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RESEARCH ARTICLE

Acute Left Heart Failure in the Emergency Room

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ABSTRACT

Acute heart failure (AHF), a rapid or gradual onset of symptoms and/or signs of heart failure severe enough for the patient to seek urgent medical attention, represents a significant and growing healthcare burden. With a prevalence of approximately 1%–2% of the adult population, over 5 million Americans and 15 million Europeans, with a yearly incidence of 550,000, rising ≥ 10% among the elderly. Despite therapeutic advances in chronic heart failure, the prognosis of AHF is poor, with in-hospital mortality ranging from ~2% in hypertensive AHF up to 40-60% in patients with cardiogenic shock, which is a life-threatening state characterized by tissue hypoperfusion resulting in severe multi-organ dysfunction and death. Although no current therapeutic approach has improved mortality in this patient population, incorporating standardized, multidisciplinary shock teams may change. In addition, correct and expedited identification and management of AHF can be challenging due to the heterogenicity of its clinical presentation, precipitant factors, and comorbid conditions. Thus, clinicians involved in patient care should perform a structured diagnostic work-up, starting with high clinical suspicion, followed by key diagnostic tests, including biomarkers, lung ultrasonography, and echocardiography, allowing recognition of the different clinical and hemodynamic profiles and providing guidance to perform further tests and therapeutic interventions. This review discusses the healthcare burden of acute heart failure, highlights the importance of its expedited recognition, and details a proposed diagnostic work-up and individualized management approach in the emergency department. We also perform a concise review of current international guideline recommendations. Future research directions are also provided.

Keywords: Acute heart failure, biomarkers, dyspnea, cardiogenic pulmonary edema

The scope of the problem

Acute heart failure (AHF) (new onset or worsening) requiring urgent therapy [1–4] represents a significant and growing healthcare burden. Its prevalence is approximately 1%–2% of the adult population, over 5 million Americans and 15 million Europeans, with a yearly incidence of 550,000, rising ≥ 10% among the elderly. Heart failure (HF) is a clinical condition characterized because all patients will have acute symptoms triggering ER visits [4–7]. AHF clinical presentation and therapeutic approaches are challenging, given the heterogenicity of the patients and precipitant factors. AHF have higher in-hospital and post-discharge mortality, increasing re-hospitalization rates [8]. Emergency providers play a significant role in managing AHF patients. Therefore, physicians involved in early management start fast-track diagnostic testing and therapeutic approaches to improve the outcome [9].

AHF is characterized by new-onset or worsening symptoms and must be considered a life-threatening medical condition requiring fast stratification and effective treatment, leading to urgent hospital admission [10]. In addition, the acute event may be caused by a primary cardiac event like ischemic heart disease, uncontrolled hypertension, acute valve insufficiency, and inflammatory or toxic factors. Chronic HF clinical worsening can occur more often with infections, uncontrolled hypertension, rhythm disturbances, or non-drug or diet adherence, especially in heart failure reduced ejection fraction (HFrEF) [10]. The most severe HF expression is cardiogenic shock, a life-threatening state characterized by tissue hypoperfusion associated with impaired tissue oxygen metabolism and hyperlactatemia, resulting in severe multi-organ dysfunction and death [11].

High clinical suspicion

High clinical suspicion must be considered in patients with or without a prior history of HF presenting with dyspnea, orthopnea, or systemic congestion. Dyspnea can be transitory or progressive, at rest or exertion, and with or without respiratory distress. In elderly populations presenting with the first episode of AHF, we must exclude ischemic heart disease (extensive coronary artery disease), myocarditis, Takotsubo, new-onset atrial fibrillation, and aortic stenosis [4].

Risk factors and prevention

Several cardiovascular and non-cardiovascular disorders may cause an AHF or worsening chronic HF leading to an in-hospital stay [12]. Therefore, primary prevention of AHF concerns the early diagnosis and treatment of HF causes. Physicians in charge must also consider risk factors, including ischemic heart disease, cardiac valvular disease, hypertension, chemotherapy, and radiotherapy. Secondary prevention concerns include avoiding chronic HF worsening and an acute event requiring hospitalization since each in-hospital stay decreases patient survival [4,7,12].

Clinical profile

The profile included males who are >70 years old and have an HF history (66%-75%) and comorbidities such as diabetes, hypertension, myocardial infarction, coronary artery disease, diabetes, atrial fibrillation, and COPD [7,12,13].

Clinical presentation

The ER physicians must determine the etiology of symptoms in patients with suspected HF based on the initial history, physical examination, biomarkers, and imaging tests [4,8]. Symptoms are often non-specific and, therefore, do not discriminate between HF and other disorders [10]. Dyspnea is the most common and sensitive presenting symptom. However, it is not a congestion-specific indicator. Other symptoms include orthopnea, paroxysmal nocturnal dyspnea, bendopnea, cough, fatigue, abdominal bloating, anorexia, and weight change (Table 1) [4,13]. Also, asthenia and adynamia could be the clinical presentation in the elderly.

