# **Original Article**

Changes in central venous oxygen saturation, lactates, and ST segment changes in a V lead ECG with changes in hemoglobin in neurosurgical patients undergoing craniotomy and tumor excision: A prospective observational study

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### Abstract

**Background and Aims:** The aim of the study was to observe the trends in central venous oxygen saturation (ScvO<sub>2</sub>), lactate, and ST segment changes with change in hemoglobin in patients undergoing acute blood loss during surgery and to assess their role as blood transfusion trigger.

**Material and Methods:** Seventy-seven consecutive patients undergoing craniotomy at a tertiary care institution were recruited for this study after obtaining written, informed consent. After establishing standard monitoring, anesthesia was induced with standard anesthetic protocol. Hemodynamic parameters such as heart rate, blood pressure (mean, systolic, diastolic), pulse pressure variation (PPV), and physiological parameters such as lactate, ScvO<sub>2</sub>, ST segment changes were checked at baseline, before and after blood transfusion and at the end of the procedure.

**Statistical Analysis:** Comparison of the mean and standard deviation for the hemodynamic parameters was performed between the transfused and nontransfused patient groups. Pearson correlation test was done to assess the correlation between the covariates. Receiver operating characteristic (ROC) curve was constructed for the  $ScvO_2$  variable, which was used as a transfusion trigger and the cutoff value at 100% sensitivity and 75% specificity was constructed. Linear regression analysis was done between the change in hemoglobin and the change in  $ScvO_2$  and change in hemoglobin and change in the ST segment. **Results:** There was a statistically significant positive correlation between the change in  $ScvO_2$  and change in  $ScvO_2$  and change in hemoglobin during acute blood loss with a regression coefficient of 0.8 and also between change in ST segment and hemoglobin with a regression coefficient of -0.132. No significant change was observed with lactate. The ROC showed a  $ScvO_2$  cutoff of 64.5% with a 100% sensitivity and 75% specificity with area under curve of 0.896 for blood transfusion requirement.

**Conclusions:** We conclude that  $ScvO_2$  and ST change may be considered as physiological transfusion triggers in patients requiring blood transfusion in the intraoperative period.

Keywords: Acute blood loss, central venous oxygen saturation (ScvO2), lactates, ST segment changes, transfusion trigger

## Introduction

Adequate oxygenation is essential for the normal functioning of various tissues in the body and is maintained by the

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combined effort of both the cardiac and the respiratory systems. A decrease in the supply of oxygen at the tissue level leads to cellular hypoxia. Hence, strategies to identify tissue hypoxia at an earlier stage and to initiate therapy before the onset of cell death would benefit the patient. The practical

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method to measure adequacy of oxygenation of the tissues is to measure the oxygen saturation of the venous blood returning to the heart or the mixed venous oxygen saturation  $(SvO_2)$ , which reflects the balance between oxygen delivery  $(DO_2)$ and oxygen consumption  $(VO_2)$  by the tissues. The mixed venous oxygen saturation (SvO<sub>2</sub>) is measured from blood in the pulmonary artery using a pulmonary artery catheter. Normal  $SvO_2$  is 68–77%. However, it has been shown that blood from superior vena cava (ScvO<sub>2</sub>) that has a higher oxygen saturation of 73-82% is an alternative to  $SvO_2$  as their trends parallel each other under varying hemodynamic conditions.<sup>[1,2]</sup> As anemia is associated with decrease in SvO<sub>2</sub>, it may be presumed that in the event of acute blood loss during surgery, a drop in ScvO<sub>2</sub> may be more reflective of the need for blood transfusion, rather than hemoglobin level alone. Moreover, dynamic changes in cardiac output and other parameters of oxygen delivery to compensate for blood loss make hemoglobin concentration alone a less sensitive marker of tissue oxygenation. ScvO<sub>2</sub> has been used to avoid hypoxia and tissue injury under such circumstances and as a transfusion trigger to guide blood transfusions.<sup>[3]</sup> Anemia is known to cause ischemic disturbances of the myocardium<sup>[4]</sup> that is a reflection of the metabolic disturbances due to the diminished oxygen carrying capacity of the blood, which manifests as ST segment changes.<sup>[5]</sup>

Acute anemia is associated with increased lactate levels.<sup>[6]</sup> Multiple studies have shown that blood lactate levels are also increased with anemia and tissue hypoxia.<sup>[7]</sup> Even in those with stable hemodynamics, elevated lactate levels are a sign of occult hypoperfusion.<sup>[8]</sup>

Hence we proposed to assess the relationship between hemoglobin levels, ST segment change, lactate levels and  $ScvO_2$ , and the need for blood transfusion, in conditions of acute blood loss in patients undergoing craniotomies, where significant blood loss requiring blood transfusion was anticipated. The aim of the study was to observe the trends in central venous oxygen saturation (ScvO<sub>2</sub>), lactate levels, and ST segment changes with change in hemoglobin levels in patients undergoing acute blood loss during surgery and to assess their role as blood transfusion triggers.

