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Acute heart failure: differential diagnosis and treatment

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Acute heart failure is a heterogeneous clinical syndrome and is the first cause of unplanned hospitalization in people >65 years. Patients with heart failure may have different clinical presentations according to clinical history, pre-existing heart disease, and pattern of intravascular congestion. A comprehensive assessment of clinical, echocardiographic, and laboratory data should aid in clinical decision-making and treatment. In some cases, a more accurate evaluation of patient haemodynamics via a pulmonary artery catheter may be necessary to undertake and guide escalation and de-escalation of therapy, especially when clinical, echo, and laboratory data are inconclusive or in the presence of right ventricular dysfunction. Similarly, a pulmonary artery catheter may be useful in patients with cardiogenic shock undergoing mechanical circulatory support. With the subsequent de-escalation of therapy and haemodynamic stabilization, the implementation of guideline-directed medical therapy should be pursued to reduce the risk of subsequent heart failure hospitalization and death, paying particular attention to the recognition and treatment of residual congestion.

Acute heart failure (AHF) is defined by a rapid or gradual onset of symptoms and/or signs of heart failure (HF) leading the patient to seek urgent medical attention with consequent unplanned hospitalization or an emergency department visit. This condition typically requires initiation or intensification of treatment.[1]

Acute heart failure may present as a clinical deterioration in patients with a previous diagnosis of HF (acute decompensated HF) or '*de novo*' in patients without a previous history of HF, and all these clinical presentations may occur as a new onset or exacerbation of pre-existing HF.[2]

Clinical presentations typically differ according to the main mechanisms involved, even if may—in certain cases—overlap:[1]

- Acutely decompensated HF: usually in a context of left ventricular (LV) dysfunction with increasing filling pressure, sodium, and fluid retention (most common form, accounting for 50–70% AHF presentations)
- Acute cardiogenic pulmonary oedema, due to fluid redistribution to the lungs leading to acute respiratory failure, it has typically a rapid onset due to increasing afterload and/or LV diastolic dysfunction or due to a severe valvular lesion; also, acute decompensated heart failure (ADHF) patients may frequently present with signs of pulmonary congestion/pulmonary oedema
- Isolated right ventricular (RV) failure, due to predominant RV dysfunction and/or pre-capillary pulmonary hypertension, typically with increased central and splanchnic venous pressure and often systemic congestion
- Cardiogenic shock, in which a severe cardiac (either LV, RV, or biventricular) dysfunction leads to inadequate

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cardiac output, systemic hypotension, and end-organ hypoperfusion, typically with a biphasic course (an initial compensatory increase of systemic vascular resistance (SVR) with a subsequent decrease in the advanced phases of shock).

Despite the improvements in HFrEF treatment, AHF is still associated with poor outcomes, with 4–10% rates of in-hospital mortality (up to 50% in CS)[3] and 30% at 1-year follow-up.[1,4]

Clinical approach to acute heart failure: one size does not fit all

A 7-item stepwise approach has been proposed for the management of AHF patients, based on the clinical profile (presence/absence of congestion and/or hypoperfusion), pathophysiology (fluid redistribution or accumulation, hypoperfusion), precipitants (e.g. infections, arrhythmias, thyroid disorders, non-adherence to therapy, uncontrolled hypertension, and so on), underlying cardiac pathology (e.g. valvular heart disease, cardiomyopathy), patient comorbidities and relevant conditions (e.g. renal or hepatic dysfunction, pulmonary disease, bleeding risk), potential iatrogenic harms associated with diagnostic procedures or treatment, patient preferences and ethical considerations, which should be integrated into the personalization of the treatment.[4]

According to clinical profile (i.e. congestion and perfusion status), 70% of HF patients present a 'warm-wet' profile at admission, and 20% a 'wet-cold' profile. Only less than 1% of patients present with a 'dry-cold' profile. Remainders have a 'dry-warm' profile (absence of congestion and hypoperfusion), a condition which should suggest an up-titration of medical therapy.[5]

Further characterization of AHF patients may be based on the pattern of fluid distribution (i.e. pulmonary and/or systemic congestion) and the presence/absence of systemic hypoperfusion. This categorization is probably among the most relevant given its therapeutic implications.