The fluid retention HF phenotype has a fast diuretic therapy response. Signs, such as elevated jugular venous pressure and displacement of the apical impulse, maybe more specific but are not easy to detect and have poor reproducibility [10]. AHF clinical presentation is challenging in obese, elderly, and COPD patients. They often have a different etiology, clinical presentation, and outcome in younger than older patients [10].

Table 1 Diagnostic accuracy of the physical exam, chest X-ray, ECG, and LUS findings in AHF patients

Physical Exam	**Sensitivity %**	**Specificity %**
Dyspnea	84	34
Jugular venous distention	39	78
Hepatojugular reflux	24	96
Third heart sound	33	99
Pulmonary crepitations	60	78
Peripheral edema	51	76
Chest X-ray		
Pulmonary venous congestion	54	96
Interstitial edema	74	97
Alveolar edema	6	99
Cardiomegaly	74	78
Pleural effusion	26	92
Pneumonia	4	92
Hyperinflation	3	92
Electrocardiogram		
Atrial fibrillation	26	93
New T-wave changes	24	92
Any abnormal finding	50	78
ST- elevation	5	97
ST depression	11	94
Lung Ultrasound		
B-profile (≥3 B lines in ≥2 areas bilaterally)	88%	90%

Modified from reference 4

Physical examination

The primary purpose is to assess the clinical stability base on blood pressure (BP) and volume status [2,4,14]. Systolic blood pressure helps identify clinical stability or instability and guides therapeutic decisions. **Hypertensive AHF** represents ≥50% of cases, and patients are more likely to be elderly and female and have heart failure preserved ejection fraction (HFpEF). The symptoms start suddenly and usually involve pulmonary congestion. The mortality rates are significantly lower, with in-hospital mortality ranging from 1.7% to 2.5% and post-discharge 2-3 months mortality from 5.4% to 6% [2]. **Normotensive AHF** represents ≥40% of the cases and usually has acute decompensated HFrEF. The symptoms develop gradually and involve significant systemic congestion. The in-hospital mortality range is from 8% to 10% [2]. **Hypotensive AHF** represents 8% of the cases, and most have advanced or end-stage HF. Clinical presentation included a low- cardiac output, tissue hypoperfusion, or cardiogenic shock. In-hospital mortality ranges from 40% to 60% in cardiogenic shock patients [11].

The signs associated with elevated ventricular filling pressures are the following [2,13–15]: jugular venous distention (JVD), jugular venous pressure (JVP) ≥10 cm H_2O, orthopnea, and hepatojugular reflux. Although an infrequent finding, bendopnea is characteristically observed while bending forward when putting on shoes or tying them up. In addition, the square-wave response in BP during the Valsalva maneuver: occurs when the BP rises during the strain phase and remains elevated throughout the strain instead of dropping, as seen in patients without HF. However, this test is rarely used in ER [4].

On the other hand, the evaluation of tissue perfusion orients the physician toward the patient's cardiac index. The perfusion assessment is more complex, given the fewer reliable findings to determine a low cardiac index, and when the cardiac index is ≤ 2.2 l/min/m^2, the patient could have had narrow pulse pressure, long capillary

refill time, cold extremities, oliguria, dizziness, or mental confusion [13,14].

Classification

Characterizing the patient phenotype is essential for therapeutic decision-making. Therefore, the classification required clinical characteristics, precipitating factors, physical examination, and ejection fraction [10]. Classifying patients by systolic blood pressure (SBP) at presentation (hypertensive, normotensive or hypotensive) is a strong predictor of outcome and mortality. It drives therapeutic decisions (i.e., inotropes vasopressors in hypotensive AHF or vasodilators in hypertensive AHF) [2,10]. Another approach is classifying patients according to the following precipitant causes requiring urgent treatment: acute coronary syndromes, hypertensive emergency, arrhythmias, severe bradycardia or conduction disturbance, mechanical cause underlying AHF, or submassive or massive pulmonary embolism [10].

Historically abnormal left ventricular ejection fraction (LVEF) is related to poor outcomes. Patients with normal LVEF (≥ 50%) have HFpEF, and those with reduced LVEF (< 40%) have HFrEF. Patients with LVEF in the range of 40%-49% are heart failure mid-range ejection fraction (HFmEF) [10]. Patients with HF complicating ST-elevation or no myocardial infarction (MI) can be classified, according to Killip and Kimball¨s classification: class I, with no clinical signs of HF; class II, HF with rales and S3 gallop; class III, with acute pulmonary edema and class IV, cardiogenic shock and hypotension (SBP <90 mmHg) with evidence of peripheral vasoconstriction, oliguria, cyanosis, and diaphoresis [10].

