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Role of Central and Mixed Venous Oxygen Saturation Measurement in Perioperative Care

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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.[1]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.[2,3] Data from across the developed world confirms that poor outcomes after high-risk surgery are a global problem.[4–6] Even for those patients who survive to leave hospital, postoperative complications remain an important determinant of long-term survival.[6] 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.[7–10] The use of fluid and inotropic therapy to enhance tissue oxygen delivery may reduce the incidence of postoperative complications.[11–14] There is an increasing body of literature describing changes in central ($Scvo_2$) and mixed venous oxygen saturation (Svo_2) during the perioperative period, which, along with a recent study in patients with severe sepsis,[15] 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 Svo_2 and $Scvo_2$ and to describe the findings of the 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 Svo_2 OR $Scvo_2$) 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, $Scvo_2$, Svo_2. 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 ($Scvo_2$) and mixed venous oxygen saturation (Svo_2) refer to the hemoglobin saturation of blood in the superior vena cava and proximal pulmonary artery, respectively.[16] Rearrangement of the Fick equation illustrates that venous oxygen content is determined by arterial oxygen content, oxygen consumption and cardiac output.[17] 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

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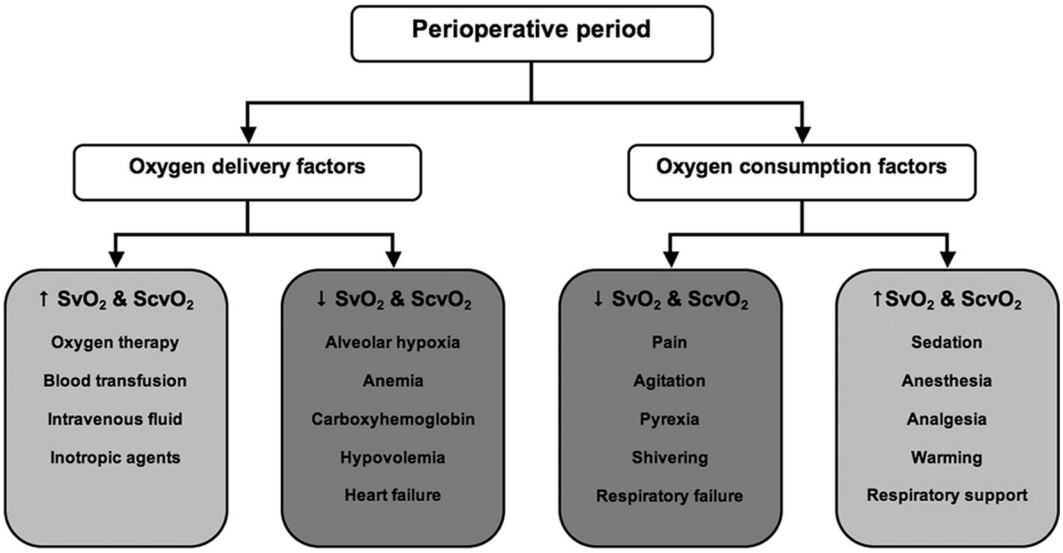

Fig. 1. Common physiologic, pathologic, and therapeutic factors that influence venous oxygen saturation ($Scvo_2$ and Svo_2) during the perioperative period. Safe use of venous saturation as a therapeutic goal requires prompt recognition of all causes of any derangement.

below, where CO refers to cardiac output, Cao_2 refers to arterial oxygen content, Cvo_2 refers to venous oxygen content, and Vo_2 refers to oxygen consumption.

$$CO = \frac{CaO_2 - CvO_2}{VO_2} \quad \therefore \quad CvO_2 = CaO_2 - \frac{VO_2}{CO}$$

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 (Do_2) and global oxygen consumption (Vo_2).[18] Vo_2 and Do_2 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 Do_2 and Vo_2 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 Svo_2 and $Scvo_2$ 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 Do_2 refers to oxygen delivery and CO to cardiac output where the Bunsen solubility coefficient for O_2 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 Svo_2 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, $Scvo_2$ 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, Svo_2 remained unchanged.[28] 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 $Scvo_2$ and Svo_2 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 Po_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 Po_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-

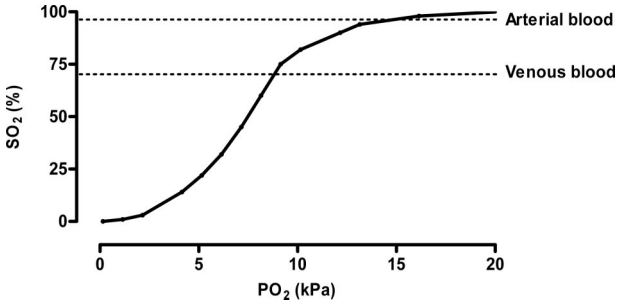

Fig. 2. Oxy-hemoglobin dissociation curve illustrating the difference in gradient at Po_2 levels typical for arterial and venous blood. The greater affinity of deoxy-hemoglobin results in a greater step change in sulfur dioxide (So_2) in venous blood than in arterial blood after an increase in fractional inspired oxygen concentration. This phenomenon has the potential to cause confusion in cases where venous saturation is employed as an endpoint for hemodynamic therapy.

