How do I use venous saturations?

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Abstract. Mixed (SvO₂) or central (ScvO₂) venous oxygen saturation is frequently used to evaluate the adequacy of global tissue oxygenation in critically ill patients. The aim of this review is to discuss the literature regarding S(c)vO₂ measurement and S(c)vO₂ - directed therapy. Both reductions in oxygen delivery and increases in oxygen consumption without subsequent adequate rise in cardiac output can result in low S(c)vO₂. Unfortunately, normal or high values do not guarantee adequate tissue oxygenation. The use of central instead of mixed venous saturation seems to be acceptable in the early hours of resuscitation of critically ill patients. Following initial resuscitation however, ScvO₂ can probably act only as a warning signal and treatment in this phase should be targeted at optimization of SvO₂ instead of ScvO₂. To guide treatment of patients with a low venous saturation, diagnosis and treatment - algorithms are available.

Introduction

Mixed (SvO₂) or central (ScvO₂) venous oxygen saturation is frequently used on the ICU to evaluate the adequacy of global tissue oxygenation. After the results of the early goal-directed therapy study in 2001 (1), venous saturation monitoring gained renewed popularity and S(c)vO₂ was recommended by the ‘Surviving Sepsis’ campaign (2). However, the use of venous oxymetry is still a matter of debate. Is S(c)vO₂ - directed therapy also beneficial following the initial hours of resuscitation? Is central or mixed venous saturation preferable? And what if S(c)vO₂ is high in patients with sepsis and there are signs of poor tissue perfusion? The aim of this review is to discuss the literature regarding S(c)vO₂ - measurement and S(c)vO₂ - directed therapy.

Physiology and pathophysiology of S(c)vO₂

Global O₂ transport can be described using the following formulas:

\[ \text{DO}_2 = \text{CO} \times \text{CaO}_2 \]
\[ \text{VO}_2 = \text{CO} \times (\text{CaO}_2 - \text{CvO}_2) \]
\[ \text{CvO}_2 = \text{CaO}_2 - \frac{\text{VO}_2}{\text{CO}} \]
\[ \text{O}_2 \text{ER} = \frac{\text{VO}_2}{\text{DO}_2} = \frac{(\text{SaO}_2 - \text{SvO}_2)}{\text{SaO}_2} \]
\[ \text{DO}_2 = \text{CO} \times \text{CaO}_2 \]
\[ \text{VO}_2 = \text{O}_2 \text{ consumption (ml/min)} \]
\[ \text{CaO}_2 = \text{arterial oxygen content} = (1.36 \times \text{Hb} \times \text{SaO}_2) + (0.0031 \times \text{PaO}_2) \]
\[ \text{CvO}_2 = \text{mixed venous oxygen content} = (1.36 \times \text{Hb} \times \text{SvO}_2) + (0.0031 \times \text{PvO}_2) \]
\[ \text{PaO}_2 = \text{arterial partial pressure of oxygen} \]
\[ \text{PvO}_2 = \text{mixed venous partial pressure of oxygen} \]
\[ \text{O}_2 \text{ER} = \text{oxygen extraction ratio} \]

When haemoglobin levels and arterial oxygen saturation remain unchanged and given the fact that the freely dissolved oxygen can be neglected (multiplier of 0.0031), SvO₂ is directly proportional to changes in the ratio of VO₂ to CO. SvO₂ thus reflects the relationship between whole-body O₂ consumption and cardiac output.

With the help of oxygen transport formulas, multiple causes of S(c)vO₂ changes can be described. VO₂ and the components of DO₂ (CO, Hb and SaO₂) interfere as is shown in Figure 1. Note that drops in S(c)vO₂ are not only caused by decreases in DO₂. Elevated oxygen consumption due to fever (3), pain, agitation (4) and increased metabolic activity in sepsis (5), are very common on the ICU. In the hours immediately after major surgery, significant reductions in ScvO₂ were observed which were not related to lower DO₂, stressing the importance of postoperative increased oxygen consumption for ScvO₂ (6).

