Chapter 23
Acute Heart Failure

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Definition

Acute heart failure (AHF) is one the most common causes of hospitalization in the elderly patients. We refer to AHF as the rapid (within minutes or days) development or progression of symptoms and/or signs of heart failure requiring urgent medical evaluation and treatment (pharmacological and/or non-pharmacological). AHF may present as a first occurrence (*de novo*) or, more frequently, as a consequence of acute decompensation of chronic HF, and may be caused by primary cardiac dysfunction or more frequently precipitated by extrinsic factors in patients with chronic heart failure. AHF may eventually be triggered by these factors in patients with previously normal or near normal cardiac function. Primary cardiac causes of AHF may result from disorders of the myocardium, endocardium, heart valves or pericardium. Acute myocardial dysfunction (ischemic, inflammatory or toxic), acute valve insufficiency or pericardial tamponade are among the most frequent acute primary cardiac causes of AHF. Decompensation of chronic stable cardiac diseases can occur without known precipitant factors but more often one or more factors, such as infections, severe hypertension, rhythm disturbances, noncompliance with diet or cardiovascular medications are present (Table 23.1).

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Table 23.1 Factors associated with the development of acute heart failure

Primary cardiac dysfunction	Triggers/precipitants
Mechanism	**Precipitants often leading to rapid deterioration**
New-onset, de-novo heart failure	C – Acute coronary syndrome
Decompensation of chronic heart failure	H – Hypertensive crisis
Cause	A – Rapid arrhythmia or severe bradycardia/conduction disturbance
Myocardial dysfunction	M – Mechanical complication (e.g. rupture of free wall, interventricular septum or papillary muscle after ACS; mitral valve chordal rupture, post-traumatic)
LV systolic dysfunction	P – pulmonary embolism
LV diastolic dysfunction	Other:
RV dysfunction	Cardiac tamponade
Valvular heart disease	Surgery and perioperative problems
Pericardial disease	Peripartum cardiomyopathy
	Precipitants usually leading to less rapid deterioration
	Concurrent diseases
	Infections (pneumonia, sepsis, endocarditis)
	Exacerbation of COPD/asthma
	Anaemia
	Kidney dysfunction/deterioration
	Endocrine (thyroid decompensations, excess catecholamine production)
	Uncontrolled hypertension
	Fluid overload
	Arrhythmias, bradycardia, and conduction disturbances not leading to sudden, severe change in heart rate
	Aortic syndromes
	Non-adherence to diet/drug therapy
	Iatrogenic causes
	Drugs causing salt retention (NSAIDs, coxibs, steroids)
	Negative inotropics (verapamil, diltiazem)
	Cardiotoxic drugs (alcohol, chemotherapies)
	Drug interactions

ACS acute coronary syndrome, *AHF* acute heart failure, *COPD* chronic obstructive pulmonary disease, *LV* left ventricular, *RV* right ventricular, *NSAID* non-steroidal anti-inflammatory drug

The pathophysiologic mechanisms causing symptoms and signs of AHF are venous congestion and reduced cardiac output impairing peripheral perfusion. Pulmonary congestion causes dyspnea, the cardinal clinical manifestation of AHF. In AHF it is usually more prominent than systemic congestion, and may be mild or lead to severe pulmonary edema. Right heart congestion may also be present, more frequently in acutely decompensated chronic HF, and will manifest as jugular venous distension, peripheral edema, hepatomegaly or splanchnic congestion. When cardiac output is compromised, symptoms or signs of peripheral perfusion impairment may be present. This may be transient (i.e. fatigue, reduced tolerance to exercise or digestion) or persistent such as low blood pressure, oliguria, confusion, and mottling of the skin or *livedo reticularis*. When systemic perfusion

is significantly compromised patients present with cardiogenic shock (CS), a clinical condition with very high short-term mortality.

Therefore, AHF is a complex syndrome that can occur in patients with severe cardiac disease or with near normal hearts, be triggered by none, one single critical precipitant or various, be isolated or accompanied by several comorbidities (Fig. 23.1). This produces a wide variability in the presentation, severity, response to treatment and prognosis of AHF, ranging from relatively benign to a short-time life-threatening condition.

Classification

Given the complexity of AHF, the variety of factors involved, clinical presentations, etiologies and potential mechanisms involved (Fig. 23.1), no single classification can fit in all clinical and prognostic relevant aspects. Therefore, several overlapping classifications based on different criteria have been proposed. Approximately 2/3 of patients with AHF present as acute decompensations of chronic HF while the others do not have a prior history of HF (*de novo* AHF). Probably, the simplest and most useful classifications are those based on clinical presentation at admission. The

