Complications after major surgery are a leading cause of morbidity and mortality. The etiology of postoperative complications is complex, but poor cardiorespiratory reserve appears to be a key factor. There is increasing interest in the use of central and mixed venous oxygen saturation to guide therapeutic interventions during the perioperative period. However, a detailed understanding of the physiologic principles of venous oximetry is essential for safe and effective use in clinical practice. Venous oxygen saturation reflects the balance between global oxygen delivery and oxygen consumption, which may be affected by a wide range of factors during the perioperative period. The purpose of this article is to describe the physiology and measurement of mixed and central venous oxygen saturation and to explore the findings of clinical investigations of their use in perioperative care.

It is estimated that 234 million major surgical procedures are performed worldwide each year. Complications after major surgery are a leading cause of morbidity and mortality. High-risk surgical patients account for more than 80% of deaths but less than 15% of in-patient procedures. Data from across the developed world confirms that poor outcomes after high-risk surgery are a global problem. Even for those patients who survive to leave hospital, postoperative complications remain an important determinant of long-term survival. It is therefore essential that we seek to improve outcomes for patients undergoing major surgery.

The etiology of postoperative complications is complex, but poor cardiorespiratory reserve appears a key factor. A number of reports indicate that poor outcomes after major surgery are strongly associated with derangements in tissue oxygen delivery that may in turn relate to impaired microvascular flow. The use of fluid and inotropic therapy to enhance tissue oxygen delivery may reduce the incidence of postoperative complications.

There is an increasing body of literature describing changes in central (ScvO₂) and mixed venous oxygen saturation (SvO₂) during the perioperative period, which, along with a recent study in patients with severe sepsis, has led to interest in the use of venous saturation as a therapeutic goal for surgical patients. However, the complexities of the physiology of venous oxygen saturation are poorly recognized. A detailed understanding of these principles is essential for the safe and effective application in clinical practice. The aim of this article is to describe the physiology and measurement of SvO₂ and ScvO₂ and to describe the findings of clinical investigations of the use of these variables in perioperative care.

Materials and Methods

Searches of the MEDLINE and Cochrane CENTRAL databases from January 1968 to December 2008 were performed by both authors using the following search terms: (venous saturation OR venous oximetry OR SvO₂ OR ScvO₂) AND (surgery OR surgical OR "operative OR operation"). Only articles published in English were included, but no restrictions were placed on source. A further online search was then carried out using the Google Scholar search engine by using the following key words: venous saturation, venous oximetry, surgery, ScvO₂, SvO₂. The resulting abstracts were screened to identify relevant investigations in adult patients undergoing major surgery. Studies were excluded if they had not been published in a peer-reviewed journal. Bibliographies of relevant articles were also screened. Manuscripts were screened initially by title and then by abstract before obtaining the full text of relevant articles.

Physiology of Venous Oxygen Saturation

The terms central (ScvO₂) and mixed venous oxygen saturation (SvO₂) refer to the hemoglobin saturation of blood in the superior vena cava and proximal pulmonary artery, respectively. Rearrangement of the Fick equation illustrates that venous oxygen content is determined by arterial oxygen content, oxygen consumption and cardiac output. The quantity of dissolved oxygen is small under standard conditions; therefore, the more conveniently measured variable of hemoglobin saturation is preferred. This is summarized in the equation.
below, where CO refers to cardiac output, CaO₂ refers to arterial oxygen content, CvO₂ refers to venous oxygen content, and VO₂ refers to oxygen consumption.

\[
CO = \frac{CaO_2 - CvO_2}{VO_2} \\
CvO_2 = CaO_2 - \frac{VO_2}{CO}
\]