The human body cannot spontaneously increase SaO₂ or haemoglobin level- at least not immediately. Increased VO₂ is thus compensated by increased CO or by elevated oxygen extraction in the peripheral tissues. An increase of CO would be the organism’s first choice to maintain VO₂. When O₂ need is not fulfilled by an adequate rise in CO, however, increased O₂ extraction ensues, decreasing the S(c)vO₂ value. Importantly, also in healthy individuals, S(c)vO₂ decreases during heavy exercise despite a marked increase in CO. Adaptation may play an important role, as healthy individuals may exhibit tissue hypoxia when ScvO₂ values drop to 30–40% for a relatively short time, whereas patients with severe chronic heart failure may live constantly in this low range without developing tissue hypoxia (7). However, these patients can increase their VO₂ only to a limited degree, as cardiac output cannot be raised and oxygen extraction is close to its limits.

In hyperdynamic septic shock, patients seldom exhibit SvO₂ levels of less than 65%. However, it is a misperception that septic patients always have normal or high venous saturations. In the early, hypovolaemic, course of severe sepsis and septic shock, ScvO₂ levels may well be below 50% (1).

A normal or high ScvO₂ or SvO₂ (>70%) may indicate a well-balanced oxygen supply for the body’s needs. Unfortunately, normal or high values do not guarantee adequate tissue oxygenation. Only if tissue is still capable of extracting oxygen, can S(c)vO₂ be reduced. In the event of microcirculatory and mitochondrial dysfunction in sepsis (8) or local necrosis (e.g. limb or bowel ischaemia), venous return may have a high O₂ content despite persistent cellular hypoxia. Venous hyperoxygenation (>80%) was found to be indicative of a defect in systemic oxygen utilization after prolonged cardiac arrest (9).

Technical aspects

Venous saturations can be measured intermittently by blood sampling from the pulmonary artery or superior vena cava, or continuously by spectrophotometry, which has been found to be accurate and stable (10). For continuous registration, either a pulmonary artery catheter equipped with a fibreoptic sensor (for SvO₂) or a fibreoptic central...
venous catheter (for SvO2), is needed. Another commercially available option for continuous ScvO2 reading is the introduction of a small separate fiberoptic probe, inserted through a previously placed central venous catheter. The latter is particularly helpful if a patient already has a central venous line.

**SvO2 versus ScvO2**

The use of central rather than mixed venous saturation has attracted the attention of ICU clinicians. Central venous catheters are routinely inserted for central venous pressure recording and the infusion of vasoactive drugs or parenteral nutrition and consequently, ScvO2 measurement does not involve extra risks. Moreover, it is less time-consuming than SvO2 measurement.

The central venous catheter sampling-site is usually situated in the superior vena cava. Blood from the inferior vena cava (e.g. effluent from intra-abdominal organs) is therefore mostly neglected and ScvO2 thus represents upper body oxygen balance. Venous O2 saturations vary among organ systems since different organs extract different amounts of O2 (11). In healthy conditions, ScvO2 exceeds SvO2 by about 2–3% (7). However, this difference changes under conditions of circulatory shock. In shock, ScvO2 exceeds SvO2 by about 5% (12;13). During redistribution in low-flow shock states, splanchnic, mesenteric and renal blood flow decreases, resulting in an increase in O2 extraction in these regions and a subsequent decrease in inferior vena cava saturation. In hyperdynamic septic shock, increased regional splanchnic metabolic rate rather than reduced perfusion, leads to lower SO2 in lower body venous return (5). Contrary to blood flow to the abdominal organs, in shock cerebral flow is maintained for some time, resulting in a delayed or absent drop in ScvO2 compared with SvO2.

Another possible explanation of a lower level of ScvO2 on comparison with SvO2, is the mixing of atrial blood with blood emanating from the coronary sinus. Although coronary sinus flow may only be a fraction of total blood flow, the effluent from the coronary sinus has a very low SO2 (44). In shock, coronary blood flow is increased as a consequence of coronary vasodilatation while oxygen extraction of the myocardium remains high (15), thereby reducing ScvO2 in comparison with SvO2.

The difference between ScvO2 and SvO2 is not equal in different ranges of cardiac output. A reversed correlation of the magnitude of the ScvO2 - SvO2 difference to CI and DO2 has been found (12;16). Again, distribution of blood flow in low-flow conditions away from renal, splanchnic and mesenteric areas and towards the brain and myocardium, is likely to explain this phenomenon.