Most AHF patients present with acutely decompensated HF, in which symptoms rely on pulmonary and/or systemic vascular congestion typically caused by LV dysfunction, even if RV involvement is not infrequent, especially in advanced HF. Management of RV failure may be particularly challenging due to the complexity of non-invasive assessment of the RV function and the different therapeutic implications. ADHF patients have a 1-year mortality rate of about 25%, while isolated right HF, despite uncommon (around 3% of all AHF diagnoses), exceeds 30% 1-year mortality.[3]

Patients with *de novo* HF have fewer comorbidities than ADHF patients and often have a catastrophic clinical presentation (cardiogenic shock or pulmonary oedema) due to acute cardiac ischemia, severe acute valvular lesion (typically regurgitant lesion), inflammatory process (e.g. myocarditis) or toxins.[6] These patients, despite a similar natural course and symptoms, tend to have a better prognosis than acutely decompensated chronic HF. In these patients, the typical mechanism is an acute haemodynamic derangement caused by LV systolic dysfunction. ADHF patients commonly present with pulmonary and/or peripheral congestion, left (and eventually right) ventricular dysfunction, and maladaptive neurohormonal activation in the context of a chronic illness in which exacerbations gradually reduce functional reserve, and in which mortality and HF chronicity are strictly interweaved.[6] Right ventricular dysfunction or frequent HF hospitalizations generally appear in advanced stages of the disease and should be considered as 'red flags' for adverse clinical outcomes. For example, in advanced HF patients, INTERMACS profiles take into account risk modifiers as frequent HF hospitalizations that define particularly high-risk situations; furthermore, recurrence of ventricular arrhythmias may denote an advanced state of the disease and is likewise considered a risk modifier due to its potential clinical relevance for patient management.[1] Finally, a diagnosis of HF <1 month before hospitalization has been independently associated with greater early dyspnoea relief and improved post-discharge survival compared to patients with chronic HF diagnoses.[7]

In the diagnostic framework of AHF patients, specific causes are addressed with the CHAMPIT acronym (acute coronary syndrome, hypertensive emergency, arrhythmias, acute mechanical cause, pulmonary embolism, infection, tamponade). After the exclusion of these specific aetiologies, the management of AHF should be tailored according to clinical presentation and phenotype.

In the early management of AHF, every effort should be made to identify high-risk patients with unstable vital signs such as those with cardiogenic shock, low output state, and/or respiratory failure, given the time-sensitivity of these high-risk conditions in which stabilizing haemodynamics should be the first goal.

Drugs, supplemental O_2/ventilatory support, and/or temporary mechanical circulatory support may be used to restore perfusion status, improve congestion, and limit end-organ damage, while also determining specific aetiology (ACS and/or mechanical complications should undergo emergency PCI or surgery).[1] From a mechanistic point-of-view, pharmacological and non-pharmacological interventions are directed to improve ventriculo-arterial coupling (optimization of circulating volume—i.e. preload—and optimization of systemic and pulmonary vascular resistances, inotropy).

Due to its dynamic nature, AHF should be addressed as a time-dependent medical urgency,[8] in which early interventions have been associated with better outcomes. Positive pressure ventilation initiation during emergency medical system transportation has been associated with improvement of gas exchange and reduced necessity of orotracheal intubation. Intravenous diuretics administration delay is also associated with increased mortality, and there is some observational evidence that the instauration of temporary mechanical circulatory support (IABP and ECMO) may also be time-dependent, with early use associated with mortality risk reduction.[8]

Determining as soon as possible, if clinically suspected, whether a cardiogenic shock is present or not and its severity should be critical since the potential divergences in patient management (e.g. immediate use of temporary mechanical circulatory support may be reasonable in severe shock with a low likelihood of restoring perfusion status with medications alone, and, conversely, a tMCS may be deemed futile when severe metabolic derangements are ongoing, and the chance of recovery is unlikely).

When failure gets worse—cardiogenic shock

Cardiogenic shock represents the most dramatic manifestation of AHF syndromes, caused by a primary cardiovascular disorder in which inadequate CO results in life-threatening tissue hypoperfusion associated with impairment of tissue oxygen metabolism and hyperlactatemia which, depending on its severity, may result in multi-organ dysfunction and death.[9]

The Society for Cardiovascular Angiography and Interventions has recently proposed a revised classification of shock severity incorporating a 3-axis model (based on shock severity, phenotype & aetiology, and risk modifiers) and reviewing various studies, including more than 20 000 patients, validating the association between the SCAI shock stage and mortality.[10]

The SCAI Shock classification is composed of five stages: stage A or at risk for cardiogenic shock (i.e. patients with large AMI or prior infarction or AHF symptoms), stage B or beginning cardiogenic shock (i.e. patients with evidence of haemodynamic instability such as hypotension or tachycardia without evidence of hypoperfusion), stage C or classic cardiogenic shock (i.e. manifest hypoperfusion with the need of pharmacological or mechanical intervention to restore perfusion), stage D or deteriorating cardiogenic shock (i.e. in which the initial support strategy fails to restore perfusion, typically with worsening haemodynamics and increasing lactate), stage E or extremis cardiogenic shock (i.e. actual or impending circulatory collapse, in which severe metabolic derangements are typically present—e.g. lactate >8 mmol/L, pH <7.2, base deficit >10 mEq/L).