Where oxygen supply is insufficient to meet metabolic requirements, increased tissue oxygen extraction results in a decrease in the oxygen content of effluent venous blood. Venous oxygen saturation therefore reflects the balance between global oxygen delivery (DO₂) and global oxygen consumption (VO₂).\(^{18}\) VO₂ and DO₂ both fluctuate significantly during the perioperative period, and it is of particular importance to recognize that changes in venous saturation may reflect a variety of physiologic and pathologic changes (fig. 1). The safe use of venous saturation as a therapeutic goal depends on the prompt recognition of the cause of any derangement. Regional variations in DO₂ and VO₂ are also commonplace and clinically relevant differences in the oxygen content of venous blood are to be expected in different parts of the circulation.\(^{19-22}\) In common with other global physiologic variables, the apparent simplicity of a single variable is often associated with a lack of sensitivity to detect regional abnormalities in an apparently stable patient. There is little published data describing the normal value of venous saturation in health. Although commonly quoted as 70%, the available data suggest this may vary from 70% to 80% in healthy individuals.\(^{23,24}\) Values of SvO₂ and ScvO₂ may often be as low as 65% in hospital in-patients before elective surgery.\(^{25}\)

**Oxygen Delivery as a Determinant of Venous Oxygen Saturation**

Global oxygen delivery is determined by cardiac output and the oxygen content of arterial blood as shown in the equation below,\(^{26}\) where DO₂ refers to oxygen delivery and CO to cardiac output where the Bunsen solubility coefficient for O₂ at 37°C is 0.02.\(^{27}\)

\[
DO_2 = CO \times [(SaO_2 \times Hb \times 1.34) + (0.02 \times PaO_2)]
\]

Adequate tissue oxygen delivery therefore depends on the adequacy of both respiratory and cardiovascular function. If oxygen consumption, hemoglobin concentration, and arterial saturation remain constant, changes in SvO₂ are therefore directly proportional to those in cardiac output; this relationship has been demonstrated in several studies in man.\(^{24,28}\) In a study of healthy volunteers, orthostatic hypotension resulted in a decrease in cardiac output from 4.3 to 2.7 l min\(^{-1}\) at the onset of presyncopal symptoms.\(^{24}\) Over the same time period, ScvO₂ decreased from 75% at baseline to 60%.\(^{24}\) A clinical series of patients undergoing one-lung ventilation demonstrated that cardiac output increased in response to sudden decreases in arterial saturation; as a consequence, SvO₂ remained unchanged.\(^{26}\) Several reports describe reduced venous saturation in patients with a reduced cardiac output due to myocardial infarction and/or heart failure.\(^{29-34}\) Changes in ScvO₂ and SvO₂ in these circumstances reflect both the severity of hemodynamic disturbances and response to treatment.\(^{29-32}\)

The affinity of hemoglobin for oxygen is affected by the partial pressure of oxygen (fig. 2). It may be anticipated from the oxyhemoglobin dissociation curve that, at higher partial pressures of oxygen, increases in P\(_O_2\) will result in only small increases in hemoglobin saturation. At lower partial pressures, such as those typical of venous blood, the same incremental rise in P\(_O_2\) will result in a greater increase of hemoglobin saturation due to the greater oxygen affinity of deoxyhemoglobin.\(^{35}\) Consequently, the change in venous saturation in re-
from alveolar hypoxia. In situations where ScvO2 or SvO2 might be used as hemodynamic endpoints, an increase in fractional inspired oxygen concentration may result in a greater increase in oxygen saturation of venous than arterial blood.36,37 The administration of supplemental oxygen may therefore be sufficient to rectify significant abnormalities in venous saturation even though these abnormalities may not specifically result from alveolar hypoxia. In situations where ScvO2 or SvO2 values are being used as hemodynamic endpoints for the administration of intravenous fluid or inotropic therapies, an increase in venous saturation resulting from an increase in fractional inspired oxygen concentration may be misinterpreted as an indication of adequate hemodynamic resuscitation. The potential for such simple interventions to mask the effects of shock emphasizes the importance of a detailed understanding of venous oximetry.