Table 2 Society for Cardiovascular Angiography and Interventions (SCAI) classification of cardiogenic shock

Stage	Description	Biomarkers	Hemodynamics
A. At risk	A patient not currently experiencing signs or symptoms of CS is at risk for its development. These patients may include those with extensive myocardial infarction or prior infarction acute and/or acute on chronic heart failure symptoms.	Normal lactate and renal function	Normotensive (SBP≥100 or patient's baseline) If hemodynamics done • Cardiac index ≥2.5 • CVP <10 • PA sat ≥65%
B. Beginning	A patient who has clinical evidence of relative hypotension or tachycardia without hypoperfusion.	Normal lactate Minimal renal function impairment Elevated BNP	SBP <90 ***OR*** MAP <60 ***OR*** >30 mmHg drop from baseline, pulse ≥100; If hemodynamics did: • cardiac index ≥2.2 • PA sat ≥65%
C. Classic	A patient who manifests with hypoperfusion requires intervention (inotrope, pressor, or mechanical support, including ECMO) beyond volume resuscitation to restore perfusion. These patients typically present with borderline blood pressure.	**May include any of:** Lactate ≥2 Creatinine doubling **OR** >50% drop in GFR Increased LFTs Elevated BNP	**May Include Any of:** SBP <90 **OR** MAP <60 **OR** >30 mmHg drop from baseline **AND** drugs/device used to maintain BP above these targets. **Hemodynamics** • cardiac index <2.2 • PCWP >15 • RAP/PCWP ≥0.8 • PAPI <1.85 • cardiac power output ≤0.6
D. Deteriorating /doom	A patient that is similar to category C but is getting worse. They have failed to respond to initial interventions.	**Any of Stage C AND:** Deteriorating	**Any of Stage C AND:** Requiring multiple pressors **OR** addition of mechanical circulatory support devices to maintain perfusion
E. Extremis	A patient experiencing cardiac arrest requiring CPR and / or ECMO is supported by multiple interventions.	**"Trying to die"** CPR (A-modifier) pH ≤7.2 Lactate ≥5	No SBP without resuscitation PEA or refractory VT/VF Hypotension despite maximal support

SBP: Systolic blood pressure; **MAP**: Mean arterial pressure, **ECMO**: Extracorporeal membrane oxygenation, **PCWP**: Pulmonary capillary wedge pressure, **RAP**: Right atrial pressure, **PAPI**: Pulmonary arterial pulsatility index, **VT**: Ventricular tachycardia, **VF**: Ventricular fibrillation.
Adapted from *Baran, DA, Grines, CL, Bailey, S, et al. SCAI clinical expert consensus statement on the classification of cardiogenic shock. Catheter Cardiovasc Interv. 2019; 94: 29– 37.* https://doi.org/10.1002/ccd.28329

Reference 16

In 2019, the Society for Cardiovascular Angiography and Interventions (SCAI) released a consensus statement paper on categorizing cardiogenic shock (Table 2) [16]. The most valuable classifications are based on a clinical presentation at admission, allowing clinicians to identify patients at high risk of complications, immediately start the direct management of specific targets, and establish personalized care in the AHF setting [10].

Work-up

Chest X-ray

This non-invasive test is low-cost, accessible, and used on patients with high clinical suspicion of HF. The AHF radiographic findings are [4,17]: Normal cardiac size or moderate cardiomegaly could suggest HFpEF, and cardiac size increase may or may not be present depending on the etiology. Pulmonary venous cephalization occurs when PCWP is >15 mmHg, interstitial edema, characterized by peripheral septal Kerley B lines, occurs when PCWP is >20 mmHg; alveolar edema presented as a "bat wing opacity," is associated with a PCWP > 25 mmHg; and small or large pleural effusion is suggesting subacute or chronic HF stage [4] (Table 1).

However, the absence of these findings cannot rule out AHF since up to 20% of patients will have no congestion on chest X-rays (Table 1) [13]. Furthermore, pulmonary edema may present atypical features like irregular distribution (pre-existing COPD or other chronic lung diseases) or unilateral or lobar in massive pulmonary embolism or giant emphysematous bulla [4]. Therefore, physicians in the ED should be cautious, notably when excluding AHF in the asymptomatic patient based on radiographic findings alone [9].

Electrocardiogram

The electrocardiogram may suggest a specific cause or precipitant of AHF (Table 1) [9]. However, ischemic heart disease is one of the most common underlying AHF etiologies; therefore, early ECG should always be obtained in AHF patients searching for rhythm abnormalities and dynamic ST changes. Furthermore, chronic HF worsening is associated with increased ventricular and supraventricular arrhythmias, particularly atrial fibrillation and flutter [9,18].

Echocardiography and point of care ultrasonography (PoC US)

Echocardiography is essential in diagnosing AHF in the ER (Table 1). The echocardiogram is a non-invasive and non-expensive test, improving clinical acuity and allowing dyspnea physiopathogenesis. Also, it quickly excludes clinical conditions that mimic an AHF (pulmonary embolism, cardiac tamponade, severe aortic stenosis, etc.). If echocardiography is unavailable, ER staff can perform cardiac and lung ultrasounds [4,8,19]: The systolic function of the left and right ventricle (ejection fraction) valve function, wall motion abnormalities, pericardial effusion, inferior vena cava evaluation, which is an estimate of right atrial pressure, and cardiac structural disorders. Also, it identifies causes that mimic left HF (cardiac tamponade, pulmonary embolism).

