Review article

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Cardiogenic shock - Back to the basics

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Abstract

The authors present a review paper that addresses the cardiac component of shock and its definition. We reviewed the concepts of oxygen delivery and consumption and approached the evaluation of these complex patients through measures that obviated the need for pulmonary artery catheters or PICCO monitoring. Hence, this review will briefly explain the concepts of oxygen delivery, oxygen consumption, oxygen extraction ratio, mixed venous saturation, lactate, mixed venous-to-arterial carbon dioxide (CO2) tension difference, and echocardiographic evaluation of cardiac output. We aimed to clarify such concepts and provide a systematic approach to evaluate this population and surrogates for cardiac output.

Key words: Cardiogenic shock, oxygen delivery, oxygen consumption, cardiac output, lactate.

Introduction

Cardiogenic shock (CS) represents a state of low cardiac output due to cardiac dysfunction. (1) European Society of Cardiology (ESC) guidelines define CS as hypotension representing a systolic blood pressure <90 mmHg despite adequate filling status, (2) for more than 30 minutes, or need for catecholamines to maintain systolic blood pressure (SBP) >90 mmHg. (3) There can be significant tissue hypoperfusion and decreased oxygenation even with preserved blood pressure. Thus, other criteria have been accepted, such as signs of clinical pulmonary congestion and signs of impaired organ perfusion, which include altered mental status, cold and clammy skin and limbs, oliguria with urine output of less than 30 ml per hour, or an arterial lactate level of more than 2.0 mmol per liter. (3) Early recognition of hypoperfusion signs identify high-risk patients regardless of hypotension, as shown in the SHOCK trial. (4)

The consensus of the European Society of Intensive Care Medicine defined shock as "a life-threatening, generalized maldistribution of blood flow resulting in failure to deliver and/or utilize adequate amounts of oxygen, leading to tissue dysoxia" in 2007 and as "a life-threatening, generalized form of acute circulatory failure associated with inadequate oxygen utilization by the cells" in an updated definition in 2014. (5) Bearing such notions in mind, a position paper from the Heart Failure Society proposed to define CS as a "syndrome caused by a primary cardiovascular disorder in which inadequate cardiac output (CO) results in a life-threatening state of tissue hypoperfusion associated with impairment of tissue oxygen metabolism and hyperlactatemia." (1)

As defined per hemodynamic parameters, CS is characterized by a reduced cardiac index (CI) inferior to 2.2 l/min/m^2 and an elevated pulmonary capillary wedge pressure (PCWP) superior to 15 mmHg. (6) CO is a key global oxygen delivery (DO2) determinant. Hence, cardiogenic shock can also be defined as a failure of global DO2 to meet oxygen consumption (VO2), resulting in tissue hypoperfusion. (7)

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This paper aims to review the hemodynamic concepts of oxygen delivery and consumption, as well as the variables related to them, to structure an approach that bears these concepts in mind. Hence, this review will briefly explain the concepts of oxygen delivery, oxygen consumption, oxygen extraction ratio, mixed venous saturation, lactate, mixed venous-to-arterial carbon dioxide (CO2) tension difference, and echocardiographic evaluation of CO.

Echocardiographic evaluation of cardiac output

Evaluation of CO is a valuable tool for the diagnosis of cardiogenic shock and the management of critically ill patients. CO is the product of the heart rate (HR) and stroke volume (SV).

SV can be estimated by echo as the product of the cross-sectional area of the left ventricle outflow tract (LVOT) and the velocity-time integral (VTI) of blood flow through it.

LVOT area is usually estimated with LVOT diameter measured in the parasternal long axis view, and VTI of LVOT is measured by placing the pulsed Doppler interrogation line at the LVOT in the apical 5-chamber view plane.

By measuring LVOT area and VTI, SV and CO can be estimated by the formulas shown in **Figure 1**. (8,9)

Studies have shown that echocardiographic evaluation of cardiac output is an accurate and precise method for evaluating patients compared to that obtained from a pulmonary artery catheter. (10,11)

CO varies between 4.0 l/min to 8.0 l/min at rest and is higher during exercise. CI represents the cardiac output adjusted to body surface area (BSA) and varies between 2.5 to 4.0 l/min/m^2. (12)

