

DECOMPENSATED HEART FAILURE AND CARDIOGENIC SHOCK

ACUTE DECOMPENSATED HEART FAILURE

Definition

Acute decompensated HF refers to rapid onset of or acute worsening of symptoms and signs of heart failure.^{1, 2} Worsening of symptoms may also be gradual leading to an unplanned hospital admission or an emergency department visit.

Aetiology

In most cases, decompensated HF arises as a result of **deterioration** in patients with a previous diagnosis of HF (either HFrEF or HFpEF), but may also be the first presentation of HF ('de novo' **acute HF**) (Figure 1 and Table 1). The most common comorbid conditions are hypertension (73%), coronary artery disease (57%), and diabetes (44%). Acute right heart failure can occur because of abruptly increased RV afterload (pulmonary embolus, hypoxia, acidemia) or decreased RV contractility (RV ischemia, myocarditis, postcardiotomy shock).³ Approximately 20% of acute HF after non-cardiac surgery patients meet the criterion for MI, whereas 80% have chronic myocardial injury with hs-cTn levels above the 99th percentile of the URL.⁴

Presentation and Prognosis

Clinical presentation depends on cardiac output and alterations in vascular compliance (Table 2). Most of the patients with acute HF present with normal or high blood pressure and with symptoms and/or signs of congestion rather than low cardiac output.⁵ Chest x-ray is variably sensitive for the presence of interstitial or alveolar edema, but natriuretic peptides, both BNP and NT-proBNP, are invariably elevated. Rising or persistently elevated blood levels of the interleukin receptor ST2 correlate with adverse clinical outcomes, during the first year after hospitalization with acute HF.⁶ Global longitudinal strain has a better prognostic value than LVEF.⁷ Renal dysfunction plays a central role in the pathophysiology of acute heart failure and the cardiorenal syndrome is a recognized complication of acute heart failure.⁸ Distinguishing true acute kidney injury from functional causes of fluctuations in serum creatinine in the context of diuresis for acute decompensated HF is critical in ensuring delivery of goal-directed medical therapies. It is exacerbated by continuing use of diuretics that reduce glomerular filtration rate.

Primary acute HF is the leading cause of hospitalization in patients over 65 years old with a high in-hospital (4%–10%) and one-year (20-30%) mortality rates (Table 3).⁴ Renal dysfunction, systolic blood pressure <115 mm Hg and an elevated troponin level are associated with worse outcome.^{9, 10} Preserved systolic function is found in up to 50% of patients and carries a better prognosis.¹⁰

Acute right ventricular (RV) failure can be defined as a rapidly progressive syndrome caused by RV dysfunction through impaired RV filling and/or reduced RV flow output and in most cases accompanied by venous congestion. Acute RV failure is often under-recognized leading to significant morbidity and mortality.¹¹

Therapy

General principles are presented in Tables 4-6, and Figures 2-9. See also Therapy of Advanced HF in the Chapter on Therapy of Chronic HF. For post-MI cardiogenic shock see also the Chapter on ACS Therapy. Patients with ACS and AHF are always considered a very high-risk group, and an immediate invasive strategy is also recommended in these patients, regardless of ECG or biomarker findings.¹²

Early coronary angiography is also indicated in acute HF patients with possible ischaemia.¹³ Serial NT-proBNP measurements are not useful for the guidance of therapy during admission for acute heart failure.¹⁴ Routine use of pulmonary artery catheter is not recommended and should be restricted to cases that do not respond to IV diuretics.¹⁵ Pulmonary capillary wedge pressure is not an accurate reflection of LV end-diastolic pressure in patients with mitral stenosis, aortic regurgitation, pulmonary venous occlusive disease, ventricular interdependence, high airway pressure, respirator treatment, or a poorly compliant LV.

Oxygen is administered via a nasal cannula (4 L/min). Non-invasive ventilation is more effective in improving symptoms but has no effect on outcome (a PEEP of 5-10 cmH₂O; FiO₂ delivery ≥ 0.40 , usually for 30 min/h). Care should be taken in serious obstructive airways disease to avoid hypercapnia.

Non-invasive ventilation (NIV) refers to all modalities that assist ventilation without the use of an endotracheal tube but rather with a sealed face-mask. NIV with positive end-expiratory pressure (PEEP) should be considered as early as possible in every patient with acute cardiogenic pulmonary oedema and hypertensive acute HF, as it improves clinical parameters including respiratory distress. NIV with PEEP improves LV function by reducing LV afterload. Potential complications are worsening of right ventricular failure and pneumothorax, and it should be used with caution in cardiogenic shock and right ventricular failure.