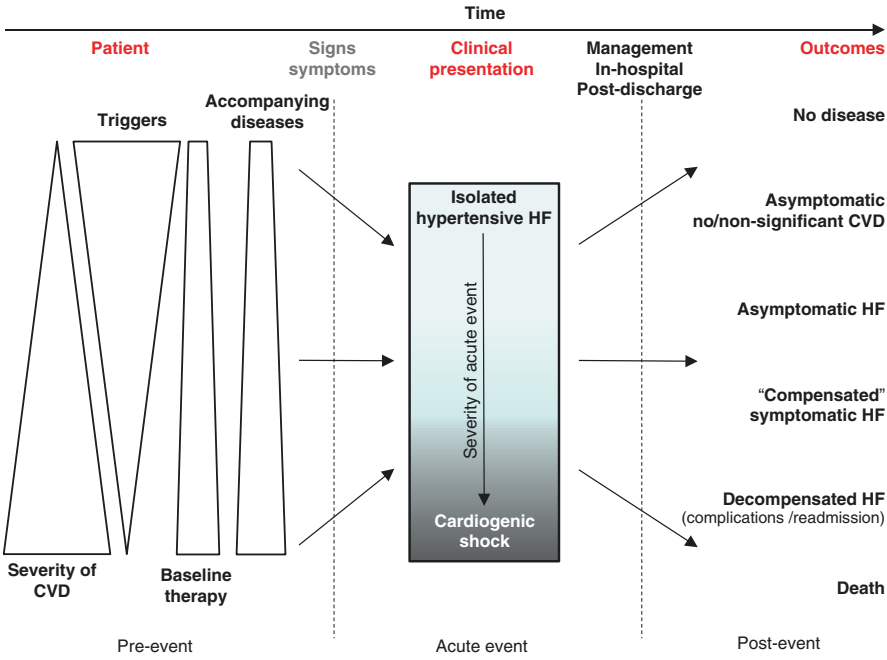

Fig. 23.1 Factors influencing the heterogeneity in etiology, clinical presentation and outcomes in patients with acute heart failure (CVD: cardiovascular disease; HF: heart failure) [3].

classification according to the level of SBP at presentation is easy to use and has a strong prognostic value. Thus, patients presenting with SBP >140 mmHg (hypertensive AHF) account for roughly half of AHF cases and have a good short- and long-term prognosis. Patients with low SBP (i.e. <90 mmHg (hypotensive AHF), are a minority (<8 %) but show the worst prognosis, with in-hospital mortality rates >15 %, particularly when signs of hypoperfusion are present (CS). In these patients, short-term mortality exceeds 30 %. The approximately other 40 % of patients with AHF present have SBP between 90 and 140 mmHg and show and intermediate risk compared with the previous two groups, with in-hospital mortality rates between 8 and 10 % [23].

One other popular classification based on physical examination, and therefore available immediately on admission, reflects the presence, or not, of clinical symptoms/signs of congestion and/or peripheral hypoperfusion [4]. The presence of congestion, either pulmonary (orthopnea, paroxysmal nocturnal dyspnoea) or systemic (peripheral oedema, jugular venous engorgement, congestive hepatomegaly, ascites, hepatojugular reflex) is defined as 'wet' vs. 'dry' for patients without congestion. Symptoms or signs of peripheral hypoperfusion (cold and clammy extremities, oliguria, mental confusion, dizziness, narrow pulse pressure) is defined as 'cold' vs. 'warm' patients for those in whom hypoperfusion is absent. It is important to emphasise that hypotension most frequently accompanies but does not equal hypopefusion. In some cases hypotension is associated with adequate perfusion. The combination of these options gives four groups: warm and dry (well perfused without congestion), warm and wet (well perfused but congested), cold and dry (hypoperfused without congestion), cold and wet (hypoperfused and congested). This classification has been proposed as a guide for initiating early medical treatment in patients with AHF [2].

Two popular classifications for AHF were developed in patients with acute myocardial infarction. Killip and Kimball [5] based on clinical status at admission, developed a classification with strong prognostic value for short-term mortality still used: Class I, no clinical signs of HF. Class II, HF with rales, S_3 gallop. Class III, with frank acute pulmonary oedema. Class IV, CS: hypotension (SBP <90 mmHg), and evidence of peripheral vasoconstriction such as oliguria, cyanosis and diaphoresis. Forrester et al. developed a classification based on cardiac index and pulmonary capillary wedge pressure (PCWP) to guide medical treatment in patients with AMI. Thus, patients in subset I would not require specific treatment, patients in subset II (high PCWP only) would mostly need diuretic therapy, patients in stage III (low CI, low PCWP) volume loading and patients in subset IV, inotropics or mechanical support [6].

Diagnostic Evaluation

The first step in diagnosis is ruling out alternative causes for dyspnea or patient´s other symptoms and signs (i.e. pulmonary infection, severe anaemia, acute renal failure). Despite advances in biomarkers and imaging, the diagnosis of AHF is based

on a careful history and physical examination. The initial diagnosis of AHF is based on the presence of clinical symptoms and signs and further confirmed by appropriate additional investigations such as ECG, chest X-ray, laboratory assessment (with specific biomarkers) and echocardiography. Typically, the clinical picture reflects fluid retention (pulmonary congestion and/or peripheral oedema) and less often is related to reduced cardiac output with peripheral hypoperfusion. Symptoms of AHF are manifestation of congestion, reflecting elevated ventricular filling pressures – left-sided may be characterized by orthopnea, paroxysmal nocturnal dyspnea, breathlessness at rest or with minimal exertion, whereas right-sided by peripheral oedema, ascites, symptoms of gut congestion. Systematic physical examination is essential in the diagnostic process of AHF and should always contain an evaluation of:

(a) Peripheral perfusion for which low systolic blood pressure and cold skin temperature are most accessible measures of hypoperfusion; additionally patient may present confusion, dizziness, anuria/oliguria.
(b) The presence of signs associated with elevated filling-pressures (left-sided: bibasal rales, an audible third heart sound, an abnormal blood pressure response to the Valsalva maneuver or right-sided: elevated jugular venous distention, hepatojugular reflux, hepatomegaly, ascites, and peripheral oedema; pleural effusions are often seen in patients with a previous history of chronic HF).