HFpEF diagnosis is more challenging than HFrEF diagnosis. Although left ventricular dilatation is frequent in HFpEF patients in early stages, LV hypertrophy and left and right atrial volume increase, reflecting filling pressures increasing diastolic dysfunction [10].

Current clinical guidelines recommend immediate echocardiography in patients with hemodynamic instability and suspected acute life-threatening structural or functional cardiac abnormalities (mechanical complications, acute valvular regurgitation, and aortic dissection). Also, early echocardiography (preferably in the ER or within 48 hours from admission) should be considered in all patients with de novo AHF and those with high clinical suspicion of AHF [10].

Point of care ultrasonography identifies inferior vena cava (IVC) diameter, and changes in respiratory variation can be used to assess the volume status. The IVC collapse index value ((IVC diameter during expiration - IVC diameter inspiration)/(IVC diameter during expiration)) in AHF with volume overload is closer to 1 compared to patients without HF, n whom it is typically between 0.25 and 0.75. This is because the volume overload dilates the IVC, preventing the diameter change during the respiratory cycle (Table 3).

Lung ultrasound

Lung ultrasound is an essential tool to assess AHF patients in the ER. It is an easy-to-learn, accessible technique for giving quick answers, showing diagnostic accuracy superior to chest X-rays [20]. The appearance of multiple, diffuse distributed B-lines in the lungs bilaterally is a handy index for the presence and congestion degree [21]. The diagnostic accuracy is high, with a sensitivity of 94% (95% CI 81–98%) and specificity of 92% (95% CI 84–96%) [22,23], while physical examination has a sensitivity of 62% (95% CI 61–64%) and a specificity of 68% (95% CI 67–69%). Chest X-ray has a sensitivity of 57% (95% CI 55–59%) and a specificity of 89% (95% CI 88–90%) for AHF diagnosis [24]. The high correlation between natriuretic peptides with lung sonography could be used to improve diagnostic accuracy. In most cases,

the lung ultrasound will be faster than natriuretic peptides [25].

Lung ultrasound is more accurate than auscultation or chest X-ray for detecting pleural effusion, consolidation, and alveolar interstitial syndrome in the critical care setting and also possesses a shallow learning curve compared to other ultrasonographic explorations [26]. In addition, Sonographic B lines (lung comets or comet tail artifacts) representing thickened interstitial or fluid-filled alveoli can be used to assess lung congestion. However, similar findings can also be observed in acute respiratory distress syndrome, pneumonia, and chronic interstitial lung disease. Other signs, such as B-line distribution and lung sliding, can be helpful in the differential diagnosis (Table 2)[26].

Additional diagnosis' role in AHF can also be used as an alternative marker of pulmonary decongestion. It can also monitor dynamic changes in B-lines resolution as a treatment response [27–29]. Finally, it predicts readmission according to the pre-discharge persistence of B line [30,31]. Based on this evidence, lung ultrasound is a cornerstone in assessing AHF patients at the ER (high sensitivity and specificity). It is easy to learn and use in diagnosing, treating, and evaluating prognosis. Large multicenter trials with a large sample of patients improving evidence level in international guidelines are mandatory.

Table 3 2021 ESC guideline recommendations for diagnostic measures in AHF [33]

Diagnostic measure	COR	LOE
Natriuretic peptides (BNP, NT-proBNP, MR-proANP) are recommended in all patients with suspected AHF at admission, during the in-hospital stay, and pre-discharge to differentiate AHF from non-cardiac causes of acute dyspnea, for treatment and prognostic purposes	I	A
A 12-lead ECG, chest X-ray, hs-c-Tns, BUN, creatinine, electrolytes, glucose, CBC, LFT, and TSH are recommended at admission and during the in-hospital stay	I	C
Echocardiography is recommended immediately in hemodynamically unstable AHF and within 48 hours when cardiac structure and function are either unknown or may have changed since previous studies	I	C
Pulse oximetry and arterial blood gas analysis are recommended at admission and during hospitalization to assess respiratory function when respiratory failure is suspected	I	C
Measuring blood lactate is recommended at admission and during hospitalization to assess perfusion status when peripheral hypoperfusion is suspected	I	C
Iron status (transferrin, ferritin) should be assessed pre-discharge for prognostic assessment and treatment	I	C

COR: class of recommendation; **LOE:** level of evidence; BNP: B-type natriuretic peptide; NT-proBNP: N-terminal pro B type natriuretic peptide; AHF: acute heart failure; ECG: electrocardiogram; BUN: blood urea nitrogen; CBC: complete blood count; LFT: liver function tests