Oxygen distribution and consumption

DO2 represents the oxygen delivery and can be calculated by the product of the total oxygen content in arterial blood (CaO2) and CO. CaO2 is estimated from hemoglobin (Hb) concentration (in g/dl), the amount of oxygen bound to it (oxygen saturation in percentage), and the partial pressure of oxygen (PO2 in mmHg) dissolved in the plasma. DO2 is dependent on Hb concentration, oxygenation, and CO, and can be calculated through the formulas shown in **Figure 2**. (7)

In the formula in **Figure 2**, k1 represents the Hüfner constant, which expresses hemoglobin oxygen capacity per gram of Hb. The maximum theoretical value is 1.39 ml/g. However, real-life values vary according to body temperature. A value between 1.36 to 1.31 ml/g is closer to the real-life value. (7,13) K2 represents the solubility coefficient of oxygen, which is 0.003 ml of oxygen per mmHg per deciliter of plasma. (7)

Normally, DO2 values vary between 900 to 1100 ml per minute or 530 to 600 ml/min/m^2 when indexed to body surface area. (14)

Oxygen consumption (VO2) represents the amount of oxygen consumed by tissues and can be determined by measuring the oxygen content in venous blood (CvO2) and using the formulas shown in **Figure 3**. (15)

Oxygen consumption can be influenced by several factors, some of which are listed in **Table 1**, adapted from McLellan and Walsh. (16)

DO2/VO2 relation and oxygen extraction ratio (O2ER)

Oxygen delivery responds to changes in any of its major three components (Hb, oxygen, and CO) and changes in VO2. For instance, CO increases to maintain a normal DO2 in acute hypoxia or acute anemia. Oxygen delivery is also responsive to metabolic needs and VO2. Exercise is an example of such a situation, with an increase of both DO2 and VO2 mediated mainly by an increase in CO. When there is an acute reduction in cardiac output (as may happen from an acute coronary infarction and cardiogenic shock), DO2 is also reduced. In such cases, to the same VO2, there is a greater oxygen extraction ratio, which is translated into a reduction in mixed venous oxygen saturation. (7)

The oxygen extraction ratio can be calculated by the formula shown in **Figure 4**. (15,16)

In a normal physiological situation, O2ER varies from 0.2-0.3. The heart is especially sensitive to a reduction of coronary DO2 since its O2ER is higher (approximately 0.6). This capacity enables the body to adapt to falling levels of DO2. (16) There is a point where the maximal capacity of O2ER is exceeded, and the critical DO2 is reached. At this point, VO2 becomes supply dependent. Normally such situations occur when the O2ER is higher than 0.6-0.8 or DO2/VO2 ratio is inferior to 2:1. (7,15)

Should the DO2 continue to decrease or the VO2 increase for the same DO2, tissue hypoxia ensues, resulting in an inefficient anaerobic metabolism and lactate increase. (17)

There is evidence that patients who can generate a high CO, DO2, and VO2 have a significantly higher survival rate than those who do not. (14,18) Some studies were designed to induce a supranormal DO2 (>600 ml/min/m^2) in the setting of shock with high doses of dobutamine. It was revealed to be ineffective or even harmful in a generalized population. (19)

Some studies in trauma and high-risk surgical pa-

tients have shown a decreased mortality when targeting a supranormal DO2. (20,21) More recent studies have also shown positive results of hemodynamic guidance with a decrease in mortality (22) without a significant increase in myocardial injury. (23)

Mixed venous saturation

Mixed venous oxygen saturation (SvO2) is defined as the percentage of oxygen saturation of hemoglobin in the pulmonary artery measured from the distal tip of a pulmonary artery catheter (PAC) and usually had SvO2≥65%. SvO2 is probably the best indicator of the adequacy of DO2, as a decrease in SvO2 is a sensitive marker of decreased CO. Cardiogenic shock is characterized by an imbalance between a decrease in CO and/or an increase in the metabolic needs that leads to a compensatory increase in oxygen extraction with a subsequent drop in SvO2. (24,25)

The major problem of SvO2 is that it can only be obtained by placing a PAC. However, this limitation could be passed by measuring central venous oxygen saturation (ScvO2). ScvO2 can be easily measured from a venous blood gas drawn central venous catheter placed preferably in the right atrium so that it could be a practical substitute, however, multiple studies have questioned the reliability of ScvO2 to predict SvO2. (24,25) In general, a good but not perfect correlation is observed, in which ScvO2 overestimates SvO2 by 3-8%, a difference that decreases in low cardiac output states such as cardiogenic shock. To overcome this difference, the place of the tip of the central vein in the right atrium is very important as this overestimation could pass from 8% to 1%, becoming ScvO2 a reasonable estimate of SvO2. (26-29) Considering these limitations, a value of ScvO2≥70% is desirable in critically ill patients.

