Received October 2006; accepted in revised form May 2007

REVIEW

How do I use venous saturations?

TC Jansen, J Bakker

Department of Intensive Care, Erasmus MC, Rotterdam, The Netherlands

Abstract. **Mixed (SvO_2) or central ($ScvO_2$) 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)vO_2 measurement and S(c)vO_2 - 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)vO_2. 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, $ScvO_2$ can probably act only as a warning signal and treatment in this phase should be targeted at optimization of SvO_2 instead of $ScvO_2$. To guide treatment of patients with a low venous saturation, diagnosis and treatment- algorithms are available.**

Introduction

Mixed (SvO_2) or central ($ScvO_2$) 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)vO_2 was recommended by the 'Surviving Sepsis' campaign (2). However, the use of venous oxymetry is still a matter of debate. Is S(c)vO_2 - directed therapy also beneficial following the initial hours of resuscitation? Is central or mixed venous saturation preferable? And what if S(c)vO_2 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)vO_2 - measurement and S(c)vO_2 - directed therapy.

Physiology and pathophysiology of S(c)vO2

Global O_2 transport can be described using the following formulas:

$DO_2 = CO \times CaO_2$

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

$CvO_2 = CaO_2 - VO_2/CO$

$O_2ER = VO_2/ DO_2 = (SaO_2 - SvO_2)/ SaO_2$

DO_2= oxygen delivery (ml/min)

VO_2= oxygen consumption (ml/min)

CaO_2= arterial oxygen content = (1.36 x Hb x SaO_2) + (0.0031 x PaO_2)

CvO_2= mixed venous oxygen content = (1.36 X Hb X SvO_2) + (0.0031 X PvO_2)

PaO_2= arterial partial pressure of oxygen

PvO_2= mixed venous partial pressure of oxygen

O_2ER= 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), SvO_2 is directly proportional to changes in the ratio of VO_2 to CO. SvO_2 thus reflects the relationship between whole-body O_2 consumption and cardiac output.

With the help of oxygen transport formulas, multiple causes of S(c)vO_2 changes can be described. VO_2 and the components of DO_2 (CO, Hb and SaO_2) interfere as is shown in Figure 1. Note that drops in S(c)vO_2 are not only caused by decreases in DO_2. 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 $ScvO_2$ were observed which were not related to lower DO_2, stressing the importance of postoperative increased oxygen consumption for $ScvO_2$ (6).

The human body cannot spontaneously increase SaO_2 or haemoglobin level- at least not immediately. Increased VO_2 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 VO_2. When O_2 need is not fulfilled by an adequate rise in CO, however, increased O_2 extraction ensues, decreasing the S(c)vO_2 value. Importantly, also in healthy individuals, S(c)vO_2 decreases during heavy exercise despite a marked increase in CO. Adaptation may play an important role, as healthy individuals may exhibit tissue hypoxia when $ScvO_2$ 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 VO_2 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 SvO_2 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, $ScvO_2$ levels may well be below 50% (1).

A normal or high SvO_2 or $ScvO_2$ (>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)vO_2 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 O_2 content despite persistent cellular hypoxia. Venous hyperoxia (>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 SvO_2) or a fibreoptic central

Correspondence:

J. Bakker
E-mail: jan.bakker@erasmusmc.nl

venous catheter (for $ScvO_2$), is needed. Another commercially available option for continuous $ScvO_2$ reading is the introduction of a small separate fibreoptic probe, inserted through a previously placed central venous catheter. The latter is particularly helpful if a patient already has a central venous line.

SvO_2 versus $ScvO_2$

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, $ScvO_2$ measurement does not involve extra risks. Moreover, it is less time-consuming than SvO_2 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 $ScvO_2$ thus represents upper body oxygen balance. Venous O_2 saturations vary among organ systems since different organs extract different amounts of O_2 (11). In healthy conditions, SvO_2 exceeds $ScvO_2$ by about 2–3% (7). However, this difference changes under conditions of circulatory shock. In shock, $ScvO_2$ exceeds SvO_2 by about 5% (12;13). During redistribution in low-flow shock states, splanchnic, mesenteric and renal blood flow decreases, resulting in an increase in O_2 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 SO_2 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 $ScvO_2$ compared with SvO_2.

