Clinical review: use of venous oxygen saturations as a goal – a yet unfinished puzzle

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Abstract
Shock is defined as global tissue hypoxia secondary to an imbalance between systemic oxygen delivery and oxygen demand. Venous oxygen saturations represent this relationship between oxygen delivery and oxygen demand and can therefore be used as an additional parameter to detect an impaired cardiorespiratory reserve. Before appropriate use of venous oxygen saturations, however, one should be aware of the physiology. Although venous oxygen saturation has been the subject of research for many years, increasing interest arose especially in the past decade for its use as a therapeutic goal in critically ill patients and during the perioperative period. Also, there has been debate on differences between mixed and central venous oxygen saturation and their interchangeability. Both mixed and central venous oxygen saturation are clinically useful but both variables should be used with insightful knowledge and caution. In general, low values warn the clinician about cardiocirculatory or metabolic impairment and should urge further diagnostics and appropriate action, whereas normal or high values do not rule out persistent tissue hypoxia. The use of venous oxygen saturations seems especially useful in the early phase of disease or injury. Whether venous oxygen saturations should be measured continuously remains unclear. Especially, continuous measurement of central venous oxygen saturation as part of the treatment protocol has been shown a valuable strategy in the emergency department and in cardiac surgery. In clinical practice, venous oxygen saturations should always be used in combination with vital signs and other relevant endpoints.

Introduction
Shock is defined as global tissue hypoxia secondary to an imbalance between systemic oxygen delivery (DO₂) and systemic oxygen demand (VO₂). Unrecognised and untreated global tissue hypoxia increases morbidity and mortality. Accurate detection of global tissue hypoxia is therefore of vital importance. Physical findings, vital signs, measuring central venous pressure and urinary output are important but insufficient for accurate detection of global tissue hypoxia [1-3]. Measurement of mixed venous oxygen saturation (SvO₂) from the pulmonary artery has been advocated as an indirect index of tissue oxygenation [4]. As a result of an extensive debate in the literature [5-7], however, use of the pulmonary artery catheter has become somewhat unpopular. In contrast, insertion of a central venous catheter in the superior vena cava via the jugular or the subclavian vein is considered standard care in critically ill patients. Just like SvO₂, the measurement of central venous oxygen saturation (ScvO₂) has been advocated in order to detect global tissue hypoxia.

Venous oxygen saturations have been the subject of research for over 50 years, but especially over the past decade the amount of literature describing changes in ScvO₂ and SvO₂ in critically ill patients, including high-risk surgical patients, increased substantially. This led to high expectations with respect to the use of venous oxygen saturation as a therapeutic goal. The aim of the present review is to summarise the evidence and to discuss the clinical utility of both SvO₂ and ScvO₂ in the treatment of critically ill patients, including high-risk surgical patients.

We performed a search of the PUBMED database from 1980 to 2010 using combinations of the following terms: SvO₂, ScvO₂, venous oxygen saturation, venous saturation, critically ill, shock, septic shock, high risk surgery, surgery, operation. The articles published in English were included when published in a peer-reviewed journal. The clinical investigations had to concern adults. Additionally, bibliographies of relevant articles were also screened.

Physiology
Understanding the physiology of venous saturations is essential for effective application in critically ill patients and during the perioperative period.
SvO₂ depends on arterial oxygen saturation (SaO₂), the balance between VO₂ and cardiac output (CO), and haemoglobin (Hb) levels. According to the Fick principle [8], SvO₂ can be described by the following formula:

\[
\text{SvO}_2 = [\text{SaO}_2 – \text{VO}_2 / \text{CO}] [1 / \text{Hb} \times 1.34]
\]

Increased VO₂ will be compensated by increased CO. If this is not adequate – that is, if oxygen demand is not met – elevated oxygen extraction occurs in the peripheral tissues and consequently SvO₂ will drop. SvO₂ thus reflects the balance between oxygen delivery and oxygen demand [9]. The normal range for SvO₂ is 65 to 75% [4,10]. Low SvO₂ is predictive of bad outcome [4,11], whereas normal or supranormal SvO₂ (or ScvO₂) values do not guarantee adequate tissue oxygenation [12,13]. If tissue is not capable of extracting oxygen (for example, in the case of shunting and cell death), venous return may have a high oxygen content despite persistent cellular hypoxia.