The pathophysiological causes of cardiogenic shock are the primary pump dysfunction and subsequent haemodynamic alterations, microcirculatory dysfunction, systemic inflammatory response syndrome, and multi-organ failure. The most frequent haemodynamic profile of cardiogenic shock is 'wet and cold', even if around 30% of patients are euvolemic ('dry and cold' profile). Up to 20% of CS may present as 'wet and warm' profile: these patients have low SVR probably due to excessive vasodilatation resulting from systemic inflammatory response syndrome or mixed shock, and most have fever and leucocytosis. Clinical inflammation is present in 20–40% of CS patients, and it is associated with a reduction of SVR (dysregulation of nitric oxide pathway), while infections complicate up to 30% of cases, and may rely on vascular accesses or bacterial translocation due to bowel mucosal damage.[9]

In the contemporary era, among cardiogenic shock subtypes, non-ischaemic form appears to be the most frequent cause of admission in CICU.[11,12] A relevant clinical issue is the identification and appropriate treatment of patients with clinical evidence of haemodynamic instability (tachycardia or relative hypotension) without hypoperfusion or those with normotensive hypoperfusion. These patients have higher mortality rates when compared to SCAI stage A patients and it has been suggested that they may also have a worse prognosis than SCAI stage C patients since a significant proportion of cardiogenic shock patients experience further clinical deterioration. Clinical decompensation in SCAI stage B may be underrecognized until the progression to higher stages of overt cardiogenic shock, associated with higher mortality.[12] It is noteworthy that the SCAI stage B class has been defined in the Cardiogenic Shock Working Group registry as the presence of hypotension or hypoperfusion (lactate 2–5 mmol/L or ALT 200–500 U/L), thus including also patients with manifest signs of end-organ damage with normal blood pressure (i.e. the so-called 'normotensive shock', in which blood pressure may be preserved by compensatory vasoconstriction). In the SCAI Shock classification, the three-axis model stresses some key clinical points such as acute vs. acute on chronic presentation, since compensatory mechanisms which intervene in chronic HF may sometimes provide a falsely reassuring clinical picture (e.g. two AHF patients, both with MAP 60 mmHg, arterial lactate of 1.8 mmol/L, the first with a central venous O_2 saturation of 65%, and the second with 40%, are very different from each other since the second is very likely to have low cardiac output and occult hypoperfusion in a chronic HF history). These differences, that are more observable in early SCAI stages (A and B), tend to disappear in stages C, D, and E.

Jentzer et al. demonstrated that patients with hypoperfusion (defined as lactate > 2 mmol/L, oliguria, or rising creatinine), even in a normal blood pressure setting, have increased mortality when compared to those with hypotension with normal perfusion.[13] These data suggest that cardiogenic shock has a wide spectrum of presentation defined by end-organ perfusion with a dynamic nature, and the recognition of hypoperfusion in normotensive patients should be incorporated in clinical decision-making.

The assessment of patients with shock and pre-shock should be multi-parametric and clinical, haemodynamic and laboratory parameters should be integrated in clinical decision-making (see *Table 1*), since a single variable may be confounding (e.g. patients with chronic advanced HF may have a low cardiac index in absence of manifest hypoperfusion since they are chronically adapted to low output state; low pulmonary artery O_2 saturation may arise from various conditions which increase oxygen extraction such as fever, stress states, anaemia, hypoxia; lactates may increase in various conditions such as liver failure, sepsis, hyperglycaemia, trauma, use of propofol, linezolid, epinephrine).

Invasive haemodynamic assessment—Swan-Ganz catheter

Correct aetiologic and haemodynamic characterization of certain conditions may be challenging, especially in unclear cases when right and/or biventricular dysfunction are present. In such situations, clinical, echocardiographic, and laboratory assessments may sometimes be insufficient to understand the degree of involvement of left or right ventricle and which one is the main determinant of shock. Invasive haemodynamic assessment may become necessary to fully understand the haemodynamic alterations involved.