Laboratory

Upon admission, patients with clinical suspicion of AHF should receive the following laboratory assessment: blood urea nitrogen, creatinine, electrolytes, liver function tests, stimulating thyroid hormone, glucose, complete blood count, and biomarkers (hs-cTn, BNP and D-dimer) [10]. A D-dimer measurement of <500 pg/dL excludes the possibility of pulmonary embolism complicating AHF. Compromised renal function is an essential predictor of AHF outcome. Blood urea nitrogen >43 mg/dL and creatinine > 2.75 mg/dL measurements are predictors of mortality, in-hospital adverse events, and therapeutic failure [32]. Serial determinations of electrolytes every 1-2 days (sodium, potassium, and magnesium) and renal function are mandatory during diuretic use, and abnormal measurements are poor prognostic variables. As evidence is scarce, a significant dilemma occurs when creatinine rises with an inadequate therapeutic response. Most physicians continue diuresis despite a modest creatinine increase. Diuretic or vasodilator therapy discontinuation is recommended with a significant

creatinine increase [33]. Liver function tests are often impaired with AHF due to hemodynamic derangements and may be helpful for management and prognosis [10]. Assessment of procalcitonin levels may be considered in patients with AHF with suspected coexisting infection, particularly for the differential diagnosis of pneumonia and to guide antibiotic therapy [10].

Table 4 Comparison of emerging American & European Guideline recommendations of acute HF management.

	ACC 2022	**COR/LOE**	**ESC 2021**	**COR/LOE**
Fluid Removal	Promptly treat fluid overload with I.V. Loop diuretics, improving symptoms and reducing morbidity. ***Side note***: The goal is the resolution of congestion, symptoms, and rehospitalization rates. Titrate drugs accordingly.	1/B-NR	I.V. Loop diuretics are the cornerstone for patients in AHF with signs of significant fluid overload aiming to improve symptoms. In cases presenting with persistent edema despite loop diuretic titration, consider combining loop diuretics with thiazide-type diuretics.	I/C IIa/B
Preload & Afterload reduction	Consider using I.V. nitroprusside or nitroglycerin as an adjuvant to diuretic therapy in normotensive patients aiming to lower pulmonary congestion.	2b/B-NR	Intravenous vasodilators may be considered to relieve AHF symptoms when SBP is >110 mmHg.	IIb/B
Approach to Hypotensive patients	In patients with CS IV, inotropic support should be used to maintain systemic perfusion and preserve end-organ performance. ***Side note:*** There is limited robust evidence to suggest the clear benefit of one inotrope over another.	1/ B-NR	Inotropic agents can be considered in patients with SBP < 90 mmHg + evidence of hypoperfusion unresponsive to standard therapy. Vasopressors such as norepinephrine can be used in patients with CS. **Side note:** Norepinephrine leads to increased LV afterload and may require inotropic dual therapy.	IIb/C IIb/B
Ventilatory Support	Not addressed	N/A	O2 is recommended in patients with SpO2 <90% or PaO2 <60 mmHg NPPV should be considered in patients with respiratory distress (RR >25 bpm, SpO2 <90%)	I/C IIa/B
VTE Prophylaxis	VTE prophylaxis is recommended if patients are not already on some form of anticoagulation.	1/B-R	VTE prophylaxis is recommended in patients not already anticoagulated and with no contraindication to it to reduce the risk of DVT and PE.	I/A
Mechanical Circulatory support	In patients with CS, temporary MCS is reasonable when the end-organ function cannot be maintained by pharmacologic means to support cardiac function. In patients with CS, management by a multidisciplinary team experienced in shock is reasonable	2a/B-NR 2a/B-NR	Unselected use of MCS in patients with cardiogenic shock is not supported and they require specialist multidisciplinary expertise for implantation.	

AHF: acute heart failure, **COR:** class of recommendation; **LOE:** level of evidence; **CS**: cardiogenic shock, **MCS**: mechanical circulatory support, **VTE**: venous thromboembolism, **SpO2**: peripheral capillary oxygen saturation, **SBP**: Systolic blood pressure. **I.V.**: intravenous, **NPPV**: non-invasive positive pressure ventilation.

Biomarkers

Natriuretic peptides, b-type natriuretic peptide (BNP), prohormone N-terminal (NT) proBNP, and mid-regional pro-atrial natriuretic peptide (mr-proANP) are released by cardiomyocytes in the setting of pressure or volume overload or ischemia [4,32–34]. The predominant hormonal effects of BNP are vasodilatation and natriuresis, antagonizing aldosterone and endothelin. These peptides have demonstrated diagnostic and prognostic utility in AHF and are now the most established HF diagnostic biomarkers in a clinical setting (Table 3).