sponse to a step change in fractional inspired oxygen concentration may differ considerably from simultaneous changes in arterial hemoglobin saturation. Clinical and laboratory investigations have shown that an increase in fractional inspired oxygen concentration results 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 $Scvo_2$ or Svo_2 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 Vo_2 and venous saturation during the perioperative period. This may reflect poor recognition of the importance of Vo_2 as a determinant of venous saturation. Considerable changes in oxygen consumption may occur during the perioperative period. Increases in Vo_2 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 Vo_2 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.[50] 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] Sympatheticolytic agents such as clonidine reduce perioperative Vo_2.[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 Vo_2.[62–65] Neuraxial blockade has both sympatheticolytic and analgesic effects,[66,67] but we are unaware of reports specifically describing effects on Vo_2.

Relationship between Svo_2 And $Scvo_2$

While the determinants of $Scvo_2$ and Svo_2 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 Do_2 and Vo_2 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 ventricle 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, Svo_2 reflects the balance between oxygen supply and demand averaged across the entire body but $Scvo_2$ is affected disproportionately by changes in the upper body.[74] In healthy individuals, $Scvo_2$ is usually 2–5% less than Svo_2,[16] largely because of the high oxygen content of effluent venous blood from the kidneys.[22] 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 $Scvo_2$ and Svo_2 may reverse, and the absolute value of $Scvo_2$ may exceed that of Svo_2 by up to 20%.[73] This lack of numerical equivalence has been demonstrated in various groups of critically ill patients, including those with cardiogenic, septic and hemorrhagic shock.[31,68–70,76–78] This has also been demonstrated in patients undergoing general anesthesia for cardiac[71,72,79] and noncardiac surgery.[69,80] Although trends in $Scvo_2$ may closely reflect those of Svo_2, 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 $Scvo_2$ is usually

more convenient than Svo_2, although $Scvo_2$ measurements cannot be cannot be used to calculate Vo_2 or shunt fraction.[72]

Measurement of Venous Oxygen Saturation

Cardiac catheterization was first performed in 1929 by Werner Forssmann, a major advance that allowed the measurement of Svo_2 and hence application of Fick's principle to measure cardiac output.[81,82] However, it was not until 1970 that the introduction of the balloon-tipped pulmonary artery catheter facilitated the routine clinical measurement of Svo_2.[81] Reports of the clinical utility of $Scvo_2$ predate those of Svo_2 by several years.[29,33] 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.[83,84] As with any form of venous oximetry, interpretation errors may arise due to intracardiac shunts, tricuspid regurgitation, and catheter misplacement.[84] 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.[85,86] 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 carboxyhemoglobin and bilirubin.

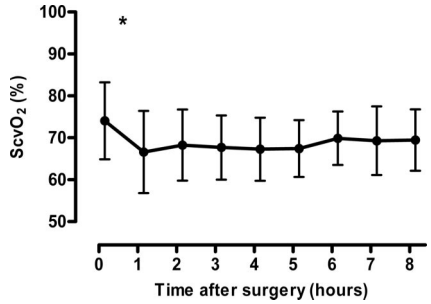

Fig. 3. Changes in central venous oxygen saturation ($Scvo_2$) after major noncardiac surgery. Reductions in $Scvo_2$ below 65% were associated with an increased incidence of postoperative complications. Note the significant decrease in $Scvo_2$ in the first hour after surgery, which may reflect increases in oxygen consumption after cessation of general anesthesia (*$P < 0.0001$). Adapted from Pearse R, *et al.* Changes in central venous saturation after major surgery and association with outcome. Critical Care 2005; 9:R694–9.

Observational Studies of Perioperative Changes in $Scvo_2$ and Svo_2

Abnormalities of venous saturation are common during and after major surgery and are associated with an increased incidence of postoperative complications.[87–91] Reductions in $Scvo_2$ and Svo_2 also have prognostic significance in heart failure, trauma, and sepsis.[92–95] These observations are no surprise, given the wide range of pathologic abnormalities that affect venous saturation in the perioperative period.[87–89]