Pulmonary artery catheter allows direct measuring of central venous pressure (CVP), pulmonary arterial systolic and diastolic pressures, pulmonary capillary wedge pressure (PCWP), cardiac output (and cardiac index) with direct or indirect Fick methods, and central venous O_2 saturation. Derived indices are systemic and pulmonary vascular resistances, LV stroke work, and cardiac power output (CPO). Right ventricular function-specific indices

Table 1 Clinical, echocardiographic, and haemodynamic markers which should aid assessment of congestion and hypoperfusion

	Clinical	Echocardiographic	Haemodynamic
Congestion	Bilateral lung crackles or rales Elevated JVP and/or hepatojugular reflux Peripheral oedema Hepatomegaly Orthopnoea Pleural effusion	Elevated LV or RV filling pressures Dilated and non-collapsing IVC Lung B-lines Altered doppler signal of hepatic, portal, and renal veins (VExUS)	Increased CVP (>12 mmHg) Increased PCWP (>15 mmHg)
Low cardiac output or hypoperfusion	Narrow pulse pressure (pulse pressure proportion < 25%) S_3 Sensation of impending doom Alteration of mental status Cold and clammy extremities, cyanosis Oligoanuria Delayed capillary refill	Low LVOT VTI	Increased arterial lactate (>2 mmol/L) Reduced cardiac index (<2.2 L/min/m^2) Reduced cardiac power output (<0.6 W) Reduced cardiac power index (<0.4 W/m^2) **Occult hypoperfusion** Pulmonary artery O_2 saturation <65% Arteriovenous delta CO_2 > 6 mmHg

include RV stroke work, CVP/PCWP ratio, and pulmonary artery pulsatility index (see *Table 2*).

The use of a Swan-Ganz catheter may allow a more accurate assessment of intracardiac pressures, distinguishing left-sided from right-sided or biventricular congestion and phenotyping cardiogenic shock subtypes. In a retrospective analysis including more than 1000 patients, right-sided congestion was associated with an increased risk of mortality when compared to euvolemia or left-sided congestion, and right atrial pressure was found to be a significant predictor of mortality even after adjusting for the SCAI stage. No differences were found in CI or CPO among survivors and non-survivors, even if the authors point out that CPO was primarily validated in acute myocardial infarction cardiogenic shock patients and its use in HF populations—in which low CO does not always correlate with low MAP—and in contemporary short-term mechanical circulatory support device-assisted patients is less well characterized.[15]

Recently, a correction of cardiac power index (CPO/BSA) has been proposed, incorporating RAP in CPI calculation, which may allow identification of patients with more severe intravascular congestion which may be missed by traditional CPI calculation, as follows: $CPI_{RAP} = (MAP - RAP) \times CI/451$. This correction has improved the prognostic yield in patients with SCAI B-D CS (with a 66% being ADHF-CS), with a cut-off <0.28 W/m^2 for patients at higher risk for in-hospital mortality.[16]

Beyond cause, three distinct phenotypes have been distinguished using machine learning. The first phenotype—noncongested—exhibited relatively lower heart rate, filling pressures, and relatively high CO and BP, thus representing the less severe form with lower in-hospital mortality. Phenotype two—'cardiorenal' shock—characterized by intermediate mortality, had more frequent LV failure with elevated PCWP and worsening kidney function, suggesting renal involvement from shock. The third phenotype—cardiometabolic shock—typically exhibit elevated lactate, high RAP, liver damage, low BP, and CO, suggesting worsening venous congestion and multi-organ involvement, with the highest mortality.[17]

These data are consistent with the fact that increased CVP confers a greater risk of organ damage since the onset of hypotension may cause rapid deterioration of a failing right ventricle by reducing coronary perfusion and transseptal gradient, and the high CVP in RV or biventricular shock reduces in a greater degree organ perfusion pressure (organ perfusion pressure = MAP − CVP) than in isolated LV shock. Thus, hypotension and high CVP lead to the rapid development of multiple abdominal organ failure (renal, hepatic failure, and ischemic bowel), the so-called 'double-hit phenomenon'; this catastrophic series of events should be immediately counteracted by increasing BP with vasopressors and reducing CVP.[18]

Haemodynamics-based medical therapy in acute heart failure and cardiogenic shock

Management of AHF should be addressed on three axes: pulmonary congestion (i.e. gas exchange), systemic congestion, and tissue perfusion.