The sensitivity and specificity of symptoms and signs to predict both clinical scenarios, i.e. elevated filling pressures or low cardiac output, is often not satisfactory, which leaves relatively big margin of uncertainty to confirm final diagnosis of AHF and initiate appropriate treatment. Thus, in the diagnostic algorithm, careful clinical evaluation should be followed by additional investigations.

A second step in diagnosis is checking if there is a precipitant that may be leading or participating in the development of AHF or if there are concomitant diseases that may be contributing to the symptoms (Fig. 23.1, Table 23.1). Some precipitants, such as very high blood pressure or rapid atrial fibrillation may trigger alone AHF, and these require immediate therapy. Identifying the presence of acute myocardial ischemia is also essential as it has its own specific treatment. Other precipitants or concomitant conditions may participate in the development or worsening of the disease (Table 23.1) and will need to be identified and corrected in addition to the general treatment of AHF.

Chest X-ray is one of the most useful test for the diagnosis of AHF. A standing chest radiograph showing pulmonary venous congestion, interstitial edema or cardiomegaly are the most specific test findings for AHF although the absence of congestion may be absent in up to 20 % of patients, particularly among those with late-stage HF in whom high pulmonary capillary wedge pressures and symptoms can coexist with few radiographic signs of HF [7]. Supine chest radiographs are of limited value in AHF. Chest X-ray is also useful to identify alternative noncardiac diseases that may cause or contribute to the patient's symptoms (i.e. pneumonia, nonconsolidative pulmonary infections etc.).

Although **ECG** is not useful *per se* for the diagnosis of AHF it may be very helpful in identifying signs of potential underlying cardiac diseases (i.e. Q waves for

chronic myocardial infarction, left bundle branch block for cardiomyopathy, low voltage for pericardial tamponade etc.) and precipitants, such as rapid atrial fibrillation or signs of acute myocardial ischemia, two of the most frequent triggers of AHF. On the other hand, the finding of an ECG without any abnormality may also be helpful as it has a high negative predictive value of 98 % for AHF [7].

Initial **laboratory test** in patients with suspected AHF should evaluate factors that may contribute to the disease, including glucose, renal function, sodium, potassium, liver function tests, and complete blood count. Also thyroid stimulating hormone and transferrin iron binding capacity may reveal correctable causes [2]. Noninvasive oxygen saturation should be measured in all patients. Depending on initial findings and clinical situation, venous or arterial blood gases may also be needed. In patients with dyspnea of unknown origin, natriuretic peptides are indicated due to their high sensitivity for HF. If the test is normal, AHF is highly unlikely (negative predictive value higher than 95 %). The most established biomarkers used for the diagnosis and management of AHF and the main causes of elevations of natriuretic peptides are listed below.

Biomarkers for the Diagnosis and Management of AHF

- BNP/NT-proBNP for diagnosis of AHF (especially for ruling-out AHF as the cause of dyspnea)
- High-sensitivity cardiac troponin for diagnosis of ACS complicating AHF
- Procalcitonin, CRP and leukocytes for diagnosis of infection complicating AHF
- MR-proANP may be used for diagnosis of AHF in grey zones of traditional natriuretic peptides
- Serum creatinine or Cystatin-C for evaluation of renal function and diagnosis of acute kidney injury
- D-dimer for the diagnosis (ruling-out) of pulmonary embolism complicating AHF

Main Causes of Elevated Natriuretic Peptide Concentrations

Cardiac

Systolic dysfunction of left and/or right ventricle.
Acute coronary syndromes
Left ventricular hypertrophy
Hypertrophic or restrictive cardiomyopathy
Valvular heart disease
Congenital heart disease
Atrial tachyarrhytmias
Myocarditis

Cardiac operations
Resuscitation
Cardioversion

Noncardiac

Elderly
Anemia
Renal dysfunction
Pulmonary diseases related with RV hemodynamic stress: obstructive sleep apnea, severe pneumonia, pulmonary hypertension, pulmonary embolism
Critical illness
Sepsis
Severe burns,
Other high cardiac output conditions (e.g. thyroid disorders)
Toxic-metabolic insults, including cancer chemotherapy and radiotherapy.

Echocardiography is the most readily available non-invasive test to evaluate structural or functional heart abnormalities. Identification of left or right ventricular systolic dysfunction, valvular abnormalities, pericardial diseases or other cardiovascular alterations is essential in therapeutic planning [1]. Therefore, an echocardiographic study should be done in every patient with AHF in whom previous cardiac function is not known and in those previously studied in whom changes may have occurred. In patients in whom there is suspicion of an acute life threatening structural or functional cardiac abnormality (i.e. acute myocardial ischemia without diagnostic ECG, mechanical complications, severe mitral regurgitation, aortic dissection) the investigation should be performed immediately as it will prompt immediate specific treatment. Echocardiography should preferably be performed within 48 h of admission to allow appropriate pharmacological treatment and long term care planning [2]. Repeat echocardiography is usually not needed for patients with known underlying cardiac condition in whom there is little clinical suspicion of a change in pathology.

Bedside **lung ultrasound** is useful in detecting AHF. The presence of sonographic B lines ("lung comets") correlate with elevated PCWP and extravascular pulmonary water [8], with sensitivity >86 % and specificity >95 % [10, 11], enhancing diagnostic accuracy of examination and measurement of natriuretic peptides [9]. Thus, chest ultrasound has been proposed as a point of care technique to diagnose AHF, particularly in the ED setting. It is also more accurate than auscultation or chest radiography for the detection of pleural effusion, consolidation, and alveolar interstitial syndrome in the critical care setting [12].

