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Cardiogenic shock — diagnostic and therapeutic options in the light of new scientific data

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Abstract

Shock is a manifestation of circulatory failure related to an inadequate supply of oxygenated blood to the tissues. One type of shock is cardiogenic shock resulting from abnormalities of myocardial structure and function, impairment of mechanical function of the heart, or arrhythmia. Most commonly, cardiogenic shock is due to an acute myocardial infarction, particularly involving the anterior wall. However, establishing the diagnosis of cardiogenic shock and determining its aetiology is not always easy. Techniques of invasive haemodynamic monitoring, measurements of specific biomarkers, and noninvasive bedside echocardiography may be helpful. The effectiveness of shock management depends on the ability to institute appropriate therapy rapidly and to remove the underlying aetiologic factor(s). We present a state-of-the-art review of basic approaches used for the diagnosis and management of cardiogenic shock.

Key words: cardiogenic shock, aetiology, diagnosis, treatment

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Shock is a manifestation of circulatory failure related to an inadequate supply of oxygenated blood to the tissues. Different classifications of shock have been proposed in the literature, but perhaps the most intuitive classification, is based on the underlying mechanisms and divides this condition into four major types:

— **Hypovolemic shock** — caused by excessive fluid loss from the body or into body cavities;
— **Obstructive shock** — related to impaired blood flow in large vessels due to such conditions as pulmonary embolism, cardiac tamponade, or tension pneumothorax;
— **Distributive shock** — caused by abnormalities related to the release of mediators in the course of severe infections (e.g. sepsis) or anaphylactic reaction;
— **Cardiogenic shock** — caused by multiple conditions affecting the myocardium [1].

Unfortunately, circulatory decompensation manifesting as shock is quite common among intensive care patients. It has been estimated that shock develops in as many as one third of patients managed in intensive care units. Epidemiological data indicates that the most common type of shock is septic shock (a form of distributive shock), followed by cardiogenic and hypovolemic shock, while other (non-septic) forms of distributive shock are seen less frequently, and the most rarely seen type is obstructive shock [2] (Fig. 1).

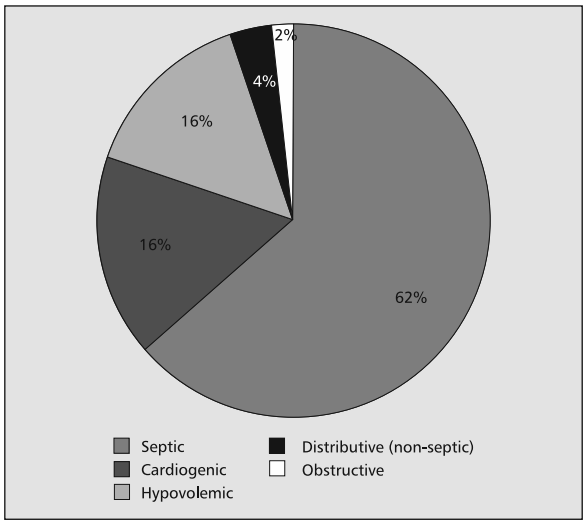

Figure 1. Distribution of various types of shock among patients treated in intensive care units

Management of shock is always difficult and may pose problems to young and experienced clinicians alike. The aim of this review is to summarise the current knowledge and recent advances related to the diagnosis and management of the second most common type of shock, which is cardiogenic shock.

AETIOLOGY OF CARDIOGENIC SHOCK

Management of shock depends on its underlying cause and thus understanding of the mechanisms leading to circulatory decompensation is the key to the institution of appropriate treatment. Although cardiogenic shock may be caused by numerous conditions affecting the myocardium, the most common underlying condition is an acute myocardial infarction, particularly a large infarct involving the anterior wall [3]. Complications of myocardial infarction, such as acute mitral regurgitation or ventricular septal rupture, may also result in shock. Although cardiac tamponade is considered a form of obstructive shock in the classification discussed above, in some large clinical registries cardiac tamponade (particularly caused by cardiac free wall rupture) has been included among causes of cardiogenic shock [2]. Other major causes of cardiogenic shock include isolated right ventricular failure, myocarditis, advanced cardiomyopathies, valvular heart disease, and arrhythmias. Figure 2 illustrates the distribution of these various causes among all cases of cardiogenic shock, and Table 1 shows a classification of causes of cardiogenic shock based on their effect on myocardial function [4].