## **Material and Methods**

After approval from the Institutional Review Board and Ethics Committee (IRB Min No. 8254), 77 consecutive patients were enrolled for the study after obtaining written informed consent. Sample size was calculated for assessing sensitivity of new test and the minimum sample required for the study with 95% confidence level was 77. Based on Vallet *et al.*,<sup>[9]</sup> with expected proportion of subjects who required blood transfusion as 50%, 12% absolute precision, and 5% type 1 error the sample size was 70. This was calculated using nmaster 1.0 software. Allowing for a dropout of 20%, the sample size calculated was 84. All adult patients, ASA (American Society of Anaesthesiologists) physical statuses 2, 3, and 4 undergoing craniotomy where significant blood loss requiring blood transfusion is expected were included in the study. Patients who were  $\geq 65$  years, pregnant women, ASA physical statuses 4 and 5, patients who underwent blood transfusion prior to surgery, patients with known coagulopathy or bleeding disorders or preexisting ST segment changes on the ECG, patients on treatment with hemoglobin augmenting substances like erythropoietin and those undergoing emergency procedures were excluded from the study [Figure 1].

Standard anesthesia protocol was followed for all enrolled patients who were premedicated with omeprazole 20 mg orally. In the operating room, standard monitoring such as pulse oximeter (SpO<sub>2</sub>), five lead electrocardiogram (ECG), and invasive blood pressure was established with a PHILIPS MP 50 monitor. Anesthesia was induced with—fentanyl (1–2 mcg/kg), propofol 1–2 mg/kg and inhalational anesthetic agent, and tracheal intubation was facilitated by vecuronium 0.15 mg/kg. The patient was on controlled ventilation with a tidal volume of 6–8 ml/kg to maintain EtCO<sub>2</sub> (end tidal carbon dioxide) of 28–35 mmHg at FiO<sub>2</sub> (fraction of inspired oxygen) of 40%. Anesthesia gas analyzer was used and a minimum alveolar concentration (MAC) of 0.8–1.0 was maintained with isoflurane.

A 7 French triple lumen polyvinyl chloride catheter with a total insertable length of 18 cm was used for the study. The position of the catheter tip at the superior vena cava—right atrial junction was guided by intravascular electrocardiography and confirmed by a chest roentgenogram postoperatively. A baseline venous blood gas was used to assess ScvO<sub>2</sub>, hemoglobin and lactate. Simultaneously, heart rate (HR), systolic blood pressure (SBP), mean blood pressure (MAP), diastolic blood pressure (DBP), pulse pressure variation (PPV), and ST segment values were recorded. The maximum allowable blood loss (MABL) for the patient was calculated from the hemoglobin value in the initial venous blood gas and dropped to the threshold value before starting the surgery. The threshold value of hemoglobin was taken as per the guidelines for transfusion<sup>[10]</sup> (10 gm% for patients with acute coronary syndrome, 9 gm% for those with ischemic heart disease or stable heart failure; 8 gm% for patients aged >75 years or with severe sepsis, and 7 gm% for all other patients). Crystalloids and colloids (maximum of 20 ml/kg) were used to replace blood volume to maintain PPV less than 12 in supine position or to the baseline value obtained after the final positioning in surgery performed in other positions.

The decision to transfuse blood was taken by the concerned anesthesiologist based on any one of the following indications.

- Blood loss exceeding the maximum allowable blood loss (on visual inspection and assessment by the anesthetist concerned) with stable hemodynamics
- Hemodynamic changes (unexplained tachycardia more than 30% and drop in SBP >30%) compared to the baseline prior to blood loss without exceeding the MABL on clinical judgement
- Venous blood gas showing a hematocrit value less than the threshold values as per guidelines.

