

## Introduction

The primary physiological task of the cardiovascular system is to deliver enough oxygen ( $O_2$ ) to meet the metabolic demands of the body. Shock and tissue hypoxia occur when the cardiorespiratory system is unable to cover metabolic demand adequately. Sustained tissue hypoxia is one of the most important cofactors in the pathophysiology of organ dysfunction [1]. Therefore determining the adequacy of tissue oxygenation in critically ill patients is central to ascertain the health of the patient. Unfortunately, normal values in blood pressure, central venous pressure, heart rate, and blood gases do not rule out tissue hypoxia or imbalances between whole-body oxygen supply and demand [2]. This discrepancy has led to increased interest in more direct indicators of adequacy of tissue oxygenation such as mixed and central venous oxygen saturations. Pulmonary artery catheterization allows obtaining true mixed venous oxygen saturation ( $SvO_2$ ) while measuring central venous oxygen saturation ( $ScvO_2$ ) via central venous catheter reflects principally the degree of oxygen extraction from the brain and the upper part of the body. This brief review discusses the role and limitations of  $SvO_2$  and  $ScvO_2$  as indicators of the adequacy of tissue oxygenation.

## Physiology of mixed venous and central venous oxygen saturation

$O_2$  delivery ( $DO_2$ ) describes whole-body oxygen supply according to the following formula:

$$DO_2 = CO \times CaO_2 \quad (1)$$

where CO is cardiac output and  $CaO_2$  is arterial oxygen content, which itself is the sum of oxygen bound to hemoglobin [product of hemoglobin concentration (Hb) and arterial  $O_2$  saturation ( $SaO_2$ )] and physically dissolved oxygen [arterial  $PO_2$  ( $PaO_2$ )]:

$$CaO_2 = (Hb \times 1.36 \times SaO_2) + (PaO_2 \times 0.0031) \quad (2)$$

Oxygen demand can be summarized in the whole-body oxygen consumption ( $VO_2$ ), which is expressed mathematically by the Fick principle as the product of CO and arteriovenous  $O_2$  content difference ( $CaO_2 - CvO_2$ ):

$$VO_2 = CO \times (CaO_2 - CvO_2) \quad (3)$$

where mixed venous  $O_2$  content ( $CvO_2$ ) is:

$$CvO_2 = (Hb \times 1.36 \times SvO_2) + (PvO_2 \times 0.0031) \quad (4)$$

Equation 3 may be transposed to:

$$CvO_2 = CaO_2 - \frac{VO_2}{CO} \quad (5)$$

As physically dissolved oxygen can be neglected, Eq. 5 may be written as:

$$Hb \times 1.36 \times SvO_2 \approx (Hb \times 1.36 \times SaO_2) - \frac{VO_2}{CO} \\ \Leftrightarrow SvO_2 \sim \frac{VO_2}{CO} \quad (6)$$

Equation 6 also demonstrates that  $SvO_2$  is directly proportional to the ratio of  $VO_2$  to CO. Thus  $SvO_2$  reflects the relationship between whole-body  $O_2$  consumption and cardiac output. Indeed, it has been shown that the  $SvO_2$  is well correlated with the ratio of  $O_2$  supply to demand [3].

### Pathophysiology of central or mixed venous O<sub>2</sub> saturation during shock

Usually VO<sub>2</sub> is independent of DO<sub>2</sub> since tissues can maintain O<sub>2</sub> needs by increasing O<sub>2</sub> extraction when DO<sub>2</sub> decreases. However, this mechanism has its limits. Below a so-called critical DO<sub>2</sub> compensatory increase in O<sub>2</sub> extraction is exhausted, and VO<sub>2</sub> becomes dependent on DO<sub>2</sub>. In this case tissue hypoxia occurs, and a rise in serum lactate levels may be observed [4].