Due to the lack of numerical equivalence, many authors have concluded that ScvO2 cannot be used as a surrogate for SvO2 in the clinical setting (12;13;17;18). Biases (mean of the differences) between the two sample sites ranged from 1% (17) to 7% (10) but more importantly, 95% confidence intervals of these biases were often clinically unacceptable (12;13;18;19). In a study with a mean bias of -5% and a 95% confidence interval of 5% to -10% (13), an ScvO2 measurement of 74% would correspond to an SvO2 of 69% with an uncertainty of the estimate ranging from 58–79%. It thus demonstrates a great variability between individual absolute values and such variability could possibly urge the clinician to take inappropriate actions; especially if the ScvO2 value is around the normal limit of 76%.

Others have stated that ScvO2 could indeed be used as a substitute for SvO2. They emphasize that from a clinical point of view, ScvO2 needs to be interpreted over time and changes in ScvO2 would be able to parallel changes in SvO2 across a wide range of haemodynamic conditions (10;19;20). In addition, the approximately 5% numerical difference between SvO2 and ScvO2 values is found to be consistent, yet less important when addressing severe cases of oxygen imbalance (21). A low ScvO2 – the range in which Rivers’ goal-directed therapy was beneficial (1) - would result in even lower SvO2 values. Thus, irrespective of whether ScvO2 equals SvO2, the presence of a low ScvO2 level is associated with adverse outcome, and correcting this value could improve this. Inserting a pulmonary artery catheter can be time-consuming (22), whereas a central venous catheter can be introduced faster or has already been inserted in the operating theatre or emergency department prior to ICU admission. Therefore, the lack of accuracy of ScvO2 - measurement could be compensated by the positive outcome-effects of ScvO2 - based therapy being started earlier (23).

**S(c)vO2 as a warning signal**

In many clinical conditions, low venous saturation is a warning signal for the development of tissue hypoxia and has been associated with adverse outcome. After normalization of vital signs following resuscitation of shock patients, the majority of the patients continued to have a low ScvO2 and needed additional therapy (24,25). In trauma patients with stable vital signs, ScvO2 was seen to be a reliable indicator of severity of injury and amount of blood loss (26). A significant subset of chronic patients with decompensated end-stage congestive heart failure (CHF) had an ScvO2 as low as 30% at presentation to the emergency department. These patients were clinically indistinguishable from those with mildly decompensated CHF and stable CHF and, once identified, required aggressive alternative management (27). ScvO2 has also been used during cardiac arrest where ScvO2 was able to assess the adequacy or inadequacy of cardiopulmonary resuscitation (28;29), and to predict short-term outcome (30).
The study of Polonen et al. on SvO₂ (and ScvO₂-guided therapy was given in the first 6 hours of treatment at a CVP of 8–12 mmHg, a MAP above 65 mmHg, and a urine output above 0.5 ml/kg/hour) resulted in a 16% absolute reduction in mortality compared to treatment without ScvO₂ monitoring (1). In this study, an important role. Rivers et al. studied early goal-directed therapy in septic shock patients with generally high SvO₂ levels, venous saturation was seen to have a prognostic significance in sepsis as its temporary reduction was associated with increased mortality (32-33).

Efficacy of S(c)vO₂ - directed therapy
SvO₂ can thus be used as a warning signal, but does the use of S(c)vO₂ also render outcome benefit? To answer this question, S(c)vO₂ has to be studied in combination with a treatment algorithm, as monitoring SvO₂ itself will never change outcome. Some have questioned the value of SvO₂ in the treatment of ICU patients (34-35), while others have suggested that SvO₂ can indeed play a beneficial role in resuscitation (36-37). So far, only a few randomized-controlled studies have been performed on the efficacy of S(c)vO₂-directed therapy. These studies indicate that timing of the intervention seems to play an important role. Rivers et al. studied early goal-directed therapy in patients with severe sepsis and septic shock and showed that maintenance of continuously measured ScvO₂ above 70% (in addition to a CVP of 8-12 mmHg, a MAP above 65 mmHg, and a urine output above 0.5 ml/kg/hour) resulted in a 16% absolute reduction in mortality compared to treatment without ScvO₂ monitoring (4). In this study, ScvO₂-guided therapy was given in the first 6 hours of treatment at the emergency department. The study of Polonen et al. on SvO₂ (and lactate)- guided therapy in post- cardiac surgery patients showed a significant reduction in complication rate and length of stay (38). This therapy was started on the ICU immediately postoperatively and lasted for 8 hours. In the preoperative setting however, optimization to achieve a SvO₂ of 65% in vascular surgery patients did not result in a reduction in complications (39). In the study of Gattinoni et al. (40), haemodynamic therapy aimed at achieving normal SvO₂ did not reduce morbidity or mortality among critically ill patients. Contrary to the two positive trials, SvO₂ - directed therapy in this negative trial was given at a later stage of ICU admission and lasted for five days (40). There was a striking difference in baseline value of venous saturation; SvO₂ was 48.6% in the Rivers study (1) and SvO₂ was 69.7% in the Gattinoni study (40).