Morphine may be required for alleviation of acute symptoms but has been associated with

worse outcome.¹⁶

Intravenous loop diuretics are essential.¹⁷ When large doses are required, a continuous infusion has greater efficacy and less ototoxicity than IV boluses, although no difference was seen in the DOSE trial.¹⁸ High doses of IV loop diuretics do not substantially worsen renal failure,¹⁸ and even if they do (creatinine rise >0.3 mg/dL) this does not necessarily indicate renal tubular injury and worse prognosis in these patients.^{19, 20} Additional use of a thiazide such as **metolazone** provides a synergistic effect, even in patients with renal failure.²¹

Acetazolamide, a carbonic anhydrase inhibitor that reduces proximal tubular sodium reabsorption, improves the efficiency of loop diuretics, potentially leading to more and faster decongestion in patients with acute decompensated heart failure with volume overload, at a dose of 500 mg IV od.²²

Diuresis is continued until physical findings (JVP) and biomarker trends suggest euvolemia. Weight loss is desirable but cannot be used as a surrogate marker for clinical outcomes. A urinary catheter is helpful.

After diuretics, **vasodilators** are the most common intravenous therapy for acute HF, but there has been no robust evidence supporting their ability to provide meaningful effects on clinical outcomes, except perhaps early symptom improvement. **Nitroglycerin** is administered with a starting dose 10-20 mcg/min IV and targeting a systolic BP not lower than 95 mm Hg. Tolerance is being developed on continuous use after 24-48 h and the efficacy and safety of IV nitrates is uncertain. Alternatively, **nitroprusside** (starting dose 0.1-0.3 mcg/kg/min with BP monitoring through an arterial line) can be given. It is light sensitive and administration line should be covered.

Ultrafiltration is an invasive fluid removal technique implemented through two large-bore peripherally inserted venous lines. It may supplement or obviate the need for diuretic therapy, particularly in non-responders,²³ but its efficacy is not established.²⁴

Beta blockers are discontinued only in hemodynamically unstable patients. Withdrawal of beta-blocker in patients with decompensated heart failure is associated with increased mortality.²⁵

Inotropes are **synthetic catecholamines**, **phosphodiesterase inhibitors**, and **calcium sensitizers**. They are indicated in development of cardiogenic shock, eg low cardiac output with hypotension and/or pulmonary congestion despite appropriate afterload reduction, and development of cardiorenal syndrome. They should be used with caution even in short-term, since they increase both in-hospital and post-discharge mortality, particularly with long-term therapy.²⁶⁻²⁸ Beta blockers should not be used concomitantly with inotropes to avoid competitive binding of b receptors.²⁹

Catecholamines mediate their cardiovascular actions through α_1 , β_1 , β_2 , and dopaminergic receptors.³⁰ β_1 -adrenergic receptor stimulation results in enhanced myocardial

contractility, and enhanced chronotropy. b2-adrenergic receptor stimulation on vascular smooth muscle cell results in vasodilation. Activation of a1-adrenergic receptors on arterial vascular smooth muscle cells results in smooth muscle contraction and an increase in systemic vascular resistance. Stimulation of D1 and D2 dopaminergic receptors in the kidney and splanchnic vasculature probably results in renal and mesenteric vasodilation through activation of complex second-messenger systems, although the mode of action of dopamine is debated. cAMP stimulation by these agents and consequent Ca overload of the sarcoplasmic reticulum and release of Ca into the cytoplasm, may trigger arrhythmias and increase mortality.

Dobutamine binds b1 and b2 receptors at a 3:1 ratio. It has minor effect on a1 receptors, and at doses <5 mcg/kg/min, the net effect is mild vasodilation. In doses <15mcg/kg/min it increases cardiac contractility without affecting peripheral resistance. It can be given by a peripheral IV line. Tolerance may develop after a few days and arrhythmias may occur at any dose as with any other inotrope.³⁰