Pulmonary congestion is very common in patients with AHF and its most dramatic presentation is acute cardiogenic pulmonary oedema, in which a sudden increase in pulmonary capillary hydrostatic pressure (>25 mmHg) leads to fluid accumulation in lungs and acute respiratory failure. These patients should be treated immediately with oxygen therapy and, in the case of SpO2 < 90%, persistent respiratory distress (respiratory rate >25/min) or increased work of breathing, with CPAP[2] or NIV (orotracheal intubation in the case of severe distress or NIV contraindication or failure).

The use of non-invasive positive pressure ventilation may reduce the risk of orotracheal intubation and improve

Table 2 Haemodynamic profiles of cardiogenic shock subtypes, from Saxena et al.[14]

Haemodynamic variables	Normotensive hypoperfusion	Hypotensive normoperfusion	LV dominant shock	RV dominant shock	BiV shock
SBP, mmHg	>90	<90	<90	<90	<90
CVP, mmHg	Variable	Variable	<14	>14	>14
PCWP, mmHg	Variable	Variable	>18	<18	Variable
CVP/PCWP	Depends on degree of LV and RV involvement	Depends on degree of LV and RV involvement	<0.86	>0.86	>0.86
Pulmonary artery pulsatility index	Depends on degree of RV involvement	Depends on degree of RV involvement	>1.5	<1.5[a]	<1.5
CI, l/min/m^2	<2.2	≥2.2	<2.2	<2.2	<2.2
SVR, dynes-s//cm^5	>1600	800-1600	800-1600	800-1600	800-1600
CPO, W	Variable	Variable	<0.6	<0.6	<0.6

BiV indicates biventricular; CPO, cardiac power output; CVP, central venous pressure; LV, left ventricular; PAD, pulmonary artery diastolic pressure; PAS, pulmonary artery systolic pressure; PAPi, pulmonary artery pulsatility index PAPi = (PAS - PAD)/CVP; PCWP, pulmonary capillary wedge pressure; RA, right atrial pressure; and SVR, systemic vascular resistance.
[a]Right ventricular (RV) dominant shock primarily attributable to RV dysfunction

survival in selected patients, while invasive positive pressure ventilation should be considered in AHF or CS in the case of NIV failure, severe hypoxia, and haemodynamic instability due to refractory shock. Positive pressure non-invasive ventilation lowers LV pre-load and afterload, reduces myocardial VO_2, and promotes hydrostatic displacement of alveolar oedema. Effects on the right ventricle include reduced venous return and increased PVR due to compression of pulmonary capillaries by PEEP, even if the improvement of oxygenation, the reduction of pulmonary congestion, and the subsequent reduction of hypoxic pulmonary vasoconstriction have an inverse beneficial effect on PVR. However, the effect of PEEP on CO depends on RV/LV interaction (e.g. in RV failure/pre-load dependence, PEEP >5 cmH_2O may decrease RV CO; in LV failure/afterload dependence, PEEP >10 cmH_2O may improve CO).

The second therapeutic mainstay should be vasodilator (e.g. nitroglycerin, nitroprusside) since it allows reduction of pre-load, SVR, LV afterload, and LV filling pressures, thus reducing PCWP.[8] It should be underlined that some patients with acute pulmonary oedema and severe hypertension may present with clinical and laboratory features of hypoperfusion (and should be treated with i.v. vasodilators rather than inotropes).[2] Usually, a moderate dose of loop diuretic should be sufficient since fluid redistribution is primarily in lungs.[8]

Systemic congestion is the most frequent phenotype in acute decompensated HF, and it causes elevation of CVP and—potentially—end-organ dysfunction due to reduced organ perfusion pressure. The first therapeutic intervention should be aggressive decongestion with early diuretic administration (monitoring urine output every 1–2 h with a goal of 1–2 mL/kg/h or U_{Na} >50–70 mmol/L). In the case of loop diuretic failure, the dose should be doubled until maximum i.v. dose (generally considered as furosemide 400–600 mg, even if doses up to 1000 mg may be acceptable in patients with severely impaired renal function),[1] and diuretic associations should be subsequently considered (thiazides, acetazolamide, metolazone, tolvaptan) to improve decongestion. In some cases, vasodilators (preferably nitroglycerin due to its venodilator capacity, or even sodium nitroprusside) may be useful to reduce CVP and improve decongestion. Finally, renal replacement therapy should be considered in the case of diuretic failure and/or refractory volume overload.[8]