A variety of physiological and pathological changes may influence venous saturation (Figure 1) and thus require different therapeutic interventions. Recognition of the aetiology of any derangement is obligatory for the safe use of venous saturation as a therapeutic goal.

**Central versus mixed venous oxygen saturation**

In general there has been considerable debate on equality or interchangeability of ScvO₂ and SvO₂ [14-16] (see Table 1). In critically ill patients, substituting SvO₂ by ScvO₂ results in large variability [16-21]. This could in part be explained by modifications of blood flow distribution and oxygen extraction by brain and splanchnic tissue. In this situation, ScvO₂ may provide the false impression of adequate body perfusion. Also, whether a positive ScvO₂–SvO₂ gradient can be used as a marker of greater oxygen utilisation and a predictor of survival remains a subject of debate [20,22,23].

In contrast, other studies have stated that ScvO₂ could indeed be used as a substitute for SvO₂ [24-26]. For example, Reinhart and colleagues performed continuous measurements of venous oxygen saturations in anaesthetised dogs over a wide range of haemodynamic conditions, including hypoxia, haemorrhage and resuscitation, and described close tracking between ScvO₂ and SvO₂ [24]. However, correlation was lowest during hypoxia, one of the areas of greatest clinical interest. Nevertheless, precise determination of absolute values for SvO₂ from ScvO₂ was not possible, as was seen before [21,27-29].

Additionally, the relationship between CO or the cardiac index and venous saturations has been evaluated in critically ill patients. So far, the results have been inconclusive for both SvO₂ and ScvO₂. Larger trials are needed before clinical recommendations can be made regarding their clinical use [19,30-33].

**Clinical use of venous oxygen saturations**

**Cardiac failure**

Venous oxygen saturations have been shown to have diagnostic, prognostic, and therapeutic qualities in critically ill patients with acute myocardial infarction (see
Table 1. Studies comparing mixed venous oxygen saturation and central venous oxygen saturation

| Study                                      | Design and subjects                          | Results                                                                 | Conclusions                                                                 |
|--------------------------------------------|----------------------------------------------|--------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| Varpula and colleagues [14]               | n = 16; septic shock; ICU; 72 paired samples | Mean SvO₂ below mean ScvO₂ at all time points; bias of difference 4.2%   | Difference between ScvO₂ and SvO₂ varied highly; SvO₂ cannot be estimated on basis of ScvO₂ |
| Martin and colleagues [16]                | n = 7; 580 comparative measurements; critically ill patients; ICU; with and without interventions | Difference ≥5% in 49% during periods of stability and in 50% during periods with therapeutic interventions | ScvO₂ monitoring not reliable                                                      |
| Chawla and colleagues [17]                | n = 32 postsurgical and medical; ICU         | SvO₂ consistently lower than ScvO₂ with mean (± SD) bias –5.2 ± 5.1%     | SvO₂ and ScvO₂ not equivalent; substitution of ScvO₂ for SvO₂ in calculation of VO₂ resulted in unacceptably large errors |
| Kopterides and colleagues [18]            | n = 37; septic shock                          | Mean SvO₂ below mean ScvO₂; mean bias –8.5%; 95% limits of agreement –20.2 to 3.3%; this resulted in higher VO₂ values | ScvO₂ and SvO₂ not equivalent in ICU patients with septic shock; substitution of ScvO₂ for SvO₂ in calculation of VO₂ resulted in unacceptably large errors |
| Ho and colleagues [19]                    | n = 20; cardiogenic or septic shock          | ScvO₂ overestimated SvO₂ with mean bias 6.9%; 95% limits of agreement –5.0 to 18.8%; changes of ScvO₂ and SvO₂ did not follow the line of perfect agreement | ScvO₂ and SvO₂ are not interchangeable numerically                                |
| van Beest and colleagues [20]             | n = 53, 265 paired samples; sepsis; ICU; multicentre | Mean SvO₂ below mean ScvO₂ at all time points; bias of difference 1.7% | SvO₂ does not reliably predict SvO₂ in patients with sepsis                                             |
| Scheinmann and colleagues [21]            | n = 24; critically ill cardiac patients; CCU | ScvO₂ levels in superior vena cava are greater than SvO₂ in shock (58 ± 13 vs. 47.5 ± 15; r = 0.55); changes in ScvO₂ reflect changes in SvO₂ (r = 0.90); ScvO₂ from right atrium is similar to SvO₂ (49.2 ± 19 vs. 49.2 ± 19; r = 0.96) | SvO₂ consistently lower than ScvO₂; Poor correlation in heart failure or shock |
| Dueck and colleagues [25]                 | n = 70; 502 comparative sets; neurosurgery   | 95% limits of agreement ranged from 6.8% to 9.3% for single values       | Numerical ScvO₂ values not equivalent to SvO₂ in varying haemodynamic conditions; trend of ScvO₂ may be substituted for the trend of SvO₂ |
| Reinhart and colleagues [26]              | n = 32; critically ill patients; ICU; continuous parallel measurements | ScvO₂ closely paralleled SvO₂ in vitro r = 0.88 and in vivo r = 0.81      | Continuous fibreoptic measurement of ScvO₂                                                                 |
| Ladakis and colleagues [28]               | n = 31 surgical and n = 30 medical; critically ill patients; ICU | ScvO₂ averaged (± SD) 7 ± 4% higher than SvO₂; ScvO₂ changed in parallel in 90% when SvO₂ changed more than 5% | Potentially reliable tool to rapidly warn of acute change in the oxygen supply/demand ratio |
| Tahvanainen and colleagues [29]           | n = 42; critically ill patients; ICU; ScvO₂, as representative of real changes in pulmonary shunt | Significant correlation between measured variables between PA blood samples and both superior vena cava and right atrial blood samples (P < 0.001) | ScvO₂ can replace SvO₂, exact SvO₂ value can only be measured from the PA itself |