Dopamine binds b1, b2, a1 and dopaminergic receptors. It is indicated in severe hypotension and worsening of renal function (cardiorenal syndrome). In “renal” doses (0.5-3 mcg/kg/min), dopamine promotes vasodilation and increased blood flow to renal tissue and has natriuretic effects on renal tubules. However, it does not increase glomerular filtration rate and a renal protective effect has not been demonstrated.³¹ In patients with acute heart failure and renal dysfunction (estimated glomerular filtration rate of 15-60 mL/min/1.73 m²), neither low-dose dopamine nor low-dose nesiritide enhanced decongestion or improved renal function when added to diuretic therapy, and there was a trend of worse outcomes in patients with preserved left ventricular systolic function (ROSE trial).³² At doses of 3-10 mcg/kg/min there is increased cardiac contractility and systemic vascular resistance. Dopamine should be given through a central line to avoid tissue extravasation. If despite this the blood pressure remains <70 mm Hg, **norepinephrine** (0.01-3 mcg/kg/min) is preferred to **epinephrine** that may promote coronary thrombosis.^{33, 34}

Milrinone inhibits phosphodiesterase 3, an enzyme in the sarcoplasmic reticulum that breaks down cAMP into AMP. It has inotropic, vasodilator (especially pulmonary) and lusitropic (improvement of diastolic relaxation) effects. It causes more significant RV afterload reduction and less myocardial oxygen consumption than the catecholamines, and no tolerance is developed with prolonged use. However, outcomes are similar to these with dobutamine in acute decompensated failure.³⁵ Milrinone may be deleterious in ischemic cardiomyopathy.³⁶

Levosimendan is a Ca sensitizer that improves contractility by enhancing binding of Ca to troponin C. Its superiority over dobutamine is controversial,³⁷ and life-threatening hypotension and cardiac arrhythmias may occur, especially at high doses.³⁸ Levosimendan or

type-3-phosphodiesterase inhibitors may be preferred over dobutamine for patients on beta-blockers as they act through independent mechanisms.³⁹ New inotropic agents are under development.²⁸

Other drugs

Vasopressin (antidiuretic hormone) causes vascular smooth muscle constriction (V1 receptors) and water reabsorption (V2 receptors). It causes less coronary and cerebral vasoconstriction than catecholamines. It is mainly used in cardiopulmonary arrest (40 u bolus).

Serelaxin, a recombinant human relaxin-2, a vasoactive peptide hormone, was recently associated with a reduction of 180-day mortality in patients admitted with acute heart failure (RELAX-AHF trial),⁴⁰ although the effects on mortality were primarily driven by reduction in mortality from other CV causes and sudden death, without apparent impact on HF deaths.⁴¹ The beneficial effects have also been seen in acute heart failure in the context of preserved LVEF.⁴² However, no effect on the incidence of death from CV causes at 180 days, or the incidence of worsening heart failure in the first 5 days was detected by the RELAX-AHF-2 trial.⁴³

Nesiritide is a recombinant BNP that was approved for normotensive patients who do not respond to adequate doses of diuretics, but no benefit was seen in the ASCEND-HF,⁴⁴ or the ROSE³² trial. It may cause arrhythmias and hypotension.

Ularitide, the chemically synthesized form of urodilatin, a human natriuretic peptide, has also been promising.⁴⁵

Other vasodilating agents are under study.⁴⁶

Iron-deficiency patients should be given IV **ferric carboxymaltose** after the acute episode.⁴⁷

Intraaortic balloon counterpulsation may be required in non-responsive cases. It can be used up to 3-4 weeks. It is contraindicated in AR or aortic dissection.

Mechanical circulatory support may be used a bridge to recovery in potentially reversible forms of acute heart failure (see Cardiogenic Shock).

Pregnancy

Recommendations for the management of acute heart failure in pregnancy are provided in Figure 10 and Table 7.⁴⁸

Discharge

Recommendations for pre-discharge and early post-discharge follow-up are presented in Table 8. In older patients who were hospitalized for acute decompensated heart failure, an early, transitional, tailored, progressive rehabilitation intervention that included multiple

physical-function domains resulted in greater improvement in physical function than usual care (REHAB-HF trial).⁴⁹

CARDIOGENIC SHOCK

Definition

Cardiogenic shock is a low cardiac output state resulting in life-threatening end-organ hypoperfusion and hypoxia.^{50, 51} It can be due to cardiac causes such as end-stage or acute heart failure, myocardial infarction, advanced valvular disease, and arrhythmias (Figure 11 and Table 8).⁵² The term **mixed cardiogenic shock** that in addition to insufficient cardiac output leading to end organ hypoperfusion, there are also underlying conditions such as low volume status, and systemic vascular resistance.⁵³ In primary CS, a low or normal SVR (eg, <1000–1200 dynes*sec/cm⁵) or SVR index (eg, <2000–2400 dynes/sec/cm⁵/m²) may be considered suggestive of a mixed cardiogenic shock state with a contribution of systemic vasodilation. In patient with primary vasodilatory shock, a normal or inappropriately or cardiac index (eg, <2.5 L/min/m²) or low CO (eg, <6 L/min) with adequate volume resuscitation, and particularly in the presence of elevated diastolic intracardiac pressures (central venous pressure ≥8–12 mm Hg and/or pulmonary capillary wedge pressure ≥12–15 mm Hg), should prompt consideration of a secondary cardiac contribution to the cause of shock.⁵³