Another possible explanation of a lower level of $ScvO_2$ on comparison with SvO_2, 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 SO_2 (14). In shock, coronary blood flow is increased as a consequence of coronary vasodilatation while oxygen extraction of the myocardium remains high (15), thereby reducing SvO_2 in comparison with $ScvO_2$.

The difference between $ScvO_2$ and SvO_2 is not equal in different ranges of cardiac output. A reversed correlation of the magnitude of the $ScvO_2$ - SvO_2 difference to CI and DO_2 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 $ScvO_2$ cannot be used as a surrogate for SvO_2 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 -16% (13), an $ScvO_2$ measurement of 74% would correspond to an SvO_2 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 $ScvO_2$ value is around the normal limit of 70%.

Others have stated that $ScvO_2$ could indeed be used as a substitute for SvO_2. They emphasize that from a clinical point of view, $ScvO_2$ needs to be interpreted over time and changes in $ScvO_2$ would be able

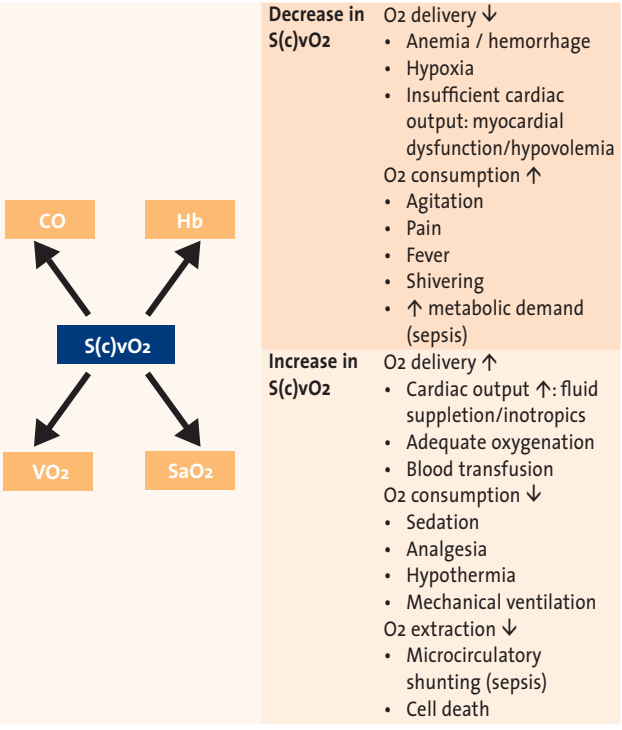

Figure 1. Multiple factors influence the value of S(c)vO2.

to parallel changes in SvO_2 across a wide range of haemodynamic conditions (10;19;20). In addition, the approximately 5% numerical difference between SvO_2 and $ScvO_2$ values is found to be consistent, yet less important when addressing severe cases of oxygen imbalance (21). A low $ScvO_2$ – the range in which Rivers' goal-directed therapy was beneficial (1) - would result in even lower SvO_2 values. Thus, irrespective of whether $ScvO_2$ equals SvO_2, the presence of a low $ScvO_2$ 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 $ScvO_2$- measurement could be compensated by the positive outcome-effects of $ScvO_2$- based therapy being started earlier (23).