CCU, cardiac care unit; CI, cardiac index; DO₂, oxygen delivery; PA, pulmonary artery; ScvO₂, central venous oxygen saturation; SvO₂, mixed venous oxygen saturation; VO₂, oxygen consumption.

Table 2. SvO₂ was particularly reduced in patients with cardiogenic shock or left ventricular failure. Patients with cardiac failure are unable to increase CO during periods of increased oxygen need. Changes in oxygen demand will therefore only be compensated by changes in oxygen extraction in the same direction and indicated by inverse changes in venous oxygen saturations. Consequently, a drop in venous oxygen saturations will be a marker of...
Table 2. Studies describing central venous oxygen saturation in clinical settings

| Study                                      | Design and subjects                                                                 | Results                                                                                     | Conclusions                                                                                     |
|--------------------------------------------|--------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| Rady and colleagues [1]                    | n = 36; critically ill patients; ED                                                  | Additional therapy is needed after haemodynamic stabilisation to normal blood pressure and heart rate | ScvO₂ can be utilised to guide therapy in this phase                                             |
| Pope and colleagues [13]                   | n = 619 registries treated with EGDT; observational study                            | Groups: ScvO₂ <70%, ScvO₂ 71 to 89%, ScvO₂ >90% Multivariate analysis: initial high ScvO₂ higher mortality | Also high ScvO₂ values predictive for mortality                                                   |
| Ander and colleagues [35]                  | Controls n = 17, high lactate group n = 22, low lactate group n = 5; chronic congestive heart failure; ED | ScvO₂ lower in high lactate group than in low lactate group (32 ± 12% vs. 51 ± 13%) and control (60 ± 6%); after treatment | Once patients with decompensated end-stage congestive heart failure are identified, these patients require aggressive alternative management |
| Scalea and colleagues [40]                 | n = 26, trauma patients with suggested blood loss                                     | Despite stable vital signs, 39% of the patients had ScvO₂ <65%; these patients required more transfusions; linear regression analysis demonstrated superiority of ScvO₂ to predict blood loss compared with normally allowed parameters | ScvO₂ is a reliable and sensitive method for detecting blood loss; it is a useful tool in the evaluation of acutely injured patients |
| Di Filippo and colleagues [41]             | n = 121 brain injury after trauma, noncontrolled study                               | Nonsurvivors showed higher lactate, lower ScvO₂ values; patients with ScvO₂ >65% showed higher 28-day mortality, ICU LOS and hospital LOS than patients with ScvO₂ <65% | ScvO₂ <65% in first 24 hours after admission in patients with major trauma and head injury is associated with prolonged hospitalisation and higher mortality |
| Pease and colleagues [65]                  | n = 118, major surgery                                                               | After multivariate analysis, lowest CI and lowest ScvO₂ were associated with postoperative complications; optimal ScvO₂ cut-off value for morbidity prediction was 64.4% in the first hour after surgery; significant reductions in ScvO₂ were observed, without significant changes in CI or oxygen delivery index | Results suggest that oxygen consumption is also an important determinant of ScvO₂; reductions in ScvO₂ are independently associated with postoperative complications |
| Rivers and colleagues [73]                 | n = 263; RCT; EGDT vs. controls; severe sepsis, septic shock; ED                   | EGDT (goal: ScvO₂ ≥70%) showed better survival (absolute 16%), lower lactate; more fluids, red cell transfusion and inotropics | EGDT provides benefits to outcome                                                                 |