In patients with AHF and implantable pacemakers or cardioverter-defibrillators, these should be routinely interrogated to assess the occurrence of atrial and/or ventricular arrhythmias as precipitants to the episode. Some of these devices can monitor thoracic impedance, which may be helpful in confirming AHF when the diagnosis is not clear.

Invasive haemodynamic monitoring with pulmonary artery (Swan-Ganz) catheterization is, in general, not needed for patients with AHF and routine use of this technique is not indicated. However, it may be helpful in some cases, particularly in unstable patients (i.e. hypotension, shock) in whom the cause or mechanism is unclear.

Other investigations must be focused only to specific clinical suspicion of causes and precipitating factors. Consequently, coronary angiogram should be performed in patients with suspected ACS and lung CT to those with suspected pulmonary embolism. However, due to unspecificity of natriuretic peptides, troponins as well as D-dimer, imaging can not be done only based on abnormal laboratory values in any AHF patient.

Risk Stratification

The mortality in AHF varies according to different features, including the clinical presentation, cause, comorbidities, and other aspects associated with the syndrome. Clinical factors associated with worse prognosis include older age, higher heart rate, lower systolic blood pressure, or lower oxygen saturation on admission, need for inotropic support, the presence of ischaemic changes in ECG, recurrent hospitalisations, renal dysfunction, COPD, anaemia, cerebrovascular events, and peripheral vascular disease. The presence of depressed left ventricular ejection fraction or a restrictive physiology in echocardiography is more frequently present in patients with worse prognosis. Laboratory tests may also be helpful for risk stratification. Worse prognosis is associated with higher levels of natriuretic peptides, cardiac troponins, serum creatinine, urea or BUN or liver function tests. Lower serum sodium or haemoglobin levels are also associated with higher mortality. Other biomarkers of myocardial injury, fibrosis or renal dysfunction, such as ST2, MR-proadrenomedullin, or cystatin C can be used for risk stratification although their additive value to standard biomarkers in clinical practice is still unclear.

Management

General Management

The need for immediate monitoring, bedrest and start of medication depends on patient's clinical stability and severity of symptoms. The management of dyspneic patient should start early after arrival to emergency department [39]. Though the management most often includes initial bed rest in semirecumbent position, continuous ECG monitoring and intravenous line, the patient with mild symptoms do not need to be monitored in bed.

Most often pharmacological and non-pharmacological treatment must be administered in parallel with the diagnostic work-up. The management of AHF is mainly

aimed to alleviate congestion, and improve perfusion and symptoms immediately. Thus, the primary goal is not to improve long-term outcomes same way as treatments for chronic HF. However, a management should not increase mortality or hospitalization indeed. The key drugs for AHF treatment are oxygen, diuretics, and vasodilators. Opiates and inotropes are used more selectively, and mechanical circulatory support is required only rarely. Non-invasive ventilation is used commonly in pulmonary oedema, but invasive ventilation is required only in minority of patients. Blood pressure, heart rhythm and rate, peripheral oxygen saturation (SpO_2) with pulse oximeter, and urine output should be monitored on a regular and frequent basis until the patient is stabilized [2]. However, in order to avoid infectious complications, one should use urinary catheter only in those, mainly oliguric and critical, patients who need measurement of hourly diuresis.

Recently, aggressive fluid and sodium restriction (at maximum 800 ml fluid and 0.8 g salt per day) compared to control group without such restrictions was shown to have no effect on weight loss or clinical stability after three days but was associated with a significant increase in perceived thirst [13]. However, moderate salt restriction is recommended (maximum 6 g per day) [2]. The degree of fluid restriction should vary depending on the estimated fluid overload. In light of the recent data, 1500 ml per day is recommended as the minimum amount of fluid per day.

Recent data show that more than one-third of patients have persistent congestion at discharge despite therapy targeting decongestion in the clinical trial setting [14].

Prompt initiation of the diagnostic work-up and appropriate treatment is mandatory for all patients admitted with a diagnosis of AHF. Patients in cardiac arrest or who require immediate resuscitation are a distinct sub-group of AHF. For the vast majority of patients, initial assessment and continued monitoring of patient's vital cardio-respiratory functions is essential to evaluate whether ventilation, peripheral perfusion and oxygenation are adequate. Typically, diagnosis and early management occurs in the emergency department, where initial assessment to identify potential life-threatening conditions requiring immediate treatment is mandatory (Fig. 23.2).

Immediate Ventilatory and Hemodynamic Stabilization

Respiratory Distress with Hypoxaemia and Peripheral Desaturation; acute Respiratory Failure

In AHF, oxygen should not be used routinely in non-hypoxaemic patients. "Wet" patients with pulmonary congestion and hypoxemia (PaO_2 <60 mmHg) or low peripheral oxygen saturation (SpO_2 <90 %) should be treated with oxygen administration to maintain oxygen saturation within the normal range (i.e. 95 %). In ACS, improper use of supplementary oxygen in normoxemic patients may be harmful [40]. In COPD, over-oxygenation may suppress ventilation and lead to hypercarbia.