The BNP cut-off value of <100 pg/mL, NT-proBNP < 300 pg/mL, and mr-proANP <120 pg/mL have a sensitivity, specificity, negative predictive value, and positive predictive value of 90%, 76%, 79%, and 89%, respectively. Both natriuretic peptides are beneficial in excluding HF, mainly when the etiology of dyspnea is unclear [6]. Also, mr-proANP cut-off values of < 120 pg/mL have an NPV (97%) than BNP and NT-proBNP, although its PPV is similar to both

Unexpectedly low BNP levels (<100 pg/ml) have been observed in end-stage HF, flash pulmonary edema (onset 1 hour), acute pulmonary edema flash (papillary muscle rupture with mitral regurgitation (onset <2 hours), massive pulmonary embolism (onset 1 hour) [35], and right-sided AHF and right ventricular myocarditis secondary to systemic lupus erythematosus [36]. The primary mechanism is that the half-life of BNP is 23 minutes. Therefore, it is expected that approximately 2 hours is required to reflect changes secondary to the left or right ventricular dysfunction [35]. However, the mechanism in the case of right ventricular myocarditis is unknown [36]. Furthermore, patients with HFpEF have a smaller left ventricular radius and thicker walls than patients with HFrEF, resulting in proportionally lower NP levels for similar degrees of AHF, suggesting different diagnostic thresholds are needed depending on whether left ventricular ejection fraction is preserved or reduced [9].

Measuring high-sensitivity cardiac troponin T or I (hs-cTn) helps detect ACS as the underlying cause of AHF. However, abnormal measurements are seen in AHF patients, even without myocardial ischemia or an acute coronary event, suggesting ongoing myocardial injury or necrosis in these patients; abnormalities are helpful for risk stratification and decision-making [10]. In addition, recent evidence showed that hs-cTn ≤99th percentile upper reference limit can be used as a marker of low-risk cardiovascular mortality even with high BNP measurements [37].

Therapeutic approach

Treatment goals

The treatment goals are to relieve symptoms and optimize the fluid volume status, restore respiratory function, gas exchange, and oxygen saturation, and improve hemodynamics and end-organ function. Additionally, addressing any underlying cause or precipitant (myocardial ischemia, arrhythmia, infection, anemia, drug toxicity, pulmonary embolism, etc.) is mandatory [4]. The first step is the initial evaluation, monitoring vital signs, airway assessment and stabilization, and optimizing the hemodynamics and tissue oxygenation [10,33,38].

Oxygen therapy and ventilatory support

Oxygen therapy is recommended in patients with AHF and SpO2 of < 90% or PaO2 of < 60 mmHg to correct hypoxemia; the goal is to achieve an SpO2 > 95% (> 90% in COPD patients due to V/Q mismatch) [4,9,10]. It is not recommended as routine therapy in patients without hypoxemia, as it may cause vasoconstriction and reduction in cardiac output. Frequent arterial blood gas is unnecessary and should be restricted to patients in whom oxygenation cannot be readily assessed by pulse oximetry. However, arterial blood gas may be helpful when precise measurements of O2 and CO2 partial pressures are needed. A venous sample might acceptably indicate pH and CO2 [10].

Non-invasive mechanical ventilation (continuous positive airway pressure or bilevel positive airway pressure) is recommended by the AHA/ACC and ESC guidelines in patients with pulmonary edema and respiratory distress because it improves respiratory effort and maintains adequate gas exchange [9,10,38] (Table 4). However, recent randomized control trials failed to demonstrate a mortality benefit over standard therapy or reduced endotracheal intubation rate. Therefore, essential prerequisites for non-invasive mechanical ventilation are hemodynamic stability, full patient cooperation, and the patient's ability to protect their airway. In addition, the response to non-invasive mechanical ventilation should be assessed after 60 minutes.

Mechanical ventilation is required in some AHF patients. It should be considered in severe respiratory distress, non-responders to non-invasive mechanical ventilation, those with cardiogenic shock, or those at high risk of hemodynamic deterioration during intervention or hospital transfer. The primary indication for mechanical ventilation is respiratory failure leading to hypoxemia (SpO2 < 90% PaO2 < 6-7 kPa), hypercapnia, and/or acidosis (pH <7.3 or PaCO2 >9-10 kPa) [2,4].

Pharmacologic therapy

Clinical instability is improved by preload and afterload reduction, inotropic stimulation, and anxiety management. However, loop intravenous diuretics remain the mainstay therapy, and the pharmacologic approach and intervention must be tailored to individual cases in the ER [4].

Fluid removal

Evidence-based treatment for AHF is limited. Therefore, the only Class I recommendation for medical therapy is intravenous loop diuretics (furosemide or bumetanide). These drugs are the first line of treatment in congested AHF patients. However, they should be avoided in those with hypoperfusion signs. The initial recommended dose is 20-40 mg of furosemide (or 1 mg/kg) for new-onset, AHF, or no diuretics use theory. Caution is warranted in very elderly patients whose 10 mg dose should be the initial dose. The diuretic should be administered in the ER as soon as possible, preferably in <20 minutes. In a prospective multicenter, observational cohort study, early treatment (<60 minutes) with intravenous loop diuretics was associated with lower in-hospital mortality in AHF patients presenting at the ER[4,39].