| Trzecki and colleagues [74]                | n = 16 pre-EGDT; n = 22 EGDT                                                       | Less PAC utilisation; more fluids and dobutamine used; similar costs                         | EGDT endpoint can reliably be achieved                                                           |
| Kortgen and colleagues [75]                | n = 30 controls; n = 30 septic shock                                                | Implementation: use of dobutamine, insulin, hydrocortisone and activated protein C increased Amount of fluids and packed blood cells unaffected | Implementation of sepsis bundle feasible Survival benefit                                         |
| Jones and colleagues [76]                  | n = 79 pre-intervention; n = 77 post-intervention; ED                               | Controls: more renal failure at baseline Greater crystalloid volume and vasopressor infusion Mortality 18 vs. 27% | Implementation resulted in mortality reduction                                                   |
| Micek and colleagues [78]                  | n = 60 before implementation order set; n = 60 after implementation order set; ED   | More appropriate antimicrobial regimen More fluids, more vasopressors Less vasopressor by time of transfer to the ICU | Shorter hospital LOS Lower 28-day mortality                                                      |
| Shapiro and colleagues [80]                | n = 51 historical controls; n = 79 septic shock                                     | Patients received more fluids, earlier antibiotics, more vasopressors, tighter glucose control, more frequent assessment of adrenal function, not more packed blood cells | Implementation sepsis protocol feasible No survival benefit                                      |
| Jones and colleagues [94]                  | Multicentre, randomised; n = 300 severe sepsis, septic shock                       | Higher in hospital mortality ScvO₂; nonsignificant difference (predefined –10% threshold) | No significantly different in-hospital mortality between normalisation of lactate clearance compared with normalisation ScvO₂ |

CI, cardiac index; ED, emergency department; EDGT, early goal-directed therapy; LOS, length of stay; PAC, pulmonary artery catheter; RCT, randomised controlled trial; ScvO₂, central venous oxygen saturation.
cardiac deterioration. Patients with low venous oxygen saturations in the early disease stage may be considered in shock [34,35]. Also, patients with sepsis and known decreased left ventricular function seem to benefit from early goal-directed therapy (EGDT) when treated for sepsis [36] according to the Surviving Sepsis Campaign guidelines [37]. Finally, in the setting of cardiopulmonary resuscitation, a ScvO2 of 72% is highly predictive for return of spontaneous circulation [38].

Trauma
In the initial assessment of trauma patients, an adequate judgement of possible blood loss is essential. Compared with conventional parameters, venous oxygen saturations are superior in predicting blood loss [39,40]. Moreover, after major trauma with brain injury, ScvO2 values below 65% in the first 24 hours are associated with higher mortality (28-day mortality 31.3% vs. 13.5%) and prolonged hospitalisation (45 days vs. 33 days) [41].

High-risk surgery
In cardiac surgery patients, SvO2 has been shown to be superior to the mean arterial pressure and heart rate as a qualitative warning sign of substantial haemodynamic deterioration. However, results on the predictive value of SvO2 for CO in clinical settings are inconsistent [42-44]. Nevertheless, continuous SvO2 monitoring enables the early diagnosis of occult bleeding or could show poor tolerance of a moderate anaemia due to the inability of the patient with chronic heart dysfunction or preoperative negative inotropic treatment (for example, β-blockers) to increase CO in the face of anaemia. Furthermore, temporary decreases of SvO2 values after cardiac surgery are of prognostic value and may predict the development of arrhythmias [45-47]. Also, probably due to an increased oxygen extraction ratio, decreased SvO2 values during weaning from mechanical ventilation are predictive for extubation failure [48-50]. Finally, good predictive values of SvO2 for mortality have been described [51,52]. This suggests beneficial effects of SvO2 monitoring, at least during and after cardiac surgery.