Tissue hypoperfusion defines the most severe AHF phenotype, in which the ineffective cardiac output due to a primary cardiac disorder determines inadequate tissue perfusion and end-organ damage.[1, 8] Almost one-third of cardiogenic shock patients are ‘euvolemic’ and respond to i.v. fluid bolus by increasing stroke volume, so 250 mL of NS or ringer lactate should be the first therapeutic measure in patients with CS with no signs of fluid overload.[9]

Inotropes and vasopressors may be considered in AHF with clinical features of hypoperfusion or persistent hypotension and, accordingly, in cardiogenic shock.[1] Their use should be limited to the lowest dose and shortest time possible. The first step should be confirming the presence of low cardiac output and adequate intravascular volume prior to administer vasoactive drugs, and, consequently, choosing which inotrope is the most appropriate in the clinical context. Adrenergic agonists (dobutamine, epinephrine, norepinephrine, dopamine), phosphodiesterase-III

Table 3 Medical management of acute heart failure according to clinical profile

Warm-dry Typically includes: normal SVR, normal PCWP, normal CVP • Up-titrate GDMT	**Wet-warm** Typically includes: normal SVR, increased CVP, and/or PCWP • Diuretics (RRT if refractory volume overload) • Consider vasodilators
Cold-dry Typically includes: high SVR, normal PCWP, normal CVP • Fluid challenge (if no signs of volume overload) • Inotropes • Vasodilators (if SBP sufficiently high)	**Wet-cold** Typically includes: high SVR, increased CVP, and/or PCWP • Inotropes • Vasopressors (if BP persistently low) • Diuretics (RRT if refractory volume overload or severe lactic acidosis) • Vasodilators (if SBP sufficiently high) • Temporary mechanical circulatory support

inhibitors (milrinone, enoximone), and calcium sensitizers (levosimendan) have different effects in terms of inotropy and variation of systemic and pulmonary vascular resistances. Some key features such as chronic beta-blocker therapy, RV dysfunction and/or pulmonary hypertension, ongoing myocardial ischemia, worsening renal function, and concomitant sepsis, should always be considered when selecting the most appropriate inotrope/vasopressor.[19]

The use of mechanical circulatory support devices should also be based on comprehensive clinical and haemodynamic assessment and after evaluating the need of single-ventricle or biventricular support. Intra-aortic balloon pump, inflating during diastole and deflating during systole, augments central aortic root pressure and coronary perfusion, and reduces LV afterload, decreasing LV work and myocardial VO_2. IABP support may provide up to 0.5–1 L/min of augmented cardiac output.[20] Despite its limited role in AMI-CS, IABP is still a valuable option in patients with ADHF-CS, since adaptation to chronic low output state may make patients more likely to benefit even from a slight increase in CO and LV afterload reduction (thus reducing mitral regurgitation). IABP insertion as a bridge to LVAD or heart transplantation has been associated with improved outcomes in chronic HF patients with CS, and additionally, the use of axillary access may allow mobilization and rehabilitation during prolonged support.

The choice of more complex mechanical circulatory support devices should be based on the presence of cardiac arrest, severe respiratory compromise, and severe RV failure. The presence of cardiac arrest and/or severe respiratory compromise should suggest the use of extracorporeal membrane oxygenation. Isolated LV failure can be managed with LV percutaneous LVAD (e.g. Impella CP, 5.0, 5.5). Isolated RV failure may be managed with RV pVAD (e.g. Impella RP). Biventricular failure without significant respiratory compromise may be managed with percutaneous LV + RV assist devices.

Haemodynamic monitoring with pulmonary artery catheter may be useful, besides diagnosis and characterization of CS, for management of patients receiving temporary mechanical circulatory support, including escalation and withdrawal of pharmacological and device therapy, and to assess candidacy to LVAD or heart transplantation in a patient who fails to recover myocardial function. The use of PA catheter allows continuous assessment of the haemodynamic and clinical effectiveness of therapeutic approaches. Invasive haemodynamic parameters should be assessed at time zero and periodically, since interventions (diuretics, inotropes, ventilation, tMCS) alter in various manners volume status, vascular tone, ventriculo-arterial coupling, and cardiac output. Finally, PA catheter should be used, together with clinical and laboratory data, to improve the weaning process of CS patients, since step-by-step de-escalation of circulatory support, as long haemodynamic and clinical stability are maintained, may be furtherly diminished until removal.[14]

Clinical variables such as creatinine, lactate, and CPO are predictors of adverse outcomes, and the combined assessment of lactate and CPO has been strongly related to in-hospital outcomes in AMI-CS patients undergoing Impella support. In the NCSI initiative, patients were divided into four groups according to arterial lactate (> or <4 mmol/L) and CPO (> or <0.6 W). Patients with lower lactate and higher CPO at 12–24 h post-index procedure had higher survival when compared to other groups.[21] A phenotype-based approach may be found in Table 3.