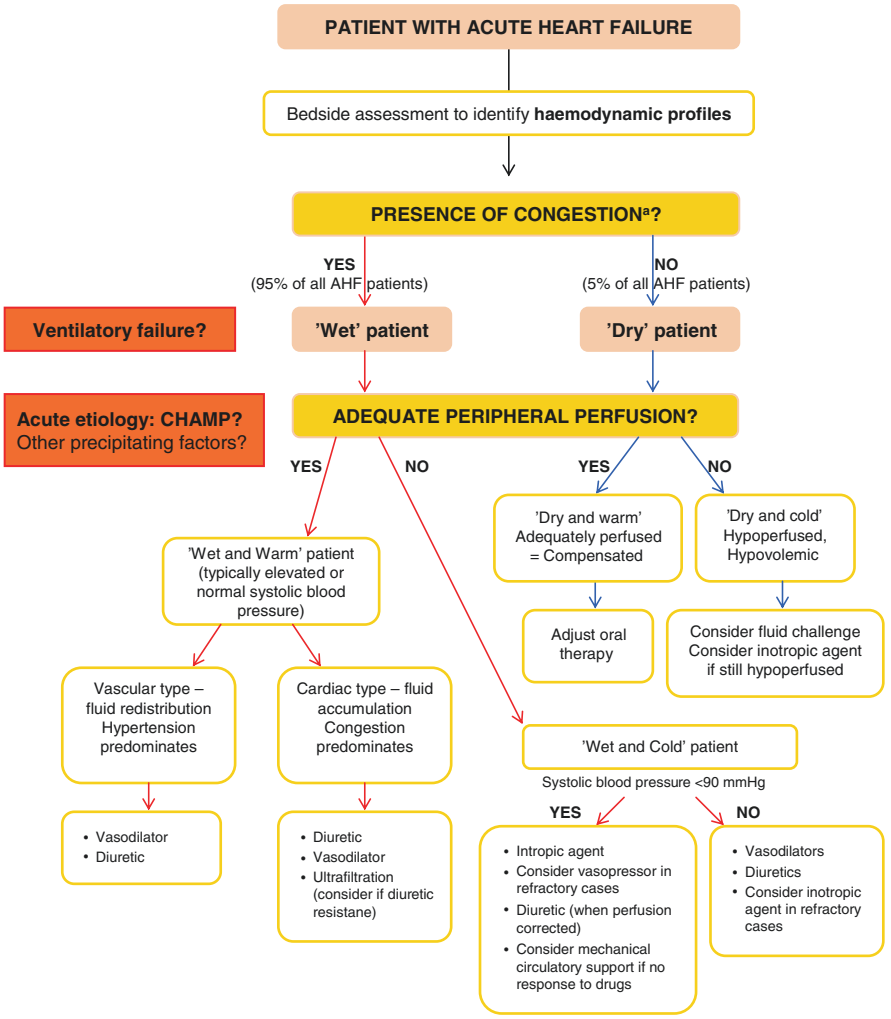

Fig. 23.2 Management of patients with acute heart failure based on clinical profile during early phase [3]. CHAMP, see Table 23.1

Ventilatory support with non-invasive ventilation (CPAP or NIPPV) should be considered in patients with significant respiratory distress, particularly for patients with acute pulmonary oedema [31]. Bilevel PPV allows also inspiratory pressure support that improves minute ventilation and is especially useful in patients with hypercarbia, most typically COPD patients. NIPPV in addition to standard medical care is an effective and safe intervention for the treatment of adult patients with acute cardiogenic pulmonary oedema.

Endotracheal intubation is rarely required and indicated only in patients with overt respiratory failure, failure to adequately respond to oxygen therapy and non-invasive ventilation, or who are inappropriate candidates for NIV because of

somnolence, anxiety or agitation. Caution has to be taken with regard side-effects of anesthetic drugs. Anesthetic drugs like propofol can induce hypotension, and have cardiodepressive side-effects. In contrast, midazolam may have less cardiac side effects and may thus be preferable in CS.

Cardiogenic Shock

Cardiogenic shock is the most severe form of AHF and the leading cause of death in acute myocardial infarction. CS is characterized by low cardiac output, hypotension and systemic hypoperfusion, resulting in end-organ dysfunction. In addition to acute cardiac cause, the contemporary diagnostic criteria for CS are 1) systolic blood pressure <90 mmHg for over 30 min despite adequate fluid resuscitation or need for vasopressor therapy to maintain systolic blood pressure ≥90 mmHg and 2) clinical signs of hypoperfusion (altered mental status, cold extremities or oliguria) or increased blood lactate level (>2–4 mmol/l). The diagnosis of CS can thus be made by clinical evaluation, instead of invasive assessment of pulmonary artery wedge pressure and cardiac index with pulmonary artery catheter routinely [1]. Electrocardiography (ECG) and echocardiography should be performed immediately after detection of the shock to assess the etiology of CS and to rule out mechanical complications. Low output syndrome caused by advanced chronic heart failure may clinically resemble CS, but the onset is more gradual and, due to adaptive mechanisms, patients may sustain the syndrome relatively long.