Before blood transfusion, hemoglobin and ScvO<sub>2</sub> were checked on a venous blood gas sample using the ABL 800 BASIC auto check machine (Radiometer, Copenhagen). Other parameters such as lactate, HR, SBP, MBP, DBP, PPV, ST segment depression were recorded. The need for vasopressors was noted. Once the decision to transfuse was made clinically by the attending anesthesiologist, blood (packed red blood cells with hematocrit of 55–60%) was transfused, irrespective of the hemoglobin value obtained on the venous blood gas. In cases where more than one unit of blood was required, patient was reassessed clinically regarding the need for transfusion on the basis of the above indication and venous blood gas was done before every transfusion and all the above mentioned parameters were recorded. A similar recording was done at the end of the procedure prior to tracheal extubation.

Statistical analysis was done in IBM SPSS (Statistical Package for the Social Sciences) version 20. Descriptive statistics were performed for variables such as age, gender, ASA physical status. Comparison of the mean and standard deviation for the hemodynamic parameters was performed between the transfused and non-transfused patient groups. Pearson correlation test was done to assess the correlation between the covariates. Receiver operating characteristic (ROC) curve was constructed for the ScvO<sub>2</sub> variable, which was used as a transfusion trigger and the cutoff value at 100% sensitivity and 75% specificity was constructed. Linear regression analysis was done between the change in hemoglobin and the change in ScvO<sub>2</sub> and change in hemoglobin and change in the ST segment. Scatter plots were also constructed for a few variables which had correlation. A P value of < 0.05 was considered as statistically significant.

### Results

The demographic profile of transfused and non-transfused patients in terms of age, gender, ASA physical status, type of tumor or duration of surgery does not show any significant difference between both the groups [Table 1]. The central venous catheter was inserted into subclavian vein in 75 subjects and into internal jugular vein in the other two. The position of the catheter tip was not satisfactory for  $ScvO_2$ sampling in seven patients and hence they were excluded from the data analysis. The hemodynamic variables such as HR, SBP, DBP, MAP, PPV, and physiological variables such as temperature, ST segment, lactate, hemoglobin, and ScvO<sub>2</sub> are compared between the groups, which required transfusion and those that did not [Table 2]. MAP was maintained at >70% of baseline value throughout the surgery with or without vasopressors. It was observed that DBP and MAP were the only hemodynamic variables that showed a statistically significant difference in between the study groups. Among the physiological variables lactate levels showed a statistically significant increase in those who required transfusion with a P value of 0.023.

The correlation between the physiological parameters in all subjects is shown in Table 3. There is a statistically significant change in ScvO<sub>2</sub> with change in hemoglobin (P = 0.032); which is observed in all patients (both transfused and nontransfused).

Linear regression analysis was performed to study the relationship between the change in  $ScvO_2$  and change in hemoglobin showed a regression coefficient of 0.837 [Figure 2] implying that every unit decrease in hemoglobin produced a change in  $ScvO_2$  of 0.837 that was statistically significant with a *P* value of 0.032.

Although a correlation between change in hemoglobin and  $ScvO_2$  in patients requiring blood transfusion was observed, with a Pearson coefficient of 0.3, this was not statistically significant. This is probably because, the number of patients who received transfusion was very small (16/70). Similarly,

Demogra profile	phic	n	Transfused n (%)	Nontransfused n (%)	Р
Age	<40	30	5 (16.7)	25 (83.3)	0.320
(years)	40-60	33	8 (24.2)	25 (75.8)	
	>60	7	3 (42.9)	4 (57.1)	
Gender	Male	35	6 (17.1)	29 (82.9)	0.227
	Female	35	10 (29.4)	24 (70.6)	
ASA	1	44	10 (22.7)	34 (77.3)	0.854
grade	2	25	6 (24)	19 (76)	
	3	1	0 (0)	100 (100)	
Type of	Meningioma	54	15 (27.8)	39 (72.2)	0.116
tumor	Glioma	4	1 (25)	3 (75)	
	Others	12	0 (0)	12 (100)	
Duration	<6 h	1	7 (16.7)	35 (83.3)	0.131
of surgery	>6 h	69	9 (32.1)	19 (67.9)	