Transition from acute to chronic phase—initiation and up-titration of guideline-directed medical therapy

When the acute phase subsides, implementation and up-titration of guideline-directed medical therapy (ARNI or ACEi/ARB, beta-blocker, MRA, and SGLT2i) should be a primary issue. The choice of one drug over others should be made according to the clinical scenario and patient comorbidities (e.g. chronic kidney disease). Neurohormonal inhibitors should be initiated when SBP and renal function are stable. Patients with low blood pressure may start with MRA and SGLT2i, therefore adding beta-blockers and lastly ACEi/ARB/ARNI if clinically feasible. If concerns for a low cardiac output state or significant residual congestion are present, beta-blocker initiation should be withheld.[22]

Residual congestion is still a significant issue in HF patients since >30% have signs or symptoms of residual congestion at discharge. Patients with tricuspid regurgitation, diabetes, anaemia, and higher NYHA class have a higher risk of residual congestion at discharge, while beta-blockers at admission, *de novo* HF, or cardiovascular procedure during hospitalization were associated with a lower risk of residual congestion. Residual congestion is associated with higher 1-year mortality (28% vs. 18.5% in those without residual congestion).[5]

The SGLT2i empagliflozin has demonstrated early, effective, and sustained decongestion in AHF patients when compared to placebo. Improved decongestion was associated with an improved probability of clinical benefit at 90-days follow-up (composite for all-cause death, HF

events, and a 5-point or greater difference in KCCQ total symptom score change from baseline to 90 days.[23]

Conclusions

Acute heart failure remains a major public health problem since its high—and increasing—incidence and significant morbidity and mortality. A standardized approach should be applied to patients with HF, to quickly identify those with high-risk features. Clinical evaluation as well as echocardiographic and laboratory parameters should be sufficient to stratify risk and guide therapy in most patients, although in some cases such as cardiogenic shock with RV involvement or need for tMCS, PA catheter placement should be considered to guide management and assess response to therapeutic interventions. Prompt recognition of RV dysfunction is advisable as increased CVP is a strong determinant of an adverse clinical outcome given the decreased perfusion pressure of abdominal organs. As last step, when clinical stabilization has been achieved, GDMT implementation should be the primary goal of the clinician to reduce the risk of death and subsequent HF events.

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Data availability

The data underlying this article are available in the article and in its online supplementary material.