As illustrated, cardiogenic shock is most commonly due to an acute myocardial infarction. It has been estimated that it may be present in as many as 3% to 9% of these patients, although some authors have suggested that these figures may be underestimated as they do not include pre-hospital deaths [5, 6]. As may be predicted, shock is more common among patients with ST segment elevation myocardial infarction compared to those admitted due to non-ST segment elevation myocardial infarction [7]. On average, it develops six hours after the onset of the infarction, but it may be expected to occur earlier if the culprit artery is the left coronary artery. The timing of shock is also of prognostic importance. Mortality in patients in whom shock develops within the first two days after the onset of ischaemia is about 45%, compared to 80% among those with late-onset shock [8]. Overall, mortality in cardiogenic shock ranges from 50% to 80% [9].

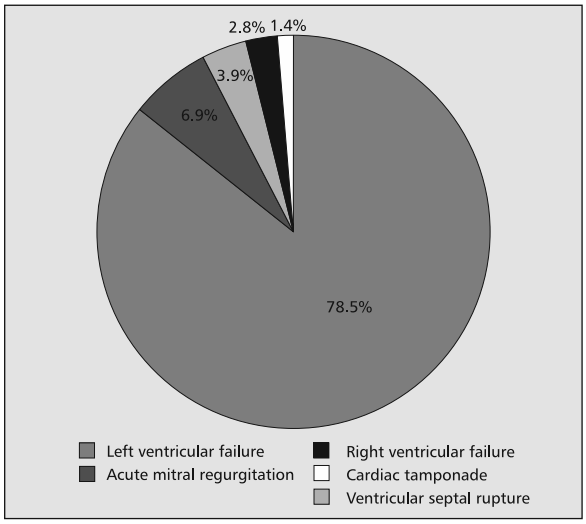

Figure 2. Aetiology of cardiogenic shock

Regardless of the cause and prognosis, cardiogenic shock is characterised by several features. It is caused by a reduction of cardiac output (systolic and diastolic dysfunction) leading to ischaemia of various body systems and organs including the central nervous system, skin, and kidneys. Changes in these systems and organs are responsible for the majority of clinical manifestations of shock. In addition, ischaemia results in a systemic inflammatory response which further complicates outcomes [10].

INVESTIGATIONS AND DIAGNOSIS

To ensure appropriate treatment, shock must be diagnosed and its cause established as rapidly as possible. Although diagnostic tests are discussed first in this paper, it should be noted that due to the life-threatening nature of the condition and the critical importance of the factor of time, treatment is often instituted before the diagnostic

Table 1. Aetiology of cardiogenic shock. Modified from [4]

Myocardial causes	Mechanical causes	Arrhythmic causes
Left or right ventricular infarction Cardiomyopathy (dilated, ischaemic, restrictive) Myocarditis Toxins or cytotoxic drugs (e.g. anthracyclines) Medications: calcium antagonists, beta-blockers, antiarrhythmic drugs, digoxin, antidepressants Ventricular hypertrophy	Valvular heart disease Mechanical complications of myocardial infarction (papillary muscle dysfunction, ventricular septal rupture, cardiac free wall rupture Hypertrophic cardiomyopathy Outflow tract obstruction by ventricular or atrial thrombus or tumour Aortic dissection Cardiac trauma	Supraventricular or ventricular arrhythmia Bradycardia

process is completed and investigations are intertwined with life-saving interventions.

Typical clinical and haemodynamic symptoms of a cardiogenic shock include [4]:

— clinical signs and symptoms:
  - peripheral hypoperfusion,
  - oliguria/anuria (urine output < 30 mL h^{-1}),
  - peripheral cyanosis,
  - symptoms of central nervous system hypoperfusion (lethargy, confusion);
— haemodynamic symptoms:
  - systolic blood pressure < 90 mm Hg over more than 90 minutes,
  - low peripheral perfusion pressure,
  - need to administer catecholamines to stabilise patient condition,
  - use of intraaortic balloon counterpulsation,
  - cardiac index < 2.2 L $min^{-1}m^{-2}$,
  - pulmonary wedge pressure >15 mm Hg.

In addition to establishing the type of shock, its underlying factor(s) should be identified. Biochemical tests, haemodynamic monitoring, and echocardiography may be helpful in this regard. In particular, the importance of the latter has recently increased. Among patients with an acute coronary syndrome, bedside echocardiography is a key investigation along with the electrocardiogram and biochemical tests [11–13]. Currently, with technical advances that have allowed miniaturisation of echocardiographic equipment, bedside echocardiography with evaluation of basic parameters may be performed not only by cardiologists but also by other clinicians. According to the American Society of Echocardiography guidelines, such examinations should include evaluation of pericardial fluid, global systolic function, and the size of the right ventricle and the vena cava inferior [14]. Evaluation of these parameters is important not only for diagnostic purposes but also to monitor treatment.