A decrease in SvO<sub>2</sub> and ScvO<sub>2</sub> represents an increased metabolic stress, because the O<sub>2</sub> demands of the body are not completely met by DO<sub>2</sub>. The causes of a decreasing SvO<sub>2</sub> are multiple and reflect the forces operative in Eqs. 5 and 6. That is, either DO<sub>2</sub> does not increase in such a way to cover an increased VO<sub>2</sub>, or DO<sub>2</sub> drops because of decrease in either arterial O<sub>2</sub> content, cardiac output, or both. Importantly, the normal cardiovascular response of increasing VO<sub>2</sub> is to increase O<sub>2</sub> extraction and cardiac output. Thus SvO<sub>2</sub> normally decreases during exercise despite increasing DO<sub>2</sub>. Therefore a drop in SvO<sub>2</sub> or ScvO<sub>2</sub> does not necessarily mean that tissue hypoxia occurs. The magnitude of the decrease indicates the extent to which the physiological reserves are stressed (Table 1). Whereas in otherwise healthy individuals anaerobic metabolism may occur when SvO<sub>2</sub> drops below its normal value of 75% to 30–40% for a substantial period of time, patients with chronic heart failure may live with an SvO<sub>2</sub> in this low range without apparent tissue hypoxia, presumably because they have adapted to higher oxygen extraction. These patients can increase their VO<sub>2</sub> to a limited degree, however, because O<sub>2</sub> extraction is close to its limits as is cardiac output.

The cardiocirculatory system may be challenged by two different conditions. Firstly, a drop in DO<sub>2</sub> can be induced by anemia, hypoxia, hypovolemia, or heart failure. Secondly, fever, pain, stress etc. may also decrease SvO<sub>2</sub> or ScvO<sub>2</sub> by increasing whole-body VO<sub>2</sub> (Table 2)

Since central venous catheterization is commonly performed for a variety of reasons in critically ill patients, it would be useful if ScvO<sub>2</sub> could function as a surrogate for SvO<sub>2</sub>. The central venous catheter sampling site usually resides in the superior vena cava. Thus central venous blood sampling reflects the venous blood of the upper body but neglects venous blood from the lower body (i.e., intra-abdominal organs). As presented in Fig. 1, venous O<sub>2</sub> saturations differ among several organ systems since they extract different amounts of O<sub>2</sub>. ScvO<sub>2</sub> is usually less than SvO<sub>2</sub> by about 2–3% because the lower body extracts less O<sub>2</sub> than the upper body making inferior vena caval O<sub>2</sub> saturation higher. The primary cause of the lower O<sub>2</sub> extraction is that many of the vascular circuits that drain into the inferior vena cava use blood flow for nonoxidative phosphorylation needs (e.g., renal blood flow, portal flow, hepatic blood flow). However, SvO<sub>2</sub> and ScvO<sub>2</sub> change in parallel when the whole-body ratio of O<sub>2</sub> supply to demand is altered [5].

**Table 1** Limits of mixed venous oxygen saturation

SvO <sub>2</sub> >75%	Normal extraction O <sub>2</sub> supply >O <sub>2</sub> demand
75% >SvO <sub>2</sub> >50%	Compensatory extraction Increasing O <sub>2</sub> demand or decreasing O <sub>2</sub> supply
50% >SvO <sub>2</sub> >30%	Exhaustion of extraction Beginning of lactic acidosis O <sub>2</sub> supply <O <sub>2</sub> demand
30% >SvO <sub>2</sub> >25%	Severe lactic acidosis
SvO <sub>2</sub> <25%	Cellular death

**Table 2** Clinical conditions and their effects on O<sub>2</sub> delivery and O<sub>2</sub> consumption and on venous oximetry