$S(c)vO_2$ 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 $ScvO_2$ and needed additional therapy (24;25). In trauma patients with stable vital signs, $ScvO_2$ 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 $ScvO_2$ 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). $ScvO_2$ has also been used during cardiac arrest where $ScvO_2$ was able to assess the adequacy or inadequacy of cardiopulmonary resuscitation (28;29), and to predict short- term outcome (30). In the

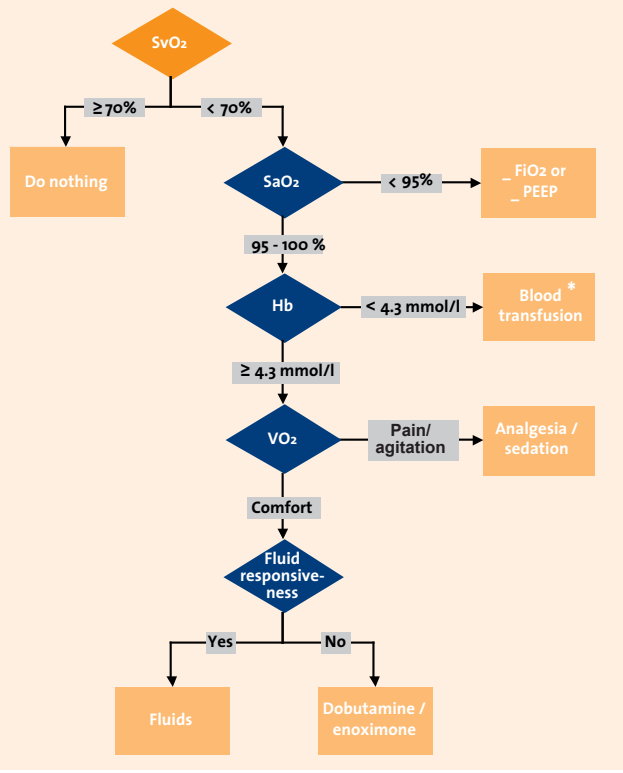

Figure 2. Diagnostic and therapeutic algorithm derived from (41): therapeutic options to be considered are presented in the rectangles. * In case of severe ischemic cardiac disease the blood transfusion threshold should be 6.2 mmol/l instead of 4.3 mmol/l (42). The trigger to use this algorithm would 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.

postoperative setting, reductions in $ScvO_2$ have been independently associated with postoperative complications (6). SvO_2 values under 70% during the first 48 hours of treatment for septic shock on the ICU has been seen as a significant independent predictor of mortality (31). Even in hyperdynamic septic shock patients with generally high $S(c)vO_2$ 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 $S(c)vO_2$ - directed therapy

$ScvO_2$ can thus be used as a warning signal, but does the use of $S(c)vO_2$ also render outcome benefit? To answer this question, $S(c)vO_2$ has to be studied in combination with a treatment algorithm, as monitoring SvO_2 itself will never change outcome. Some have questioned the value of SvO_2 in the treatment of ICU patients (34;35), while others have suggested that SvO_2 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 $S(c)vO_2$-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 $ScvO_2$ 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 $ScvO_2$ monitoring (1). In this study, $ScvO_2$-guided therapy was given in the first 6 hours of treatment at the emergency department. The study of Polonen et al. on SvO_2 (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 SvO_2 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 SvO_2 did not reduce morbidity or mortality among critically ill patients. Contrary to the two positive trials, SvO_2 -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; $ScvO_2$ was 48.6% in the Rivers study (1) and SvO_2 was 69.7% in the Gattinoni study (40).

Clinical guidelines

How should we incorporate the use of $S(c)vO_2$ into the clinical assessment of the cardiocirculatory system on the ICU? In chronic heart failure patients, a low $S(c)vO_2$ does not necessarily signify acute problems, just as normal or high venous saturations do not always guarantee adequate tissue oxygenation. Therefore, $S(c)vO_2$ 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 $S(c)vO_2$ can be targeted. Pinsky and Vincent proposed a clinically useful diagnostic and therapeutic algorithm based on SvO_2 (41). A similar algorithm is shown in Figure 2. Applying such an algorithm, all possible causes of low $S(c)vO_2$ 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 $S(c)vO_2$ 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 $S(c)vO_2$ 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 $S(c)vO_2$, 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 SvO_2 or $ScvO_2$ in the early resuscitation of patients with severe sepsis and septic shock (2). Following initial resuscitation, however, $ScvO_2$ can probably act only as a warning signal and definitive treatment in this phase should be directed on the basis of SvO_2 instead of $ScvO_2$ mea-

surement. 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.

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