In some cases, pulmonary artery catheterisation may be useful to monitor patients with cardiogenic shock. It may provide information on such parameters as left and right ventricular filling pressures, systemic and pulmonary vascular resistance, right ventricular ejection fraction, and oxygen saturation. Although it has not been shown to improve outcomes, it is safe (does not increase mortality rate) and may be helpful, e.g. by facilitating drug dosing [15]. Another parameter important not only for diagnostic purposes but also when establishing therapeutic targets is blood oxygen saturation. For example, it may be useful to monitor mixed venous oxygen saturation (SvO_2) or related parameters. It has been shown that management protocols that included SvO_2 were associated with a large decrease in mortality during the initial hours of shock treatment [16].

Table 2. Therapeutic targets during shock management

Therapeutic targets
Mean arterial pressure ≥ 60 mm Hg
Pulmonary wedge pressure ≤ 18 mm Hg
Central venous pressure 8–12 mm Hg
Urine output ≥ 0.5 mL h^{-1} kg^{-1}
Arterial blood pH 7.3–7.5
Central venous oxygen saturation ($ScvO_2$) ≥ 70% (at arterial oxygen saturation [SpO_2] ≥ 93% and haemoglobin level ≥ 9 g dL^{-1})

The Acute Cardiovascular Care Association (ACCA) has recently issued the ACCA Clinical Decision-Making Toolkit, a set of algorithms related to the management of acute cardiovascular conditions which is freely available from the European Society of Cardiology website [17]. It includes a summary of basic recommendations regarding treatment of cardiogenic shock. This tool may be useful when making therapeutic decisions. For example, it lists therapeutic targets during shock management (Table 2).

In addition to making the diagnosis and treatment plans, it is also useful to determine prognosis early. For this purpose, risk stratification schemes are helpful, depending on the underlying aetiology of shock (i.e. in most patients with cardiogenic shock, risk scores developed for acute coronary syndromes), and measurements of various biomarkers of proven value in various acute cardiovascular conditions [18–20]. B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NTpro-BNP) levels are often elevated in intensive care patients regardless of the reason for their admission, and elevated levels of these biomarkers are independent predictors of mortality [21]. In patients with cardiogenic shock, elevated BNP or NTpro-BNP level may be related to both left and right ventricular dysfunction and may predict outcomes [22, 23]. Recently, an increasing number of novel biomarkers have been reported which are also useful in patients with cardiogenic shock. Fibroblast growth factor 23 (FGF-23) level increases with disease severity, correlates with BNP level, and is associated with worse outcomes [24]. Other biomarkers of proven usefulness include interferon-γ (INF-γ), tumour necrosis factor-α (TNF-α), macrophage inflammatory protein-1β (MIP-1β), granulocyte-colony stimulating factor (G-CSF), monocyte chemoattractant protein-1β (MCP-1β), angiopoietin-1 and -2 (Ang-1 and Ang-2), and the Th17/Treg ratio [25–27].

MANAGEMENT OF CARDIOGENIC SHOCK

Early management of shock is aimed at the normalisation of haemodynamic parameters and the prevention of further organ damage and deterioration of the clinical status of the patient. Basic approaches are summarised by the mnemonic VIP:

V (ventilate) — oxygen supply,
I (infuse) — fluid therapy,
P (pump) — administration of vasoactive drugs.

An algorithm for the management of cardiogenic shock is shown in Table 3. However, this is symptomatic treatment and if possible management should be directed at the underlying cause. As described above, most cases of cardiogenic shock are secondary to a myocardial infarction. If this diagnosis is made, prompt reperfusion therapy should be pursued. It has been shown that coronary revascularisation by percutaneous coronary angioplasty or coronary artery bypass grafting reduces both in-hospital and long-term mortality in patients with cardiogenic shock and complicated myocardial infarction [3, 28].

The management of shock also includes fluid therapy and ventilator therapy which, along with correction of ion disturbances, allow normalisation of the acid-base balance. In a significant proportion of cases, however, such an approach is not sufficient and patients require drug therapy [29]. Based on data from the ACCA Clinical Decision-Making Toolkit, basic drugs used in the treatment of shock, including their mechanisms of action and dosage, are summarised in Table 4. Unfortunately, these medications are suboptimal and their use may be associated with complications including arrhythmias and increased myocardial oxygen demand. In some patients, haemodynamic improvement is not possible despite use of these drugs.