Goal-directed therapy has been shown to improve outcome after major general surgery [53]. Originally, the goals in the protocol group were supranormal haemodynamic and oxygen transport values (cardiac index >4.5 l/minute/m², DO2 >600 ml/minute/m², VO2 >170 ml/minute/m²). In this group a significant reduction of complications, hospital stay, duration of mechanical ventilation and mortality was achieved when the pulmonary artery catheter was placed preoperatively [54]. Such a strict predefined concept holds certain risks, however, and should not be translated to all patients [55-57]. Meta-analyses of haemodynamic optimisation in high-risk patients revealed haemodynamic optimisation to be beneficial only when interventions were commenced before development of organ failure [58,59]. Several of the studies described showed improved outcome, possibly including long-term survival, when goal-directed therapy was commenced before surgery [54,60-62]. Perhaps owing to methodological shortcomings, a multicentre trial that randomised surgical patients to pulmonary artery catheter guided or conventional management failed to show a difference in outcome [63,64]. More recently a reduction in postoperative complications and duration of hospital stay was described when goal-directed therapy was used postoperatively [65-67]. However, the abovementioned findings do not provide definite answers on how to use venous saturations as a therapeutic goal. Only one interventional trial used ScvO2 as a therapeutic goal in perioperative care [68]. In this study the intervention group received therapy to achieve an estimated oxygen extraction ratio <27% after predefined goals for arterial pressure, urine output, and central venous pressure had been achieved. Fewer patients developed organ failure in the ScvO2 group [68].

Sepsis and septic shock
In a large multicentre study, three different cohorts of a very heterogeneous population of critically ill patients were compared for survival after different strategies for haemodynamic therapy had been applied: control versus supranormal values for the cardiac index (>4.5 l/minute/m²) or normal values for mixed venous saturation. In total, the anticipated goal was only achieved in one-third of the patients. There was no significant reduction in morbidity or mortality in any group [69]. An important reason for this may be the late timing of the intervention (that is, after occurrence of organ failure), implying that all patients suffered severe damage and received significant treatment before inclusion.

Global tissue hypoxia as a result of systemic inflammatory response or circulatory failure is an important indicator of shock preceding multiple organ dysfunction syndrome. The development of multiple organ dysfunction syndrome predicts the outcome of the septic patient [37]. Treatment strategies aimed at restoring the balance between DO2 and VO2 by maximising DO2 have not been successful [57,69,70].

In line with studies over several decades [1,21,27,35,40,71] and based on recommendations [72], Rivers and colleagues randomised 263 patients with severe sepsis or septic shock to standard therapy or EGDT. Compared with the conventionally treated group, the ScvO2 guided group received more fluids, more frequently dobutamine, and more blood transfusion during the first 6 hours. This resulted in an absolute reduction in 28-day mortality of 16% [73].
A large number of studies that implemented certain treatment protocols in the emergency department – including antibiotic therapy and tight glucose control, for example [74-79] – showed a significant decrease in mortality. EGDT endpoints (central venous pressure 8 to 12 mmHg, mean arterial pressure ≥65 mmHg, and ScvO₂ ≥70%) can well be achieved in an emergency department setting, suggesting that a multifactor approach is a useful strategy in the treatment of sepsis [74-80]. Of note, three of these studies described similar populations with a high percentage of end-stage renal disease in the control group being prone for higher mortality [76,77,79,81]. Although attainment of ScvO₂ >70% has been reported as a prominent factor for survival [82], several studies that used EGDT without this specific target were also able to achieve a survival benefit [83-85]. In summary, as shown by Nguyen and colleagues [86], the use of (modified) EGDT implies early recognition of the critically ill patient and enforces continuous reassessment of treatment. This observation seems to be the greatest gain in the treatment of patients with severe sepsis or septic shock over the past decade.

Earlier studies that enrolled patients admitted to the ICU were unable to show a decrease in mortality after aggressive haemodynamic optimisation [57,69]. In contrast, more recent studies that used modified EGDT protocols were able to show a significant decrease in mortality [85,87,88], suggesting that compliance to dedicated sepsis bundles after the emergency department stage can still be useful.