For those on chronic diuretic therapy, the initial intravenous dose should be at least equivalent to the oral dose. The peak effect is seen at the 1st and 2nd hour following intravenous administration and remains by the 6th hour. After, the administration can be given as a bolus or continuous infusion without any difference in effectiveness and immediately after patients arrive at the ER [4,39].

A loop diuretic can be titrated up, or dual treatment with a loop diuretic and thiazide (bendroflumethiazide or metolazone) or spironolactone may be used in patients with treatment failure suspicion. In addition, renal dose dopamine (evidence IIb-B) could potentiate the effect of loop diuretics [38]. Therefore, the lowest dose compatible with stable signs and symptoms should be used after acute congestion improves. Isolated ultrafiltration is an effective alternative for managing congestion: a) removes fluid rapidly, b) avoids the maladaptive renal tubular autoregulatory responses induced by diuretics, and c) has a higher Na+ clearance. However, excessively high isolated ultrafiltration can lead to hypotension, renal hypoperfusion, and acute renal failure requiring dialysis [2,6,40,41].

Endpoints for adequate diuresis include symptom resolution, vital signs, and end-organ function (renal and liver) improvement. Therefore, the diuresis effect should be monitored with careful measurement of fluid intake or output, vital signs, body weight, daily serum electrolytes, magnesium, BUN, and creatinine [2,4].

Preload and Afterload Reduction

Intravenous vasodilators (nitroglycerine, isosorbide dinitrate, nitroprusside, and nesiritide) are the second drugs for symptomatic AHF relief. However, evidence indicating any prognostic benefit is scarce. They optimize preload by decreasing venous tone and afterload by decreasing arterial tone, thus increasing volume stroke. Intravenous vasodilators are recommended for patients with pulmonary edema normotensive or hypertensive (SBP > 100 mmHg) [4]. It should be avoided in hypotensive patients and those with left ventricular outflow tract obstruction [2,6,10,33,38].

The ESC guidelines recommend cautious opioid use in patients with severe dyspnea and anxiety to reduce the sympathetic drive. However, dose-dependent side effects and controversies regarding these patients' potentially elevated mortality risk remain a concern [10].

In patients with chronic HF and ß-blocker therapy, acute cessation is associated with higher in-hospital and short-term mortality. The mechanisms are sympathetic nervous system reactivation inducing myocardial ischemia and ventricular arrhythmias. Evidence supports the continuation of ß-blockers at home unless patients require vasopressors or inotropes on admission. However, in current guidelines, no formal recommendations are given [42,43]. In the ER setting, the physician in charge should decide whether to continue and increase the ß-blocker dose or stop administration and restart after stabilization [4].

Hypotension approach

Inotropic agents represent a rescue therapy for low cardiac output patients. However, this therapy is unfrequent in the AHF setting. The most used sympathomimetics are dobutamine, dopamine, norepinephrine, and epinephrine. The phosphodiesterase inhibitors are milrinone, enoximone, and calcium sensitizers, such as levosimendan. Unfortunately, despite beneficial hemodynamic effects, none of these agents improve clinical outcomes and increase mortality [2,38,40,41].

Patients with HFpEF presenting with hypotension should not receive inotropic therapy and may require a vasopressor aside from diuretic therapy. Dynamic left ventricular outflow obstruction should not receive inotropic sympathomimetics therapy to avoid worsening obstruction in hypotension patients. Instead, they should be treated with beta-blocker therapy, a vasopressor (e.g., phenylephrine or norepinephrine), and intravenous fluid if pulmonary

edema is absent. Dynamic left ventricular outflow obstruction occurs in hypertrophic cardiomyopathy patients [44].

Circulatory Support

Close monitoring of BP, fluid balance, and urine output are essential. Routine invasive hemodynamic evaluation with a pulmonary artery catheter is not indicated for AHF diagnosis. However, it may be helpful in selected cases of hemodynamically unstable patients (hypovolemia suspicion plus pulmonary edema). Also, routine arterial or central venous line use for diagnostic purposes is not indicated [10].

Percutaneous, short-term mechanical circulatory support may be indicated early during the initial resuscitation and stabilization phase, especially with sustained drug-resistant hypotension and pulmonary congestion. The intra-aortic balloon pump is the most widely used mechanical circulatory support therapy. In addition, it can be used to bridge until the implantation of a ventricular assist device or heart transplant in the case of cardiogenic shock [10]. Table 4 shown American and European Guideline recommendations of acute HF management.