CS ranges from low-output advanced, end-stage chronic HF to new onset, de-novo CS. It is most often caused by STEMI or other acute coronary syndromes (80 %) [34]. The specific treatment is immediate revascularization. However, although in about 80 % of cases it is caused by ventricular dysfunction, mechanical complications such as acute mitral valve incompetence or ventricular septal defect may be the precipitant requiring immediate intervention with either circulatory support or urgent surgery in selected cases [16]. Other etiologies include chronic heart failure, valvular disease, myocarditis, Tako-Tsubo, high-risk pulmonary embolism among others. Pharmacologic therapy aims to improve organ perfusion by increasing cardiac output and blood pressure. After fluid challenge, pharmacologic management consists of inotropic agent and vasopressor as needed. Treatment is guided by the continuous monitoring of organ function and hemodynamics. Pulmonary artery catheter may be used. As vasopressor, norepinephrine is recommended (over dopamine) when mean arterial pressure needs pharmacologic support [35]. Dobutamine is the most commonly used adrenergic inotrope. Levosimendan may also be used [36] Phosphodiesterase III inhibitors may be another option, especially in non-ischemic patients. However, rather than combining several inotropes, mechanical circulatory support has to be considered when there is inadequate response. Extra-corporeal life support is a promising tool for both oxygenation and assistance for heart. Recently, the IABP-SHOCK II trial showed that use of intraaortic balloon pump (IABP) did not improve outcomes in patients suffering from AMI and CS [37, 38]. Therefore, routine use of IABP cannot be recommended [2].

Further Management – Initial In-hospital Phase

After stabilization of oxygenation, ventilation and circulatory status, the next step in clinical profiling is the identification of precipitants/causes leading to decompensation to avoid further deterioration and/or development of life-threatening conditions if not treated/corrected urgently (Fig. 23.2).

Acute Co-morbidities

Acute Coronary Syndrome

Coronary artery disease (CAD) is the most common cause of HF. Most patients admitted with AHF have a history of CAD often with prior myocardial infarction [45]. Acute myocardial ischaemia may cause AHF or trigger decompensation of chronic HF while AHF can lead to worsening of chronic myocardial ischaemia. In AHF registries, up to 40 % of patients may have acute coronary syndrome (ACS) as a precipitating factor [46]. More than one quarter of patients with myocardial infarction develop signs and symptoms of HF [44]. Early identification of ACS in patients with AHF is essential as this implies the need for urgent management per ACS guidelines [43]. Cardiogenic shock is the most severe form of AHF complicating ACS.

It is important to emphasise that the use of high sensitive cardiac troponin assays has led to a very high proportion of AHF patients showing elevated troponin levels in the early phase in the absence of clinically apparent ischaemia and ACS. Although this finding has prognostic implications, there is currently no evidence showing that a strategy to protect or prevent further myocardial injury would lead to improved outcomes.

Arrhythmias

Arrhythmias are a common precipitating cause in AHF, ranging between *15 and 30 %* [45, 46]. These range from tachyarrhythmias to severe bradycardia or conduction disturbance. This clinical profile at presentation warrants consideration of either electrical cardioversion or temporary pacing [2]. AHF patients with incessant ventricular arrhythmias constitute most challenging scenario, as arrhythmias and haemodynamic instability operate here in a vicious circle, perpetuating each other. Urgent angiography (with resultant revascularization, if needed) and electrophysiological testing with radiofrequency ablation are indicated in selected cases [47].

Patients with AHF and atrial fibrillation should be fully anticoagulated (e.g. with s.c. low-molecular weight heparin), if not already anticoagulated and with no contraindication to anticoagulation, as soon as AF is detected to reduce the risk of systemic arterial embolism and stroke. Electrical cardioversion is recommended in patients haemodynamically compromised by AF and in whom urgent restoration of sinus rhythm is required to improve the patient's clinical condition rapidly. Electrical

cardioversion or pharmacological cardioversion with amiodarone should be considered in patients when a decision is made to restore sinus rhythm non-urgently ('rhythm control' strategy). This strategy should only be employed in patients with a first episode of AF of <48 h duration (or in patients with no evidence of left atrial appendage thrombus on transesophageal echocardiography) [2]. Intravenous administration of digoxin, amiodarone and in patients with stable haemodynamics small doses of beta blocker should be considered for control of rapid ventricular rate in HFrEF and also cautious use of verapamil or diltiazem in HFpEF.

Pacing is recommended in patients haemodynamically compromised by severe bradycardia or atrioventricular block to improve the patient's clinical condition. Ventricular pacing may worsen stroke volume significantly.

Hypertensive Heart Failure

AHF precipitated by rapid and excessive increase in arterial blood pressure typically manifests as acute pulmonary oedema, though less extreme presentations are also common. Prompt reduction in blood pressure should be considered as a primary therapeutic target in this wet-warm, vascular type presentation. Aggressive blood pressure reduction with vasodilators initiated as soon as possible aiming to lowering by 25 % during the first hours, and cautiously thereafter [2, 48]. In a recent small clinical trial, intravenous calcium-channel blocker clevidipine safely and rapidly reduced blood pressure and improved dyspnoea [42].

Acute Mechanical Cause Underlying AHF

An acute mechanical cause may rapidly precipitate haemodynamic deterioration leading to AHF and often CS. It is relatively rare and usually occurs as a complication of ACS (ventricular septal defect, free wall rupture, acute mitral regurgitation). It is less frequently caused by aortic dissection, acute valvular incompetence (due to trauma or endocarditis), prosthetic valve failure or thrombosis. After diagnosis, generally by immediate echocardiography, either surgical or percutaneous intervention may improve the outcome in selected cases, if performed urgently [2].

Acute Pulmonary Embolism

Patients with acute pulmonary embolism who present with signs and symptoms of AHF, typically in the form of arterial hypotension and/or shock are in the highest risk group. The detailed diagnostic and therapeutic algorithms are presented in the recent ESC guidelines [41]. In brief, if acute pulmonary embolism is confirmed as underlying cause of haemodynamic compromise, immediate specific treatment is recommend with primary reperfusion either with thrombolysis, catheter-based approach or surgical embolectomy.