Variables	Transfused n=16			Nontransfused n=54			Р
	Mean (SD) Baseline	Mean (SD) End	∆ Mean (SD)	Mean (SD) Baseline	Mean (SD) End	Δ Mean (SD)	
Heart rate (beats/min)	80.8 (13.6)	91.5 (13.2)	10.7 (11.3)	81.7 (11.6)	91.7 (10.2)	10.1 (11.7)	0.721
Systolic blood pressure (mmHg)	116.2 (13.8)	112.5 (12.2)	3.7 (20.5)	112.8 (17.2)	117.6 (16.9)	4.9 (14.7)	0.229
Diastolic blood pressure (mmHg)	70.4 (10.5)	65.8 (12.6)	4.5 (17.5)	67.5 (11.3)	73.8 (12.3)	6.3 (12.8)	0.026*
Mean arterial pressure (mmHg)	84.2 (9.8)	78.8 (11.4)	5.4 (17.0)	81 (11.9)	87.8 (13.6)	6.85 (13.4)	0.012*
Pulse pressure variation	8.0 (2.7)	8.0 (3.2)	0 (4.0)	7.9 (2.7)	7.5 (2.2)	0.4 (2.9)	0.503
ST segment (mm)	0.7 (0.5)	0.6 (0.6)	0.2 (0.5)	0.6 (0.6)	0.5 (0.5)	0.0 (0.4)	0.561
Temperature	36.1 (0.6)	35.9 (0.7)	0.2 (0.9)	36.1 (10.3)	36.2 (0.5)	0.0 (0.5)	0.358
Lactate (mmol/l)	2.4 (0.9)	5.1 (2.1)	2.7 (1.7)	2.3 (1.4)	4.0 (1.7)	1.7 (1.4)	0.023*
Hemoglobin (g/dl)	10.7 (1.6)	8.4 (1.4)	2.2 (1.5)	11.9 (1.6)	10.3 (1.7)	1.6 (1.8)	0.183
Central venous oxygen saturation (%)	84.3 (4.4)	84.0 (5.7)	0.3 (5.1)	83.2 (6.1)	0.84.1 (6.2)	0.7 (5.7)	0.817

Table 2: Comparison of the means of hemodynamic and physiologic variables between transfused and nontransfused natients between baseline and end of the surgery

#### **Table 3: Correlation between the physiological** parameters in all participants

Variables	Pearson correlation coefficient	Р
Change in ScvO <sub>2</sub> with change in hemoglobin	0.262	0.032*
Change in lactate with change in ScvO <sub>2</sub>	-0.099	0.421
Change in lactate with change in hemoglobin	-0.166	0.172
Change in ST segment with change in $ScvO_2$	0.018	0.885
Change in ST segment with change in hemoglobin	018	0.888
*Statistically significant		

#### **Table 4: Correlation between the physiological** parameters in transfused and nontransfused patients

	Transfused	l <i>n</i> =16	Nontransfused n=		
	Pearson coefficient	Р	Pearson coefficient	Р	
ScvO <sub>2</sub> vs Hb	0.300	0.259	0.210	0.138	
$ScvO_2$ vs lactate	0.06	0.820	0.047	0.739	
Lactate vs Hb	-0.076	0.771	-0.104	0460	
$SevO_2$ vs ST	0.389	0.136	-0.156	0.274	
ST vs Hb	0.608	0.012*	-0107	0.450	

\*Statistically significant

the lactate levels also did not show any correlation with either change in Hb or ScvO<sub>2</sub> despite significant change in lactate levels observed among those who received transfusion.

However, while comparing the physiological parameters in transfused and nontransfused patients, it was observed that there was a statistically significant correlation between change in Hb and change in ST segment in patients requiring blood transfusion [Table 4]. This correlation, however was not observed in patients not requiring blood transfusion or in the total study population. Linear regression analysis performed to observe the relationship between change in Hb and change in ST segment showed that for every unit decrease in Hb, there is a statistically significant decrease in ST segment of -0.132 (*P*-value = 0.012) [Figure 3].



Figure 1: Flowchart depicting the flow of the study participants

Receiver operator curve analysis [Figure 4] was performed to assess the usefulness of ScvO<sub>2</sub> measurement as a physiological transfusion trigger compared to hemoglobin. The threshold value obtained for ScvO<sub>2</sub> was 64.5% with a 100% sensitivity and 75% specificity with area under curve (AUC) of 0.896 which shows that ScvO<sub>2</sub> may also be used as an accurate alternative transfusion trigger.

#### Discussion

This study assessed the relationship between hemoglobin levels and ScvO<sub>2</sub>, ST segment change, lactate levels in conditions of acute blood loss in patients undergoing craniotomies; where significant blood loss requiring blood transfusion was anticipated.