#### Decrease in ScvO<sub>2</sub>/SvO<sub>2</sub>

##### O<sub>2</sub> consumption ↑

Stress  
Pain  
Hyperthermia  
Shivering

##### O<sub>2</sub> delivery ↓

CaO<sub>2</sub> ↓ (anemia, hypoxia)  
Cardiac output ↓

#### Increase in ScvO<sub>2</sub>/SvO<sub>2</sub>

##### O<sub>2</sub> delivery ↑

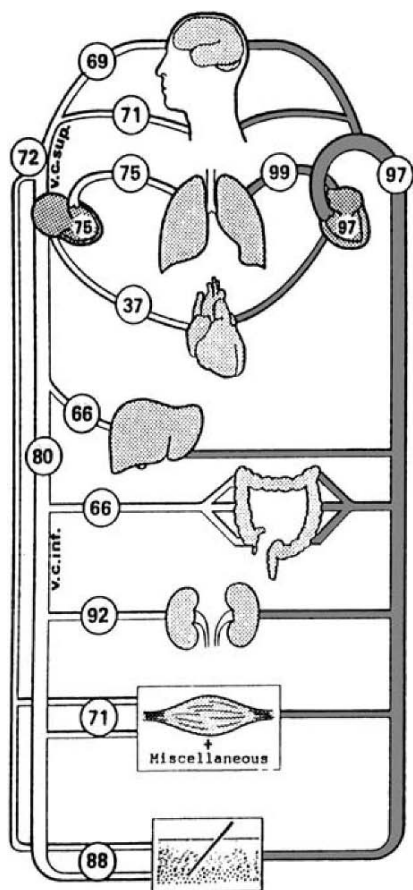
CaO<sub>2</sub> ↑  
Cardiac output ↑

##### O<sub>2</sub> consumption ↓

Analgesia  
Sedation  
Mechanical ventilation  
Hypothermia

The difference between the absolute value of ScvO<sub>2</sub> and SvO<sub>2</sub> changes under conditions of shock [6]. In septic shock ScvO<sub>2</sub> often exceeds SvO<sub>2</sub> by about 8% [7]. During cardiogenic or hypovolemic shock mesenteric and renal blood flow decreases followed by an increase in O<sub>2</sub> extraction in these organs. In septic shock regional O<sub>2</sub> consumption of the gastrointestinal tract and hence regional O<sub>2</sub> extraction increases despite elevated regional blood flows [8]. On the other hand, cerebral blood flow is maintained over some period in shock. This would cause a delayed drop of ScvO<sub>2</sub> in comparison to SvO<sub>2</sub>, and the correlation between these two parameters would worsen. Some authors therefore argued that ScvO<sub>2</sub> cannot be used as surrogate for SvO<sub>2</sub> under conditions of circulatory shock [9].

However, changes in SvO<sub>2</sub> are closely mirrored by changes in ScvO<sub>2</sub> under experimental [10] and clinical conditions [7] despite a variable difference between these two variables. This may explain why Rivers et al. [11] were able to use ScvO<sub>2</sub> higher than 70% in addition to conventional hemodynamic parameters as therapeutic endpoint for hemodynamic resuscitation to improve outcome in patients with severe sepsis and septic shock. From a physiological point of view, SvO<sub>2</sub> monitoring for “early goal directed therapy” should provide similar re-



**Fig. 1** Arterial and venous oxygen saturations in various vascular regions [2]

sults. Given the fact that  $ScvO_2$  exceeds  $SvO_2$  on average by 8% in patients with septic shock, an  $SvO_2$  of about 62–65% should suffice as endpoint for hemodynamic resuscitation in these conditions, although this has not been tested prospectively. However, the placement of pulmonary artery catheters and the potentially higher risk of this should not result in a delay in the start of the resuscitation of critically ill patients.

Venous oximetry can reflect the adequacy of tissue oxygenation only if the tissue is still capable of extracting  $O_2$ . In the case of arteriovenous shunting on the microcirculatory level or cell death,  $SvO_2$  and  $ScvO_2$  may not decrease or even show elevated values despite severe tissue hypoxia. As demonstrated in patients after prolonged cardiac arrest, venous hyperoxia with an  $ScvO_2$  higher than 80% is indicative of impaired oxygen use [12].

## Conclusion

Low values of  $SvO_2$  or  $ScvO_2$  indicate a mismatch between  $O_2$  delivery and tissue  $O_2$  need. While measurement of  $SvO_2$  requires the insertion of a pulmonary artery catheter, measurement of  $ScvO_2$  requires only central venous catheterization.  $ScvO_2$  directed early goal-directed therapy improves survival in patients with septic shock who are treated in an emergency department. However,  $ScvO_2$  values may differ from  $SvO_2$  values, and this difference varies in direction and magnitude with cardiovascular insufficiency.  $ScvO_2$  should not be used alone in the assessment of the cardiocirculatory system but combined with other cardiocirculatory parameters and indicators of organ perfusion such as serum lactate concentration and urine output.

## References

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