Cardiovascular Medication

Systematic approach with clear therapeutic goals and safety limits and regular, close monitoring of treatment response, e.g. symptom relief, urine volume or blood pressure control are essential for management. The medications should be chosen according to the patient's clinical profile, most importantly congestion and hypoperfusion.

Diuretics

In the treatment of patients with signs of fluid overload and congestion, especially wet and warm patients (cardiac type) diuretics are the mainstay of therapy. Diuretics increase renal salt and water excretion and may cause some vasodilation. However, in patients with signs of hypoperfusion one should correct perfusion before starting diuretics.

In AHF, intravenous furosemide is the most commonly used first-line diuretic. The dose should be modified according to previous renal function and previous dose of diuretics. Typically, the dose should be at least equal to the pre-existing oral dose used at home. Consequently, patients without a history of renal failure and without previous use of diuretics or de-novo AHF may respond to iv boluses of 20–40 mg whereas those with chronic renal failure and previous use of diuretics usually require higher doses like 40–80 mg iv. Torasemide is another alternative and dose is usually 10–20 mg iv [2]. There is no data to recommend one way of delivering diuretics over another, i.e. bolus dosing or continuous infusion [15].

In patients with insufficient response to furosemide, thiazide-type diuretics or mineralocorticoid receptor antagonists (most often spironolactone) can be combined. The decision depends on plasma potassium level and renal function. A combination of a loop and a thiazide (e.g. bendroflumethiazide) or thiazide-like diuretic (metolazone) is usually only needed temporarily and requires careful monitoring to avoid hypokalemia, renal dysfunction, and hypovolaemia [14].

Vasodilators

Vasodilators decrease both venous and arterial tone and thus preload and afterload. Consequently, they may also increase stroke volume [18].

Vasodilators are especially useful in hypertensive – wet and warm, vascular type-patients in which they should be uptitrated rapidly [49]. Vasodilators should be avoided in patients with systolic blood pressure <90 mmHg and in patients with symptomatic hypotension. Vasodilator should be used with caution in patients with significant mitral or aortic stenosis.

Nitrates include nitroglycerin and isosorbide dinitrate (ISDN). They can be given as sublingual tablets, oral spray, infusions, orally or by dermal patches. Tolerance to nitrates may occur and may necessitate change from nitrate e.g. to nitroprusside.

Intravenous nitrates when used in the treatment of AHF in emergency department, improve short-term symptoms and appear safe. However, they have not been shown to impact mortality [16]. Use of high dose transdermal and sublingual ISDN, in addition to standard AHF care, seems an interesting option that has to be explored [17].

Nitroprusside is a more pronounced arterial vasodilator. In hypertensive crisis, nitroprusside is preferred over nitrates. Prolonged use of sodium nitroprusside is limited by its potential toxic accumulation of isothiocyanate [18].

Nesiritide—a human BNP that acts mainly as a vasodilator— alleviates dyspnea but increases hypotension. It is current role among vasodilators is unsettled. Thus, nesiritide cannot be recommended for routine use in AHF [19].

Digoxin

Digoxin has cholinergic properties, and is a mild inotrope. It is mostly indicated in patients with atrial fibrillation and rapid ventricular rate and given in boluses of 0.25–0.5 mg iv, if not used previously.

Inotropes and Inodilators

Inotropes increase stroke volume and cardiac output, and decrease left ventricular filling pressure. They should be used in patients with reduced with organ hypoperfusion. Most commonly they are indicated in CS [2, 24]. Inotropes may also be effective in advanced heart failure patients with severely depressed left ventricular function and congestive heart failure. Dobutamine is the most commonly used inotrope. However, especially adrenergic inotropes (dobutamine, dopamine, epinephrine) may cause tachyarrhythmias, increase oxygen consumption and induce myocardial ischaemia. Inappropriate use of inotropes may increase mortality and inotropes have to be used with caution, as short as possible, starting low and with adequate monitoring [2, 21].

Levosimendan is a calcium sensitizing drug that enhances troponin C sensitivity to intracellular calcium, thereby enhancing cardiac inotropy and lusitropy. Levosimendan also causes peripheral vasodilation by opening smooth muscle ATP dependent potassium channels. Levosimendan may be better than dobutamine for treating AHF patients with a history of CHF or those on beta-blocker therapy [22].

Intravenous milrinone is a phosphodiesterase III inhibitor with inodilating action. It is not recommended in the treatment of patients hospitalized for an exacerbation of chronic heart failure. Milrinone may be especially deleterious in acutely worsened ischemic HF [23].

In theory, large doses (>5 μg/kg/min) of dopamine have inotropic activity via beta receptor activation and higher doses (10–20 μg/kg/min) vasoconstrictor activity via alpha adrenergic stimulation. However, the individual effects may vary a lot which makes these theories less well adapted to clinical practice. Dopamine was recently shown to be ineffective in improving diuresis in AHF [20].

The use of epinephrine (adrenaline) should be restricted for resuscitation protocols since it increases mortality when used in CS [25].

Vasopressors

Drugs with prominent peripheral arterial vasoconstrictor action such as norepinephrine (noradrenaline) may be given to patients in CS with marked hypotension. These agents are given to raise blood pressure and redistribute cardiac output from the extremities and splanchnic vascular beds to the vital organs. However, this is at the expense of an increase in LV afterload. Dopamine was compared with noradrenaline in treatment of various shock patients. A subgroup analysis suggested that noradrenaline would have less side-effects and lower mortality [26].