The ultimate approach to improve haemodynamic parameters is mechanical circulatory support. Currently, a number of devices are used that are characterised by varying effectiveness and mechanisms of action. Differences between these devices are related to their insertion route (percutaneous or surgical), the effect on cardiac chambers (left, right or biventricular support), and their ability to be combined with extracorporeal membrane oxygenation (ECMO) [30]. Currently available devices include intra-aortic balloon pump (IABP), veno-arterial ECMO, the Impella pump, and the TandemHeart device

Clinical experience with IABP is extensive, and an improvement of haemodynamic parameters has been observed over the years, but the large randomised IABP-Shock II study showed that the use of IABP was not associated with a reduction of 30-day mortality among patients with myocardial infarction complicated by cardiogenic shock [31]. Few randomised studies of the use of Impella pumps and TandemHeart devices have been reported, but some of them have compared outcomes to the use of IABP. These approaches have not been shown to reduce 30-day mortality compared to IABP [30]. Thus, if IABP does not reduce short-term mortality, and other studies do not show the

Table 3. Cardiogenic shock management algorithm. Modified based on the ACCA Clinical Decision-Making Toolkit [17]

0 min	**Early risk assessment and monitoring:** Initiate O_2 at high flow Establish vascular access	**Risk stratification:** Age: 65–74, ≥ 75 years Heart rate > 100 beats min^{-1} Systolic blood pressure < 100 mm Hg Pulse pressure ≤ 25 mm Hg (cardiac index < 2.2 L $min^{-1}m^{-2}$)
5 min		Orthopnoea (pulmonary wedge pressure > 22 mm Hg) Tachypnoea (> 20 min^{-1}), > 30 min^{-1} (!) Killip class II–IV Clinical symptoms of tissue hypoperfusion/hypoxia: — cold extremities — decreased urine output (< 40 mL h^{-1}) — reduced capillary refill — alteration in mental status
15 min	**Initial resuscitation:** Obtain arterial and central venous access with a catheter capable of measuring central venous oxygen saturation Perform transthoracic echocardiography to evaluate left (and right) ventricular function and detect potential mechanical complications of myocardial infarction	**Correct:** hypoglycemia and hypocalcemia **Treat:** sustained brady- and tachyarrhythmias Infuse normal saline 20–30 mL kg^{-1} body weight over 30 minutes until central venous pressure is 8–12 mm Hg or perfusion improves (up to 500 mL)
60 min	Refer patient for coronary angiography as rapidly as possible if symptoms and/or laboratory findings indicate myocardial ischaemia	**Consider:** mechanical ventilation to improve patient comfort (to reduce fatigue, stress) or correct acidosis or hypoxemia **Inotropic support:** dobutamine and/or vasopressor drugs
	Consider mechanical circulatory support in drug-resistant cardiogenic shock	

Table 4. Drugs used in the management of cardiogenic shock

	Drug type		Clinical effects	Dosage
β-adrenergic effect	Levosimendan	Calcium sensitiser	Vasodilatation, positive inotropic effect	0.05–0.2 μg $kg^{-1}min^{-1}$
	Isoprenaline	β_1, β_2 agonist	Positive chronotropic effect (pulmonary vasodilatation)	0.5–5 μg min^{-1} (0.25–2.5 mL of 1:250,000 solution) IV
	Dobutamine	$\beta_1, \alpha_1/\beta_2$ agonist	β_2 receptor-mediated vasodilatation, positive inotropic and chronotropic effect	2–20 μg $kg^{-1}min^{-1}$
	Dopamine	β, α, and dopaminergic agonist	Peripheral vasodilatation (e.g. visceral and renal vessels)	4 μg $kg^{-1}min^{-1}$
			Positive inotropic and chronotropic effect	4–8 μg $kg^{-1}min^{-1}$
			Vasoconstriction at high doses	> 8 μg $kg^{-1}min^{-1}$
α-adrenergic effect	Norepinephrine	α_1, β agonist	Vasoconstriction, positive inotropic effect	0.05–0.2 μg $kg^{-1}min^{-1}$ titrate to on effect

superiority of the Impella pump and the TandemHeart device over IABP, it may be expected that these two interventions also have no effect on outcomes. It is worth noting, however, that only short-term outcomes were evaluated in the IABP-Shock II study, and studies on the effect of IABP on long-term outcomes are eagerly awaited. Further development of mechanical circulatory support is necessary to culminate in the introduction of devices that would improve not only haemodynamic parameters but also patient outcomes.

In summary, both the diagnosis and the management of cardiogenic shock are difficult and require extensive knowledge and clinical experience. Despite significant advances regarding the development of diagnostic methods and approaches to predict patient outcomes, management remains a challenge and some authors have indicated that mortality trends in cardiogenic shock have not improved significantly in recent decades [5]. We are still awaiting new therapeutic methods that would improve patient survival. Removal of the factor(s) underlying circulatory decompensation continues to be the most effective treatment approach.

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