Aetiology and Pathophysiology

Cardiogenic shock due to heart failure accounts for 16% of all types of shock, the remainder being due to sepsis or anaphylaxis (62%), hypovolemia (16%), and other causes such as tamponade, pulmonary embolism and pneumothorax.⁵⁴ Cardiogenic shock occurs in 5-8% of patients with ST-elevation myocardial infarction and 2.5% of non-STEMI. Predominant RV shock represents 5% of all cardiogenic shock cases.⁵⁵ Risk factors for development of shock in the context of MI include delayed reperfusion, old age, anterior MI, hypertension, diabetes mellitus, multivessel coronary artery disease, history of prior MI or heart failure, and left bundle-branch block. Mechanical complications of MI, including rupture of the ventricular septum (mortality >80%), free wall, or papillary muscles and chordae cause 12% of CS cases. Abnormalities of ventricular relaxation and compliance, neurohormonal changes, excessive nitric oxide production, and inappropriate vasodilation as part of the systemic inflammatory response syndrome caused by the MI, and excessive use of medications such as beta blockers, ACE inhibitors, morphine and diuretics have been postulated as additional responsive factors. Although LVEF may be moderately depressed (in the SHOCK trial mean LVEF was 30%) it is still a prognostic indicator.⁵⁶

Diagnosis

The patient typically presents with cool and clammy extremities, decreased urine output (<0.5 ml/kg/h), and altered mental status (obtundation, disorientation, and confusion). Haemodynamic status is compromised with systolic blood pressure <90 mm Hg or mean arterial pressure <60 mm Hg, and cardiac index < 2.2 L/min/m², and capillary wedge pressure >15 mm Hg (Table 9, and Figure 12).

The clinical examination and chest radiograph are not reliable predictors of pulmonary capillary wedge pressure, and pulse oximetry may be unreliable due to peripheral vasoconstriction. Pulmonary artery and pulmonary wedge pressures can be measured with a pulmonary catheter or with Doppler echocardiography. A short mitral deceleration time (≤ 140 ms) is highly predictive of pulmonary capillary wedge pressure ≥ 20 mm Hg in CS. In patients with post-MI cardiogenic shock, the short-term mortality risk is predicted by clinical comorbidity parameters as those used by the IABP-SHOCK II risk score.⁵⁷ Despite advances in temporary mechanical circulatory support technology in the past 2 decades, studies have reported 30% to 50% mortality at 6 to 12 months, though this may exceed 70% depending on severity of shock and individual patient factors.⁵²

Therapy

General measures are presented in Tables 10-12, and Figures 13-18. Mortality even with optimum therapy is approximately 50%.⁵¹ In the 2016-2020 registry of the Cardiogenic Shock Working Group (CSWG) on 3455 patients, there was a 35% in-hospital mortality, with higher mortality among patients with acute MI CS (42%).⁵⁸ Despite advances in revascularization and increasing use of mechanical circulatory support during the past 2 decades, RCTs have largely failed to identify treatment strategies that reliably improve mortality other than early revascularization for acute MI-CS.⁵¹ The first trial to demonstrate any benefit with mechanical circulatory support was the DanGer Shock RCT, which showed that early use of a microaxial flow pump in select patients with (STEMI)- related shock.⁵⁹ Pregnant patients in cardiogenic shock/dependent on inotropes should be transferred early to a facility where mechanical circulatory support is available.⁶⁰ The VIP rule, ie ventilate (oxygen administration), infuse (fluid resuscitation), and pump (vasoactive agents), is useful. Arterial oxygenation and near-normal pH should be maintained if necessary, with ***mechanical ventilation via mask or intubation in case of hypoxemia and pH <7.30*** . Positive end-expiratory pressure decreases preload and afterload. An abrupt decrease in arterial pressure after the initiation of invasive mechanical ventilation strongly suggests hypovolemia, and a decrease in venous return. The use of sedative agents should be kept to a minimum to avoid further decreases in arterial pressure and cardiac output.