Other Pharmacological Therapy

Opiates relieve pain, dyspnea and anxiety. Common, dose-dependent side-effects include nausea, hypotension, bradycardia, and respiratory depression In AHF, opiates should be given cautiously and confined to patients with severe dyspnea, mostly with pulmonary oedema [2].

Anxiolytics or sedatives may be needed in a patient with anxiety or delirium. Cautious use of diazepam or lorazepam seems the safest approach [2].

Venous thromboprophylaxis with low-molecular weight heparin or another anticoagulant should be used [2].

Tolvaptan is a vasopressin antagonist that promote aquaresis. It may be temporarily used in resistant hyponatraemia. Thirst and dehydration are its typical side-effects [2].

Drugs Under Research

There are few drugs being investigated for the use in AHF. Among them are serelaxin, istaroxime, omecamtiv mecarbil and ularitide. Serelaxin is recombinant human relaxin-2 peptide, which regulates maternal adaptations in pregnancy. Serelaxin has potential benefits for decongestion given its effects on arterial compliance, cardiac output, and renal blood flow [27]. Istaroxime is a novel intravenous drug that both inhibits the activity of sodium-potassium ATPase and stimulates sarcoplasmic reticulum calcium ATPase isoform 2a (SERCA2a). It consequently improves both relaxation (lucitropy) and inotropy [28]. Omecamtiv mecarbil is a cardiac myosin activator. It increases the efficiency of heart muscle contraction via selectivity for a subset of cardiac myosins [29]. Ularitide is a synthetic analogue of urodilatin, a member of the family of A-type natriuretic peptides (ANP) [30]. We need to wait until results from ongoing trials to give recommendations for their use.

Devices

Ultrafiltration

Ultrafiltration involves removal of plasma water across a semipermeable membrane in response to a transmembrane pressure gradient. It can not be recommended as first line therapy [32, 33]. The use of ultrafiltration should be confined to patients that fail to respond to diuretic-based strategies.

Mechanical Circulatory Support

Mechanical circulatory support (MCS) is reserved to patients with cardiogenic shock that is unresponsive to pharmacological and other first-line management. MCS systems improve circulation by unloading the heart and maintaining appropriate end-organ perfusion. Short-term MCS from days to a few weeks is most commonly accomplished with percutaneous cardiac support devices. Intra-aortic balloon pulsation should not be used routinely in cardiogenic shock. The veno-arterial extracorporeal life support (ECLS), in other words, extracorporeal membrane oxygenation (ECMO) systems are relative easy and fast to implant and are being increasingly used. However, the evidence behind these strategies is still limited. A more comprehensive view about the short- and long-term MCS is given in another chapter of this book.

Criteria for Discharge from the Hospital and Follow up in High Risk Period

Patients should only be discharged when they have been hemodynamically stable, euvolaemic, have stable renal function, and have been established on oral medication for at least 24 h.

Chronic disease modifying, life prolonging medications (ACEi or ARBs, beta blockers and MRAs) should be continued at the highest tolerated dose and uptitrated or initiated again after clinical stabilization according to the patients' vital signs, hemodynamic status, underlying renal function and electrolyte values.

Follow-up plan must be in place prior to discharge and clearly communicated to the primary care team. Patients, ideally, should be seen by their general practitioner or primary care cardiologist within 1 week of discharge and by the hospital based cardiology team within 2 weeks [2]. All patients should be enrolled in disease management programme and followed up by a multi-professional heart failure service. They also ensure continuation and uptitration of disease modifying therapy for heart failure with reduced ejection fraction, if appropriate.

Compliance is listed among the most important precipitating factors for AHF. Recognition of compliance problems along with other potential precipitating factors is critical step for optimal management of AHF. On the other hand, every patient following an attack of AHF should have an acceptably detailed plan of care that ensures the achievement of optimal medical therapy and compliance with all the necessary measures. Table 4 describes the relevant actions for optimization of discharge and early follow up management in hospitalized HF patients.

Table 4. Instructions for the Optimization of Management of AHF Patients at Hospital Discharge

- Exacerbating factors addressed
- Transition from intravenous to oral therapies successfully completed
- Optimal decongestion and hemodynamics achieved
- Initiation or up-titration of pharmacologic therapy achieved and stable for 24 h, including chronic disease-modifying therapies for patients with reduced LVEF or cause of limitation of up-titration or intolerance to a drug documented
- Evaluation of co-morbidities
- Ambulation prior to discharge to assess functional capacity after therapy
- Patient and family education completed, including clear discharge instructions (daily weight measurements, diet instructions, vaccination, sodium intake etc.)
- Management plan documented and sent to those in charge of post-discharge care
- Follow-up programme scheduled, nurse visit or telephone follow-up 3 days after discharge in selected high-risk patients and doctor's office visit preferentially after 7–14 days
- Referral for disease management programme (e.g. evaluation for device therapy, heart transplantation or palliative care)

Future Directions

- The incidence of acute heart failure is increasing
- The role of early treatment in emergency department is underscored
- Results from randomized clinical trials will give us new data on intravenous drug therapies
- Patients must be clinically characterized in a systematic manner in order to provide individualized goal-directed treatment
- Treatment response has to be assessed systematically and decongestion has to be evaluated appropriately
- Cardiogenic shock remains a clinical challenge conferring high mortality
- More knowledge is needed about modern treatments of cardiogenic shock including pharmacotherapy and mechanical circulatory support
- More emphasis must be paid to prevent early rehospitalization after discharge from a hospital admission for AHF
- Ways to prevent early rehospitalization need to be explored

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