The incorporation of venous saturation can be used to estimate cardiac output, better understand the patient's physiological state, and define an end metabolic target in the resuscitation process. (25,26)

Mixed venous-to-arterial carbon dioxide (CO2) tension difference

In the case of hypoxia, apart from the production of lactate, other changes are observed, including defects in CO2 clearance. Therefore, determining the CO2 arteriovenous difference may help evaluate tissue oxygenation. (25) The mixed venous-to-arterial CO2 tension difference (P[v-a]CO2) is the difference between carbon dioxide tension (PCO2) in mixed venous blood (sampled from a PAC) and the PCO2 in arterial blood. (30) Under normal physiological conditions, this difference should not exceed six mmHg. (31)

A P(v-a)CO2>6 mmHg is associated with a significantly lower mean cardiac output when compared to P(v-a)CO2≤6 mmHg. (32) Different studies have found its value to be inversely correlated to CI, whether central or mixed PCO2 is used. Levels greater than six mmHg have been shown to reveal persistent hypoperfusion despite the normalization of ScvO2. (33)

There is evidence that patients that reach a normal P(v-a)CO2 (≤6 mmHg) after six hours of resuscitation have greater decreases in blood lactate and Sequential Organ Failure Assessment score than those who fail to normalize P(v-a)CO2 (>6 mmHg). Patients that achieve both goals of P(v-a)CO2≤6 mmHg and ScvO2>70% after the first six hours of resuscitation have the greatest blood lactate decrease, which was found to be an independent prognostic factor of ICU mortality. (30)

Lactate monitoring

Hyperlactatemia is known to be associated with adverse outcomes in critical illness. In general, elevations of lactate indicate the presence of tissue hypoxia and anaerobic metabolism. The magnitude of this increase has been directly correlated to the prognosis of the patient with acute critical illness. (25) In cardiogenic shock patients, there is also increasing evidence that supports the notion of lactate as a prognostic factor. (34,35) As an example, in ST-segment-elevation myocardial infarction (STEMI) patients complicated with cardiogenic shock, increased lactate values (that is >6.5 mmol/l) were independently associated with in-hospital death. (36) The strict relationship between lactate and hemodynamic impairment was verified when a short-term increase in mean arterial pressure with norepinephrine was associated with a significant reduction in lactate levels, better cardiac performance, and improved microcirculatory variables. (37)

No single cut-off value of lactate is associated with a worse outcome. Still, a lactate value higher than 2.0 mmol/l has been suggested as a diagnostic criterion for impaired end-organ perfusion. (3)

Other than CS, lactate seems useful to identify a subset of patients with STEMI at higher risk for early death and in-hospital complications, being related to hemodynamic derangement. The prognostic impact of hyperlactatemia on mortality has been documented in patients with cardiac arrest, even if there is no cut-off value of lactate to be associated with worse outcomes or to guide resuscitation or hemodynamic management. (38)

Beyond its importance as a prognostic marker in

critically ill patients, lactate could be an important energy source in these patients. In this point of view, hyperlactatemia can be viewed as part of a stress response to an increased metabolic rate, sympathetic nervous system activation, accelerated glycolysis, and a modified bioenergetics supply. An infusion of labeled lactate in healthy and cardiogenic shock patients showed that 50% of the lactate was oxidized and 20% used for glucose synthesis, without differences between the two groups. In other words, increased lactate levels are, at the same time, an indication of stress response and a source of energy for the heart. (38)

Conclusion

Through this series of evaluations, with or without knowledge of echocardiography, we can guide our therapy according to the notion of tissue hypoperfusion, reduced delivery of oxygen, reduced cardiac output, and increased oxygen extraction.

We can argue that there might be an increased oxygen extraction in an initial state of adaptation without significant hypoperfusion and consequent hyperlactacidemia. By means of arterial and central venous blood gas, we can determine O2ER, which portraits an accurate picture of the oxygen delivery. Evaluation of pH levels and acid-base balance should be considered as well.

Using the ScvO2 and the P(v-a)CO2 can further aid this determination by supporting the presence of a normal or decreased cardiac output. Finally, hyperlactacidemia represents the stage where there is definite tissue hypoperfusion, and the point when the compensatory measures have failed (**Figure 5**).