Fluid administration in order to ensure adequate right-sided filling pressure and LV preload are necessary. Fluids (usually crystalloid solutions) should be infused rapidly but without exceeding 300 - 500 ml over 20 - 30 minutes. When the RVEDP is > 20 mm Hg, ventricular septum shift towards the LV may impair systolic function, and to avoid pulmonary oedema, the central venous pressure should be monitored.

Inotropic and especially **vasopressor** agents should be used in the lowest possible doses. Preferred agents are dopamine (2-50 mcg/kg/min) with or without dobutamine (2-40 mcg/kg/min) and norepinephrine (0.01-3 mcg/kg/min) for more severe hypotension.³⁰ Norepinephrine is associated with fewer arrhythmias than other inotropes,⁵⁰ and, in patients who have undergone successful primary angioplasty, results in less refractory shock than epinephrine (0.01-1 mcg/kg/min).³⁴ A combination of the inotrope levosimendan (0.05-0.2 mcg/kg/min) with the vasopressor noradrenaline may be the most effective management option,⁶¹ but no randomised data exist.

In cases of decompensated chronic pulmonary hypertension, milrinone often induces hypotension and potentially RV ischaemia, making dobutamine the preferred option. However, if acute RV failure is secondary to left heart failure, milrinone or levosimendan may offer greater benefit. Norepinephrine should be used alongside inodilators to maintain systemic pressure.¹¹

In post-MI shock, *early revascularization* with PCI or CABG (even in suitable patients >75 years of age) remains the cornerstone of therapy offering >10% increases in survival.^{56, 62} The survival benefit may be seen as long as 48 hours after MI and 18 hours after shock onset. Fibrinolysis can be considered when PCI cannot be accomplished in a timely fashion.⁵⁰ The mean arterial pressure should be kept between 85 to 100 mm Hg.⁶³

Percutaneous VSD closure is an evolving therapeutic modality in post-MI patients.

Intensive insulin therapy improves survival in hyperglycemic critically ill patients and is recommended for use in complicated MI.

Routine use of **intra-aortic balloon pumping** theoretically improves coronary and peripheral perfusion via diastolic balloon inflation and augments LV performance via systolic balloon deflation with an acute decrease in afterload. However, its use is not justified for post-MI cardiogenic shock following the IABP-SHOCK II trial.^{64, 65}

Mechanical circulatory support

Long-term mechanical support (**LVAD**) and short-term venoarterial extracorporeal membrane oxygenation provides cardiorespiratory support (**ECMO**, **Impella**, **Tandem Heart**) may be used as a bridge to recovery. Commercially available devices for short-term mechanical circulatory support are presented in Table 12.⁶⁶⁻⁷⁰ Additional LV unloading with the Impella device may be beneficial in patients with cardiogenic shock treated with ECMO (**ECMELLA** approach). Bleeding and thrombotic complications jeopardize outcomes in patients with

cardiogenic shock supported with percutaneous ventricular assist devices, and a standardized anticoagulation management protocol guided by parallel measurements of anti-Xa activity and APTT has been proposed.⁷¹ Venoarterial extracorporeal membrane oxygenation (*ECMO*), especially with LV unloading (*ECMELLA* approach) may reduce mortality but randomized data-derived evidence is conflicting. There has been observational evidence from registries that such approaches may reduce mortality albeit at a high complication rate.⁷²⁻⁷⁵ However, randomised clinical trials on mechanical circulatory support have been neutral by means of survival.⁷⁶⁻⁷⁹ Extracorporeal life support (V-A ECMO) also failed to reduce mortality in the ECLS-RCT.⁸⁰ Previous randomized trials did not show a clinical benefit of microaxial flow pumps in patients with acute myocardial infarction and cardiogenic shock, and registry studies have consistently shown excess bleeding among patients who received a microaxial flow pump. However the larger DanGer Shock RCT demonstrated that the routine use of a microaxial flow pump (IMPELLA CP) with standard care in the treatment of patients with STEMI-related cardiogenic shock promoted heart recovery and led to a lower risk of death from any cause at 180 days than standard care alone.^{81, 82} Algorithms for the use of temporary mechanical circulatory support in cardiogenic shock following acute MI or in the context of heart failure have been provided by AHA and ACC (Figures 14-17).⁶⁸

The management of cardiogenic shock in **pregnancy** is presented in Figure 10 and Table 7.⁴⁸

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