**Oxygen Consumption as a Determinant of Venous Oxygen Saturation**

Few studies have explored the relationship between Vo2 and venous saturation during the perioperative period. This may reflect poor recognition of the importance of Vo2 as a determinant of venous saturation. Considerable changes in oxygen consumption may occur during the perioperative period. Increases in Vo2 resulting from pain, anxiety, or shivering may all result in a decrease in venous saturation,38–42 whereas the corresponding treatments may rectify such derangements.43 Experimental data suggests that the extent of such derangements may correlate with the magnitude of oxidative stress.44 General anesthesia results in a decrease in Vo2 through reductions in general motor activity, work of breathing, neuronal activity, and body temperature. These changes are the result of anesthesia itself as well as neuromuscular blockade and invasive ventilation.45–49 Volatile anesthetic agents decrease the basal metabolic rate, with reductions in sympathetic tone and cardiac output being more pronounced at higher doses.40 Intravenous hypnotics such as benzodiazepines appear to exert similar effects on metabolic demand by blunting the sympathetic neurohumoral response.51,52 and intravenous anesthetic agents such as propofol similarly reduce metabolic demand, with the probable exception of ketamine, which usually increases myocardial inotropy by increasing general sympathetic activity.53,54 Sympathomimetic agents such as clonidine reduce perioperative Vo2.55,56 Reductions in neuronal oxygen consumption occur with the administration of volatile anesthetic agents, barbiturates, benzodiazepines, and propofol.57–61 Opiates may similarly reduce perioperative Vo2.62–65 Neuraxial blockade has both sympathomimetic and analgesic effects,66,67 but we are unaware of reports specifically describing effects on Vo2.

**Relationship between Svo2 and Scvo2**

While the determinants of Scvo2 and Svo2 are very similar, the relationship between the two variables is complex and they cannot be used interchangeably.68–73 Regional variations in the balance between Do2 and Vo2 result in differences in the hemoglobin saturation of blood in the superior and inferior vena cavae.74 Streaming of caval blood continues within the right atrium and complete mixing only occurs during ventricular contraction. The drainage of myocardial venous blood directly into the right atrium via the coronary sinus and cardiac chambers via the Thebesian veins results in further discrepancies.16 Consequently, Svo2 reflects the balance between oxygen supply and demand averaged across the entire body but Scvo2 is affected disproportionately by changes in the upper body.74 In healthy individuals, Scvo2 is usually 2–5% less than Svo2,16 largely because of the high oxygen content of effluent venous blood from the kidneys.72 This relationship changes during periods of hemodynamic instability because blood is redistributed to the upper body at the expense of the splanchnic and renal circulations.75 In shock states, therefore, the observed relationship between Scvo2 and Svo2 may reverse, and the absolute value of Scvo2 may exceed that of Svo2 by up to 20%.75 This lack of numerical equivalence has been demonstrated in various groups of critically ill patients, including those with cardiogenic, septic and hemorrhagic shock.71,72,77–80 Although trends in Scvo2 may closely reflect those of Svo2, absolute values differ and the variables cannot be used interchangeably.68–72 This observation is sometimes cited in support of continued use of the pulmonary artery catheter. However, there is no evidence to suggest one variable is of greater clinical value than the other. As the use of the pulmonary artery catheter declines, measurement of Scvo2 is usually
more convenient than \( S\text{v}O_2 \), although \( S\text{c}vO_2 \) measurements cannot be used to calculate \( V\text{O}_2 \) or shunt fraction.\(^7\)

**Measurement of Venous Oxygen Saturation**

Cardiac catheterization was first performed in 1929 by Werner Forssmann, a major advance that allowed the measurement of \( S\text{v}O_2 \) and hence application of Fick’s principle to measure cardiac output.\(^8\)\(^1\),\(^8\)\(^2\) However, it was not until 1970 that the introduction of the balloon-tipped pulmonary artery catheter facilitated the routine clinical measurement of \( S\text{v}O_2 \).\(^8\)\(^1\) Reports of the clinical utility of \( S\text{c}vO_2 \) predate those of \( S\text{v}O_2 \) by several years.\(^2\)\(^9\),\(^3\)\(^3\) Measurement of venous saturation may be performed either intermittently by blood sampling and cooximetry or continuously through the use of a spectrophotometric catheter.

**Intermittent Blood Sampling and Cooximetry**

Cooximetry involves the measurement of hemoglobin saturation by spectrophotometry by using widely available blood gas analysis technology. The differences in light absorption spectra between oxygenated and deoxygenated hemoglobin allow calculation of the hemoglobin saturation of blood. This also allows the identification of other forms of hemoglobin such as methemoglobin and carboxyhemoglobin. Cooximetry is a reliable and well-established technique. However, in clinical practice it may be inconvenient to make frequent measurements by using this approach. Specific errors result from sample contamination, delayed measurement, and sampling from the incorrect site.\(^8\)\(^3\),\(^8\)\(^4\) As with any form of venous oximetry, interpretation errors may arise due to intracardiac shunts, tricuspid regurgitation, and catheter misplacement.\(^8\)\(^4\) When taking blood samples, syringe aspiration should be gentle enough to avoid high negative pressure that may increase the aspiration of pulmonary capillary blood and hence produce falsely high readings for oxygen saturation.

