels. Circulation. 2003;108(1):13–6.
33. Maisel A, Mueller C, Adams K Jr, et al. State of the art: using natriuretic peptide levels in clinical practice. Eur J Heart Fail. 2008;10(9):824–39.
34. Pivetta E, Goffi A, Lupia E, et al. Lung ultrasound-implemented diagnosis of acute decompensated heart failure in the emergency department - a SIMEU multicenter study. Chest. 2015;148(1):202–10.
35. Collins S, Storrow AB, Albert NM, et al. Early management of patients with acute heart failure: state of the art and future directions. A consensus document from the Society for Academic Emergency Medicine/ Heart Failure Society of America Acute Heart Failure Working Group. J Card Fail. 2015;21(1):27–43.
36. Agricola E, Bove T, Oppizzi M, et al. "Ultrasound comet-tail images": a marker of pulmonary edema∗: a comparative study with wedge pressure and extravascular lung water. Chest. 2005;127(5):1690–5.
37. Liteplo AS, Marill KA, Villen T, et al. Emergency thoracic ultrasound in the differentiation of the etiology of shortness of breath (ETUDES): Sonographic B-lines and N-terminal pro-brain-type natriuretic peptide in diagnosing congestive heart failure. Acad Emerg Med. 2009;16(3):201–10.
38. Gallard E, Redonnet JP, Bourcier JE, et al. Diagnostic performance of cardiopulmonary ultrasound performed by the emergency physician in the management of acute dyspnea. Am J Emerg Med. 2014.
39. Vital FM, Ladeira MT, Atallah AN. Non-invasive positive pressure ventilation (CPAP or bilevel NPPV) for cardiogenic pulmonary oedema. Cochrane Database Syst Rev. 2013;5:CD005351.
40. Levy P, Compton S, Welch R, et al. Treatment of severe decompensated heart failure with high-dose intravenous nitroglycerin: a feasibility and outcome analysis. Ann Emerg Med. 2007;50(2):144–52.
41. Collins S, Storrow AB, Kirk JD, Pang PS, Diercks DB, Gheorghiade M. Beyond pulmonary edema: diagnostic, risk stratification, and treatment challenges of acute heart failure management in the emergency department. Ann Emerg Med. 2008;51(1):45–57.
42. Cotter G, Metra M, Milo-Cotter O, Dittrich HC, Gheorghiade M. Fluid overload in acute heart failure ? re-distribution and other mechanisms beyond fluid accumulation. Eur J Heart Fail. 2008;10(2):165–9.
43. Cotter G, Metzkor E, Kaluski E, et al. Randomised trial of high-dose isosorbide dinitrate plus low-dose furosemide versus high-dose furosemide plus low-dose isosorbide dinitrate in severe pulmonary oedema. Lancet. 1998;351(9100):389–93.
44. Adams KF Jr, Fonarow GC, Emerman CL, et al. Characteristics and outcomes of patients hospitalized for heart failure in the United States: rationale, design, and preliminary observations from the first 100,000 cases in the acute decompensated heart failure national registry (ADHERE). Am Heart J. 2005;149(2):209–16.
45. Johnson W, Omland T, Hall C, et al. Neurohormonal activation rapidly decreases after intravenous therapy with diuretics and vasodilators for class IV heart failure. J Am Coll Cardiol. 2002;39(10):1623–9.
46. den Uil CA, Brugts JJ. Impact of intravenous nitroglycerin in the management of acute decompensated heart failure. Curr Heart Fail Rep. 2015;12(1):87–93.
47. Wakai A, McCabe A, Kidney R, et al. Nitrates for acute heart failure syndromes. Cochrane Database Syst Rev. 2013;(8):CD005151.
48. Alexander P, Alkhawam L, Curry J, et al. Lack of evidence for intravenous vasodilators in ED patients with acute heart failure: a systematic review. Am J Emerg Med. 2015;33(2):133–41.
49. Cuffe MS, Califf RM, Adams KF Jr, et al. Short-term intravenous milrinone for acute exacerbation of chronic heart failure: a randomized controlled trial. JAMA. 2002;287(12):1541–7.
50. Lund LH, Benson L, Dahlstrom U, Edner M, Friberg L. Association between use of beta-blockers and outcomes in patients with heart failure and preserved ejection fraction. JAMA. 2014;312(19):2008–18.
51. Pathak A, Lebrin M, Vaccaro A, Senard JM, Despas F. Pharmacology of levosimendan: inotropic, vasodilatory and cardioprotective effects. J Clin Pharm Ther. 2013;38(5):341–9.
52. Hogan CJ, Dalawari J, Nassiry A, Ward KR. Sublingual microvascular perfusion defects in acutely decompensated heart failure. Acad Emerg Med. 2008;15(5):S61.