Clinical guidelines
How should we incorporate the use of S(c)vO₂ into the clinical assessment of the cardiocirculatory system on the ICU? In chronic heart failure patients, a low S(c)vO₂ does not necessarily signify acute problems, just as normal or high venous saturations do not always guarantee adequate tissue oxygenation. Therefore, S(c)vO₂ alone should not be used in the clinical assessment of the cardiocirculatory system, but combined with other indicators of organ hypoperfusion such as oliguria, altered mental state, hyperlactataemia and poor peripheral perfusion. Once a clinical problem has been defined using these indirect parameters, improvement of S(c)vO₂ can be targeted. Pinsky and Vincent proposed a clinically useful diagnostic and therapeutic algorithm based on SvO₂ (41). A similar algorithm is shown in Figure 2. Applying such an algorithm, all possible causes of low S(c)vO₂ can be evaluated in a stepwise manner and treated accordingly. Since the oxygen delivering capabilities of stored red blood cells have been debated and adverse effects of red blood cell transfusion have been reported, best evidence suggests a restrictive transfusion policy on the ICU (transfusion threshold 4.3 mmol/l) with the exception of severe ischaemic cardiac disease (threshold 6.2 mmol/l)(42). How should we deal with a high S(c)vO₂ in combination with signs of persistent tissue hypoxia (e.g. hyperlactataemia), possibly representing limitations in oxygen extracting capability? Administration of nitroglycerin has been shown to reverse microcirculatory shutdown and shunting in septic shock patients (43). This has led to implementation of vasodilator use in clinical practice in some clinics, including ours. Nevertheless, to the best of our knowledge, no study has yet tested the hypothesis that vasodilators such as nitroglycerine can decrease elevated S(c)vO₂ by improving the microcirculation and hence, oxygen extraction capability. So far, evidence on this topic remains scarce and no evidence-based clinical guidelines can be given. Until then, our practical recommendation would be to use vasodilators in hyperlactataemic patients with a high S(c)vO₂, following adequate fluid resuscitation.

Conclusion
Mixed or central venous oxygen saturation represents the balance between global oxygen delivery and consumption. The use of central instead of mixed venous saturation seems to be acceptable in the early hours of resuscitation of critically ill patients. The Surviving Sepsis campaign has acknowledged this by recommending the use of SvO₂ or ScvO₂ in the early resuscitation of patients with severe sepsis and septic shock (2). Following initial resuscitation, however, ScvO₂ can probably act only as a warning signal and definitive treatment in this phase should be directed on the basis of SvO₂ instead of ScvO₂ mea-

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Figure 2. Diagnostic and therapeutic algorithm derived from (41): therapeutic options to be considered are presented in the rectangles. In case of severe ischemic cardiac disease the blood transfusion threshold should be 6.2 mmol/l instead of 4.3 mmol/l (42). The trigger to use this algorithm would be ongoing hypotension despite initial fluid resuscitation efforts or, in the setting of normotension, oliguria, persistent tachycardia, metabolic acidosis, hyperlactatemia, altered mental status or poor peripheral perfusion.
Placement of a pulmonary artery catheter is thus warranted in patients with persistent, therapy-resistant circulatory shock (41). To guide treatment of patients with a low venous saturation, diagnosis and treatment algorithms are available.

References