**Continuous Measurement Using an Indwelling Fiberoptic Catheter**

The introduction of optical fiber technology has allowed the continuous measurement of venous saturation by spectrophotometry using indwelling pulmonary artery or central venous catheters. The major benefit of this approach is the provision of continuous data allowing the detection of sudden fluctuations in venous saturation, which are common during the perioperative period.\(^9\)\(^5\),\(^8\)\(^6\) The principle disadvantages of this technology are the additional cost and signal drift, although the latter can be addressed by recalibration. Advances in the technology have addressed the problem of interference from other optically active compounds such as carboxyhemoglobin and bilirubin.

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*SHEPHERD AND PEARSE*
Cardiothoracic Surgery

Alterations in $\text{SvO}_2$ have been described in patients undergoing cardio-thoracic surgery, although no reports of changes in $\text{ScvO}_2$ were identified. Derangements in $\text{SvO}_2$ occur before any changes in mean arterial pressure or heart rate are observed, and they appear to correlate well with changes in cardiac index. Early work in patients undergoing both cardiac and pulmonary surgery demonstrated that sustained reductions in $\text{SvO}_2$ below 65% were associated with a higher incidence of complications, particularly arrhythmias. Increases in oxygen extraction ratio, derived through measurement of $\text{SvO}_2$, have also been associated with postoperative organ failure and prolonged intensive care stay. During lung transplantation, changes in $\text{SvO}_2$ reflected adverse clinical events, although this series is too small to support any more detailed conclusions. During cardiopulmonary bypass, $\text{SvO}_2$ may prove a more specific indicator of global oxygen delivery; pump flow (or cardiac output) and metabolic rate are generally constant in these circumstances.

Trauma

The effects of hypovolemia on venous saturation have been described in both animals and humans. Fluctuations in $\text{SvO}_2$ and $\text{ScvO}_2$ closely mirror periods of hemorrhage and subsequent resuscitation in anesthetized dogs. A case series of ten victims of mainly hemorrhage and subsequent resuscitation in anesthetized dogs. Venous saturation may provide a useful indication of the severity of blood loss that is more reliable than conventional cardiovascular variables such as heart rate and arterial and central venous pressure. A single small case series describes the use of normal levels of $\text{SvO}_2$ as a therapeutic target in trauma patients in which the authors suggest a survival benefit. However, the study has a number of limitations, and the data do not appear to support such conclusions.

Interventional Trials Utilizing $\text{ScvO}_2$ and $\text{SvO}_2$ as Therapeutic Targets in the Perioperative Period

Noncardiac Surgery

Our literature search identified only one interventional trial using $\text{ScvO}_2$ as a therapeutic goal in perioperative care. This was a multicenter trial of 135 patients undergoing major abdominal (including aortic) surgery. All patients received fluid challenges, dobutamine up to 15 $\mu$g · kg$^{-1}$ · min$^{-1}$ and blood transfusions to achieve predefined goals for arterial pressure, urine output, and central venous pressure. These same therapies were administered in the intervention group to achieve the additional goal of an estimated oxygen extraction ratio of less than 27%, the value of which was calculated using intermittent measurements of $\text{ScvO}_2$. Trial interventions were continued until an unspecified time on the first postoperative day. Dobutamine was administered more frequently and in greater doses to the $\text{ScvO}_2$ group ($2.6 \pm 4.0 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ vs. $0.4 \pm 2.2 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$; $P = 0.001$). Volumes of intravenous fluid and transfused blood were similar in the two groups, although fluid challenges were commenced earlier stage in the $\text{ScvO}_2$ group. Fewer patients in the $\text{ScvO}_2$ group developed organ failure (8 of 68 patients [11.8%] vs. 20 of 67 patients [29.8%]; $P < 0.05$). The duration of hospital stay was also reduced in the $\text{ScvO}_2$ group (11.5 ± 3.8 days vs. 13.4 ± 6.1 days; $P < 0.05$), whereas mortality was low in both groups (2.9% vs. 3.0%; absolute values not reported). This was an important investigation with encouraging findings. However, there are some limitations that prevent full interpretation of the results. The report provides little information regarding the standardization of interventions that are frequent confounders in trials of this size. In particular, there is little or no description of those interventions likely to limit excessive $\text{Vo}_2$. These include anesthesia, analgesia, temperature maintenance, postoperative sedation, ventilation, and other aspects of postoperative critical care. It is unclear why the investigators chose to use estimated oxygen extraction ratio as a hemodynamic goal rather than absolute values of $\text{ScvO}_2$.