References

1. McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M *et al*. 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J* 2021;**42**:3599–3726.
2. Masip J, Frank Peacok W, Arrigo M, Rossello X, Platz E, Cullen L *et al*. Acute heart failure in the 2021 ESC heart failure guidelines: a scientific statement from the Association for Acute CardioVascular Care (ACVC) of the European Society of Cardiology. *Eur Heart J Acute Cardiovasc Care* 2022;**11**:173–185.
3. Chioncel O, Mebazaa A, Harjola VP, Coats AJ, Piepoli MF, Crespo-Leiro MG *et al*. Clinical phenotypes and outcome of patients hospitalized for acute heart failure: the ESC heart failure long-term registry. *Eur J Heart Fail* 2017;**19**:1242–1254.
4. Arrigo M, Jessup M, Mullens W, Reza N, Shah AM, Silwa K *et al*. Acute heart failure. *Nat Rev Dis Primers* 2020;**6**:16.
5. Chioncel O, Mebazaa A, Maggioni AP, Harjola VP, Rosano G, Laroche C *et al*. Acute heart failure congestion and perfusion status—impact of the clinical classification on in-hospital and long-term outcomes; insights from the ESC-EORP-HFA heart failure long-term registry. *Eur J Heart Fail* 2019;**21**:1338–1352.
6. Raffaello WM, Henrina J, Huang I, Lim MA, Suciadi LP, Siswanto BB *et al*. Clinical characteristics of de novo heart failure and acute decompensated chronic heart failure: are they distinctive phenotypes that contribute to different outcomes? *Card Fail Rev* 2021;**7**:e02.
7. Greene SJ, Hernandez AF, Dunning A, Ambrosy AP, Armstrong PW, Butler J *et al*. Hospitalization for recently diagnosed versus worsening chronic heart failure from the ASCEND-HF trial. *J Am Coll Cardiol* 2017;**69**:3029–3039.
8. Shiraishi Y, Kawana M, Nakata J, Sato N, Fukuda K, Kohsaka S *et al*. Time-sensitive approach in the management of acute heart failure. *ESC Heart Fail* 2021;**8**:204–221.
9. Chioncel O, Parissis J, Mebazaa A, Thiele H, Desch S, Bauersachs J *et al*. Epidemiology, pathophysiology and contemporary management of cardiogenic shock—a position statement from the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2020;**22**:1315–1341.
10. Naidu SS, Baran DA, Jentzer JC, Burkhoff D, Hall SA, Henry TD *et al*. SCAI SHOCK stage classification expert consensus update: a review and incorporation of validation studies. *J Soc Cardiovasc Angiogr Intervent* 2022;**1**:100008.
11. Jentzer JC, van Diepen S, Barsness GW, Henry TD, Menon V, Rihal CS *et al*. Cardiogenic shock classification to predict mortality in the cardiac intensive care unit. *J Am Coll Cardiol* 2019;**74**:2117–2128.
12. Kapur NK, Kanwar M, Sinha SS, Thayer KL, Garan AR, Hernandez-Montfort J *et al*. Criteria for defining stages of cardiogenic shock severity. *J Am Coll Cardiol* 2022;**80**:185–198.
13. Jentzer JC, Burstein B, van Diepen S, Murphy J, Holmes DR Jr, Bell MR *et al*. Defining shock and preshock for mortality risk stratification in cardiac intensive care unit patients. *Circ Heart Fail* 2021;**14**:E007678.
14. Saxena A, Garan AR, Kapur NK, O'Neill WW, Lindenfeld J, Pinney SP *et al*. Value of hemodynamic monitoring in patients with cardiogenic shock undergoing mechanical circulatory support. *Circulation* 2020:1184–1197.
15. Thayer KL, Zweck E, Ayouty M, Garan AR, Hernandez-Montfort J, Mahr C *et al*. Invasive hemodynamic assessment and classification of in-hospital mortality risk among patients with cardiogenic shock. *Circ Heart Fail* 2020;**13**:E007099.
16. Baldetti L, Pagnesi M, Gallone G, Barone G, Fierro N, Calvo F *et al*. Prognostic value of right atrial pressure-corrected cardiac power index in cardiogenic shock. *ESC Heart Fail* 2022;**9**:3920–3930.
17. Zweck E, Thayer KL, Helgestad OKL, Kanwar M, Ayouty M, Garan AR *et al*. Phenotyping cardiogenic shock. *J Am Heart Assoc* 2021;**10**:e020085.
18. Hrymak C, Strumpher J, Jacobsohn E. Acute right ventricle failure in the intensive care unit: assessment and management. *Can J Cardiol* 2017;**33**:61–71.
19. Farmakis D, Agostoni P, Baholli L, Bautin A, Comin-Colet J, Crespo-Leiro MG *et al*. A pragmatic approach to the use of inotropes for the management of acute and advanced heart failure: an expert panel consensus. *Int J Cardiol* 2019;**297**:83–90.
20. Abraham J, Blumer V, Burkhoff D, Pahuja M, Sinha SS, Rosner C *et al*. Heart failure-related cardiogenic shock: pathophysiology, evaluation and management considerations: review of heart failure-related cardiogenic shock. *J Card Fail* 2021;**7**:1126–1140.
21. Basir MB, Kapur NK, Patel K, Salam MA, Schreiber T, Kaki A *et al*. Improved outcomes associated with the use of shock protocols: updates from the national cardiogenic shock initiative. *Catheter Cardiovasc Interv* 2019;**93**:1173–1183.
22. Cox ZL, Nandkeolyar S, Johnson AJ, Lindenfeld J, Rali AS *et al*. In-hospital initiation and up-titration of guideline-directed medical therapies for heart failure with reduced ejection fraction. *Card Fail Rev* 2022;**8**:e21.
23. Biegus J, Voors AA, Collins SP, Kosiborod MN, Teerlink JR, Angermann CE *et al*. Impact of empagliflozin on decongestion in acute heart failure: the EMPULSE trial. *Eur Heart J* 2023;**44**:41–50.