At any moment, an echocardiographic evaluation can be used to determine the SV, CO, and CI, all of which might alter our treatment strategy. Filling pressures and altered contractility can further the personalization of the management of critically ill patients in cardiogenic shock.

Table 1. Several factors that can influence oxygen consumption

Factors that increase VO2	Factors that decrease VO2
Exercise	Sedation, analgesia, neuromuscular blocking agents, antipyretics
Trauma	Hypovolemia, shock states
Inflammation, sepsis, pyrexia	Mechanical ventilation
Shivering	Hypothermia
Pain	
Agitation	
Physiotherapy	

Figure 1. Equations for the calculation of stroke volume and cardiac output

$$\text{LVOT area} = (\textbf{LVOT diameter}/2)^2 \times \pi$$

$$\text{SV} = \text{LVOT area} \times \textbf{VTI LVOT}$$

$$\text{CO} = \text{SV} \times \textbf{HR}$$

Legend: LVOT=left ventricle outflow track; SV=stroke volume; VTI=velocity-time integral; CO=cardiac output; HR=heart rate.

Figure 2. Oxygen delivery and total arterial oxygen blood content equation

$$DO2 = CO \times CaO2$$

$$DO2 = CO \times [(k1 \times Hb \times SpO2) + (k2 \times PO2)]$$

Legend: DO2=oxygen delivery; CO=cardiac output; CaO2=arterial blood oxygen content; Hb=hemoglobin; SpO2=oxygen saturation; PO2=oxygen partial pressure.

Figure 3. Oxygen consumption and total venous oxygen blood content equation

$$CvO2 = [(k1 \times Hb \times SvO2) + (k2 \times PO2)]$$

$$VO2 = CO \times (CaO2 - CvO2)$$

Legend: CvO2=venous blood oxygen content; Hb=hemoglobin; SvO2=mixed venous oxygen saturation; PO2=oxygen partial pressure; VO2=oxygen consumption; CO=cardiac output; CaO2=arterial blood oxygen content; CvO2=venous blood oxygen content.

Figure 4. Oxygen extraction ratio equation

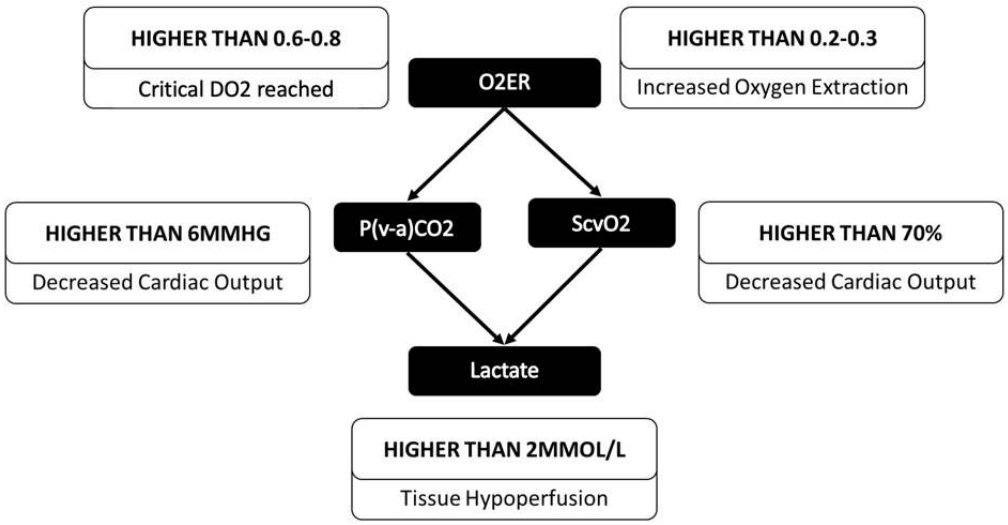
$$O2ER = VO2/DO2$$

or

$$O2ER = (CaO2 - CvO2)/CaO2$$

Legend: O2ER=oxygen extraction ratio; VO2=oxygen consumption; DO2=oxygen delivery; CaO2=arterial blood oxygen content; CvO2=venous blood oxygen content.

Figure 5. Integrated approach scheme



Legend: DO2=oxygen delivery; O2ER=oxygen extraction ratio; P(v-a)CO2=mixed venous-to-arterial carbon dioxide tension difference; ScvO2=central venous oxygen saturation.

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