Although this may reduce the effects of alveolar hypoxemia as a confounder, the use of $\text{ScvO}_2$ to calculate oxygen extraction ratio is considered unreliable. In common with a number of similar trials, the small sample size limits the generalizability of the findings. Although the multicenter design offsets this somewhat, much larger trials are clearly needed to resolve the question of effectiveness in routine clinical practice.

In an earlier study of patients undergoing peripheral vascular surgery, the use of $\text{SvO}_2$ as a therapeutic endpoint for inotropic therapy was not associated with any change in outcome. Patients undergoing aortic reconstruction or limb salvage procedures were admitted to intensive care 12 hours preoperatively for pulmonary artery catheter placement. Initial values of $\text{SvO}_2$ were surprisingly low but responded significantly in the intervention group (59.1% to 68.8%). However, final $\text{SvO}_2$ values were similar in the two groups (70.0% vs. 70.1%) perhaps explaining the similar outcomes.

Cardiothoracic Surgery

Polonen et al. randomized 196 patients undergoing elective cardiac surgery to a protocol involving the administration of intravenous fluid and inotropic therapy to attain a target $\text{SvO}_2$ of at least 70% in the first 8 h after surgery. Dobutamine was administered in doses of up to 15 $\mu$g · kg$^{-1}$ · min$^{-1}$ where the target $\text{SvO}_2$ was not achieved with intravenous fluid alone. Control group patients were administered intravenous fluid and dobutamine to meet goals for pulmonary artery occlusion pressure, cardiac index, arterial pressure, and hematocrit. $\text{SvO}_2$ was similar in the two groups at baseline (control group 67 ± 6% vs. $\text{SvO}_2$ group 67 ± 6%), but there were greater improvements in $\text{SvO}_2$ in the $\text{SvO}_2$ group (control group 69 ± 5% vs.
Svo2 group 71 ± 4%; P < 0.001). Svo2-guided therapy was associated with a reduction in both hospital stay (7 [5–8] days vs. 6 [5–7] days; P < 0.05) and the number of patients developing complications (11 patients [5.6%] vs. 2 patients [1.0%]; P < 0.01). It is uncertain whether such a small mean difference in Svo2 of 2% is a true reflection of these improved clinical outcomes. In common with other trials, the intervention protocol principally targeted Svo2 by increasing Do2. In addition, the authors report measures in all patients that would have minimized excessive Vvo2. These include postoperative sedation and ventilation that was discontinued only when the patient was normothermic and hemodynamically stable. Hemodynamic therapy to attain a target value for Svo2 is more appropriate in this context as confounding factors of decreased venous saturation are minimized. This treatment approach is possible after cardiac surgery where postoperative intensive care admission is a standard of care; this is not always the case for high-risk noncardiac surgery.2,3

Conclusions

Svo2 and Svo2 reflect important pathophysiological changes in oxygen delivery and consumption that occur during the perioperative period. The most appropriate clinical interventions to rectify abnormalities of venous saturation may therefore vary widely. Supplemental oxygen, respiratory support, blood products, intravenous fluid, inotropic therapy, anesthesia, analgesia, sedation, and rewarming are all commonly used perioperative interventions that affect venous oxygen saturation. Small clinical trials suggest that the use of venous saturation as a therapeutic goal for hemodynamic therapy may reduce postoperative complication rates. However, these studies are not large enough to demonstrate a mortality benefit and are poorly generalizable. Further research is required to establish the most appropriate treatment algorithms for the use of Svo2 and Svo2 in perioperative care. Large, prospective, randomized control trials should then be undertaken to confirm the effects of such an approach on clinical outcomes.

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