Low incidences of low ScvO₂ values at ICU admission [89] or emergency department presentation [90] do occur together with baseline mortality, however, compared with the original EGDT study [73,89,90]. For clinical appreciation of the above-mentioned results, a thorough look into the data is needed. Interestingly, fewer patients were intubated before the first ScvO₂ sampling in the EGDT study [73], and this could partially explain the difference of initial ScvO₂ values between both studies [73,89]: due to higher DO₂ (pre-oxygenation) and lower VO₂ (sedation, paralysis; lower work of breathing), ScvO₂ may very well improve in response to emergency intubation in the majority of patients [91]. This hypothesis partially explains the differences between populations [73,89,90] and provides another piece in the puzzle on the value of ScvO₂ [92]. Nevertheless, applicability of the results of the EGDT trial may be dependent on the geographical setting and the underlying healthcare system [92,93].

Additionally, no difference in outcome was found between a resuscitation protocol based on lactate clearance and a ScvO₂-based protocol [94], and ScvO₂ optimisation does not always exclude a decrease in lactate levels [95]. Also, the pursuit of ScvO₂ >70% does not always seem to be the optimal solution. Recent data suggest that patients with initially high ScvO₂ values may also have adverse outcomes [12,13], probably due to impaired oxygen utilisation. High ScvO₂ values may thus represent an inability of the cells to extract oxygen or microcirculatory shunting in sepsis [96].

Finally, as a reflection of an increased respiratory muscle oxygen extraction ratio, a reduced ScvO₂ or SvO₂ predicts extubation failure in difficult-to-wean patients [48,97]. However, a successful intervention to increase ScvO₂ in this context is not yet known. Nevertheless, it is conceivable that in the future ScvO₂ will be used as a parameter in weaning protocols for a subset of patients [97,98].

Continuous measurement

Should continuous measurement be considered when venous saturations are used as a therapeutic goal? It may be argued that changes in venous saturations may occur rapidly, particularly in haemodynamically unstable patients, and that discontinuous spot measurements by drawing intermittent blood samples may miss these changes. Accordingly, continuous measurement of SvO₂ in septic shock patients revealed a higher frequency of short-term changes in SvO₂ in nonsurvivors. Variations in SvO₂ could thus be of prognostic importance [99]. However, the lack of therapeutic guidelines and cost-effectiveness issues question the clinical use of continuous measurement of SvO₂ in critically ill patients [5,7,58]. Continuous measurement in perioperative care allows detection of fluctuations. Low SvO₂ values have been associated with increased complications and morbidity, especially in cardiac surgery [100]. The use of SvO₂ values >70% as a target seems promising in cardiac surgery and during cardiopulmonary resuscitation [38,43].

There are currently two commercially available devices to measure ScvO₂ continuously. Continuous ScvO₂ measurement as part of treatment protocol has shown to be a valuable strategy in the emergency department [71,73] and in cardiac surgery [101]. Additionally, Reinhart and colleagues concluded that continuous ScvO₂ measurement in the ICU setting is potentially reliable [26]. However, continuous and intermittent measurements of SvO₂ or ScvO₂ have never been compared systematically.

Conclusions

The ongoing debate on differences between SvO₂ and ScvO₂ and their interchangeability should focus on well-defined populations. SvO₂ and ScvO₂ are clinically useful but both variables should be used with knowledge and caution. Evaluating the available evidence in a clinical setting, we conclude that low venous oxygen saturations are an important warning sign for the inadequacy of DO₂
to meet oxygen demands. Low values may warn the clinician about cardiocirculatory or metabolic impairment and should urge for further diagnostics and appropriate action, whereas normal or high values do not rule out persistent tissue hypoxia. Based on the numerous clues for its usefulness discussed in this article, the use of venous oxygen saturations seems especially useful in the early phase of disease or injury. In clinical practice, venous oxygen saturations should always be used in combination with vital signs and other relevant endpoints.

Abbreviations
CO, cardiac output; DO₂, systemic oxygen delivery; EGDTr, early goal-directed therapy; Hb, haemoglobin; SaO₂, arterial oxygen saturation; ScvO₂, central venous oxygen saturation; SvO₂, mixed venous oxygen saturation; VO₂, systemic oxygen demand.

Competing interests
The authors declare that they have no competing interests.

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