Noncardiac Surgery

Two studies have been performed in noncardiac surgical patients with complementary findings. In the first observational study of 117 patients, the lowest recorded value of $Scvo_2$ in the early postoperative period was independently associated with subsequent complications, the optimal cut-off for the lowest $Scvo_2$ value being 64.4%.[87] Interestingly, a considerable decrease in $Scvo_2$ was observed within the first hour after surgery, possibly as a consequence of increased Vo_2 after the cessation of general anesthesia (fig. 3). In a further multicenter observational study of 60 patients, the mean value of $Scvo_2$ was found to be reduced at various time points throughout the perioperative period in patients who developed complications.[88] The optimal cutoff value in this study for the *mean* $Scvo_2$ value was 73%. These investigations not only provide strong evidence to support the role of $Scvo_2$ as a therapeutic target, but they are also highly consistent in suggesting the most appropriate target value to be an $Scvo_2$ value of approximately 75%. However, these findings do not indicate how venous saturation should be used as a therapeutic goal. A range of factors influence Vo_2, Do_2, and therefore venous saturation during the perioperative period, not all of which are pathologic in nature. The most appropriate therapy to achieve a venous saturation endpoint may vary.

Cardiothoracic Surgery

Alterations in Svo_2 have been described in patients undergoing cardio-thoracic surgery, although no reports of changes in $Scvo_2$ were identified.[89–91] Derangements in Svo_2 occur before any changes in mean arterial pressure or heart rate are observed,[96] and they appear to correlate well with changes in cardiac index.[86] Early work in patients undergoing both cardiac and pulmonary surgery demonstrated that sustained reductions in Svo_2 below 65% were associated with a higher incidence of complications, particularly arrhythmias.[97] Increases in oxygen extraction ratio, derived through measurement of Svo_2, have also been associated with postoperative organ failure and prolonged intensive care stay.[90,91,98] During lung transplantation, changes in Svo_2 reflected adverse clinical events, although this series is too small to support any more detailed conclusions.[99] During cardiopulmonary bypass, 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.[100,101]

Trauma

The effects of hypovolemia on venous saturation have been described in both animals and humans.[73,102,103] Fluctuations in Svo_2 and $Scvo_2$ closely mirror periods of hemorrhage and subsequent resuscitation in anesthetized dogs.[73,102] A case series of ten victims of mainly penetrating trauma described similar changes in Svo_2.[103] 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.[102,103] A single small case series describes the use of normal levels of Svo_2 as therapeutic target in trauma patients in which the authors suggest a survival benefit.[104] However, the study has a number of limitations, and the data do not appear to support such conclusions.

Interventional Trials Utilizing $Scvo_2$ and Svo_2 as Therapeutic Targets in the Perioperative Period

Noncardiac Surgery Our literature search identified only one interventional trial using $Scvo_2$ as a therapeutic goal in perioperative care.[105] This was a multicenter trial of 135 patients undergoing major abdominal (including aortic) surgery. All patients received fluid challenges, dobutamine up to 15 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and blood transfusions to achieve predefined goals for arterial pressure, urine output, and central venous pressure.[105] 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 $Scvo_2$. Trial interventions were continued until an unspecified time on the first postoperative day. Dobutamine was administered more frequently and in greater doses to the $Scvo_2$ group (2.6 ± 4.0 *vs.* 0.4 ± 2.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$; $P = 0.001$). Volumes of intravenous fluid and transfused blood were similar in the two groups, although fluid challenges were commenced earlier stage in the $Scvo_2$ group. Fewer patients in the $Scvo_2$ 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 $Scvo_2$ group (11.3 ± 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 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 $Scvo_2$. Although this may reduce the effects of alveolar hypoxemia as a confounder, the use of $Scvo_2$ to calculate oxygen extraction ratio is considered unreliable.[68,73,76,80,106] In common with a number of similar trials, the small sample size limits the generalizability of the findings.[11–13] 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 Svo_2 as a therapeutic endpoint for inotropic therapy was not associated with any change in outcome.[107] Patients undergoing aortic reconstruction or limb salvage procedures were admitted to intensive care 12 hours preoperatively for pulmonary artery catheter placement. Initial values of Svo_2 were surprisingly low but responded significantly in the intervention group (59.1% to 68.8%). However, final 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 Svo_2 of at least 70% in the first 8 h after surgery.[108] Dobutamine was administered in doses of up to 15 $\mu g \cdot kg^{-1} \cdot min^{-1}$ where the target 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. Svo_2 was similar in the two groups at baseline (control group $67 \pm 6\%$ *vs.* Svo_2 group $67 \pm 6\%$), but there were greater improvements in Svo_2 in the Svo_2 group (control group $69 \pm 5\%$ *vs.*

Svo_2 group 71 ± 4%; $P < 0.001$). Svo_2-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 Svo_2 of 2% is a true reflection of these improved clinical outcomes. In common with other trials, the intervention protocol principally targeted Svo_2 by increasing Do_2. In addition, the authors report measures in all patients that would have minimized excessive Vo_2. 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 Svo_2 is more appropriate in this context as confounding causes 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

$Scvo_2$ and Svo_2 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 $Scvo_2$ and Svo_2 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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