ECMO in the ER

Extracorporeal membrane oxygenation (ECMO) shows an exponential increase in respiratory and cardiac failure in adult patients. ECMO is a centrifugal pump capable of propelling up to 8 L/min of blood and venous drainage and arterial return cannulas. A hollow fiber membrane oxygenator is spliced into the circuit that not only provides blood oxygenation but also carbon dioxide (CO2) clearance via sweep gas flow [45]. Indications for Veno-arterial ECMO use in cardiac failure include severe refractory cardiogenic shock, refractory ventricular arrhythmia, active cardiopulmonary resuscitation for cardiac arrest, and acute or decompensated right heart failure providing biventricular support [46,47]. The most typical indication of vA-ECMO is cardiogenic shock refractory to medical therapy [48,49]; recent evidence suggests high survival rates (51% to discharge), being used as rescue therapy [50]. Percutaneous cannulation is now preferred over surgical cannulation in most patients. Percutaneous cannulation can be done quickly in the ER and is increasingly performed by intensivists, cardiologists, interventional radiologists, and other related specialists [51].

The ELSO's current recommendations for VA ECMO in adult cardiac patients are as follows [49]

- ECMO should be considered for patients who experienced cardiogenic shock within the first 6 hours, those with conditions refractory to conventional pharmacological and fluid therapy, those with reversible cardiocirculatory collapse, and those eligible for alternative cardiocirculatory assistance, such as those with ventricular assist devices (VADs) or transplantation.
- Etiologies compromising appropriate ECMO function (aortic regurgitation) should be considered to represent potential contraindications.
- Age, per se, is not an absolute contraindication.
- A prognostic score may provide information regarding decision-making before ECMO.
- Poor life expectancy, severe liver disease, acute brain injury, vascular disease, and immunocompromised represent exclusion criteria for ECMO application.

Conclusions

AHF, a life-threatening medical condition requiring urgent assessment, represents a significant and growing healthcare challenge. Despite therapeutic advances in chronic heart failure, the prognosis of AHF is poor, with in-hospital mortality ranging from ~2% in hypertensive AHF up to 40%-60% in cardiogenic shock patients. Currently, no therapeutic intervention has convincingly improved mortality in this population. Therefore, clinicians involved in early therapeutic approaches and fast-track risk stratification to improve immediate outcomes in a heterogeneous population are mandatory. In addition, combining lung ultrasonography with echocardiography is cost-effective in identifying early lung congestion severity and the triggering mechanism. Finally, recent evidence points to the mortality benefits of multidisciplinary cardiogenic shock teams and the early use of advanced mechanical circulatory support.

Future research focused on optimizing public health programs and strategies for primary and secondary cardiovascular risk reduction could reduce the incidence of AHF. Also, the development of novel myotropic, inotropes, or therapeutics could improve the outcome for patients with advanced heart failure and/or cardiogenic.

Take-home message

- Acute HF is a life-threatening medical condition requiring urgent evaluation and treatment, typically leading to urgent in-hospital admission.

- AHF comprises a broad spectrum of clinical conditions with different pathophysiologies and precipitating factors.
- In patients presenting with dyspnea and/or systemic or pulmonary congestion, with or without a prior history of HF, fast and effective management is critical in AHF high clinical suspicion patients.
- It is mandatory to exclude severe and extensive coronary artery disease, myocarditis, aortic valve disease, and atrial fibrillation in the elderly populations presenting with the first episode of AHF.
- Initial and careful SBP, congestion, and perfusion evaluation established the patient's underlying hemodynamic state and clinical profile.
- The diagnostic work-up has to include classification and decision-making. However, clinical correlation is fundamental for starting therapy.
- Normal or moderate cardiac size on chest X-ray, associated with pulmonary or systemic congestion, could suggest HFpEF.
- Echocardiography is mandatory in all AHF-suspected patients.
- BNP cut-off value of <100 pg/mL and NT-proBNP <300 pg/mL have a sensitivity, specificity, negative predictive value, and positive predictive value of 90%, 76%, 79%, and 89%, respectively, to exclude HF.
- Unexpectedly low BNP measurements (<100 pg/ml) can be detected in end-stage HF, flash pulmonary edema (onset 1 hour), acute pulmonary edema secondary to papillary muscle rupture with mitral regurgitation (onset <2 hours), massive pulmonary embolism (onset 1 hour) right-sided AHF, and right ventricular myocarditis secondary to systemic lupus erythematosus.
- Routine invasive hemodynamic evaluation with a pulmonary artery catheter is not indicated for diagnosing AHF.
- A routine arterial blood gas is not needed and should be restricted to patients in whom oxygenation cannot be readily assessed by pulse oximetry.
- Non-invasive mechanical ventilation is recommended in AHF patients with respiratory distress.
- Diuretic therapy remains the mainstay therapy for AHF. However, a better understanding of the underlying pathophysiology of the patient's condition establishes the start of preload and afterload reduction and/or inotropic support.
- If an ECMO team is available, ECMO should be started in the ER in cardiogenic shock patients.
- Early treatment with intravenous loop diuretics reduces in-hospital mortality.
- Home therapy with ß-blockers must be discontinued in the acute phase. Restart ß-blockers when clinical conditions improve, enhancing in-hospital stay and short-term prognosis.
- Optimal treatment initiation, once hemodynamic stability is achieved, improves the outcome in HFrEF or HFpEF patients.

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