The major finding of the study was a significant correlation between the change in hemoglobin and change in ScvO<sub>2</sub> with a Pearson coefficient of 0.262 (*P*-value = 0.032) in all patients irrespective of blood transfusion. A similar correlation



**Figure 2:** Correlation between changes in  $ScvO_2$  with change in hemoglobin in all patients



Figure 3: Correlation between changes in ST segment with change in hemoglobin in patients requiring blood transfusion



**Figure 4:** ROC curve analysis illustrating the usefulness of  $ScvO_2$  measurement as a transfusion trigger

was also established in patients receiving blood transfusion. However it did not reach statistical significance, because of the small numbers (only 22.8% of the patients received blood transfusion). In patients requiring blood transfusion, a statistically significant correlation was observed between the change in Hb and change in the ST segment (P value of 0.012) with a regression coefficient of 0.135. There was no correlation observed between ScvO<sub>2</sub> and lactate levels or ST segment changes.

Red blood cell transfusion in the perioperative period improves the delivery of oxygen at the tissue level by increasing the hemoglobin content. However, the adequacy of tissue oxygenation is a fine balance between oxygen delivery and consumption. An imbalance in any one of the two arms can cause tissue hypoxia. Traditionally, the means of improving the oxygen delivery during periods of ongoing blood loss was attributed to improving the hemoglobin concentration and therefore guidelines for blood transfusion in the perioperative period<sup>[11]</sup> stress on the role of hemoglobin value as the transfusion trigger.<sup>[12]</sup> Despite this, the indication, time and the amount of blood transfused is quite unclear in an acutely changing scenario such as perioperative or intraoperative blood loss. Furthermore, changing hemodynamics either due to the body's compensatory mechanisms such as sympathetic stimulation or the hemodynamic manipulation by the anesthesiologist often does not portray the actual situation.

In such a setting, monitoring of physiological variables which either indicate global oxygenation such as  $ScvO_2$ , lactates or those which indicate regional oxygenation such as ST segment may throw light on the balance between  $O_2$  delivery and consumption and help to guide the decision regarding the need for blood transfusion rather than relying on hemoglobin value alone. Numerous studies have demonstrated that trends in  $ScvO_2$  parallel that of  $SvO_2$  in the animal model<sup>[13]</sup> and also in human subjects.<sup>[14]</sup>

As pulmonary artery catheterization is expensive and includes inherent risks, and central venous catheterization is less expensive, safe and a routine procedure in the surgical settings, we measured ScvO<sub>2</sub> as a substitute for mixed venous oxygen saturation (SvO<sub>2</sub>). Pearse et  $al.^{[15]}$  used ScvO<sub>2</sub> guided goal directed therapy in patients admitted to the intensive care unit (ICU) after major surgeries and reported an uncomplicated postoperative course for patients with  $ScvO_2 > 64.4\%$  as compared to those with  $ScvO_2 < 64.4\%$ . Scalea et al.<sup>[16]</sup> analyzed ScvO<sub>2</sub> values in trauma patients admitted to the ICU and found that patients who had ScvO<sub>2</sub> less than 65% had more serious injuries, significantly larger estimated blood losses and required more transfusions than those patients with ScvO<sub>2</sub> greater than 65%. In their study linear regression coefficients showed that ScvO<sub>2</sub> was better than HR, MAP, CVP, PPV, and urine output in predicting estimated blood loss. This is similar to the ScvO<sub>2</sub> cutoff of 64.5% (100% sensitivity and 75% specificity) for blood transfusion observed in our study.

An observational study by Adamczyk *et al.*<sup>[17]</sup> in postoperative patients recommended that  $\text{ScvO}_2$  could be used as a transfusion trigger along with the current blood transfusion guidelines to improve utilization of blood products. The threshold value for  $\text{ScvO}_2$  with the best sensitivity and specificity was 69.5% (sensitivity of 82% and specificity of 76% with AUC of 0.83  $\pm$  0.059)<sup>[17]</sup> which is very similar to that observed in our study.

In an animal model, Kocsi *et al.*<sup>[3]</sup> showed that  $ScvO_2$  reflects changes of  $VO_2/DO_2$  (oxygen extraction ratio) in normovolemic anemia better than hemoglobin alone. It is also more reliable in identifying the point when compensatory mechanisms fail and oxygen delivery begins to decline as compared with hemoglobin concentration alone and hence can be considered as an additional guideline for blood transfusion.<sup>[3]</sup>

Our study is in congruence with other studies which found no correlation between  $\text{ScvO}_2$  and lactate levels.<sup>[18,19]</sup> We did observe a statistically significant difference in the lactate levels between the groups that received and did not receive blood transfusion (*P*-value = 0.0180) but change in serum lactate levels cannot be used as a physiological transfusion trigger in neurosurgical patients as they have high baseline lactate levels.<sup>[20]</sup>

As shown by Shakuntala *et al.*<sup>[21]</sup> we also observed that in the group which had acute blood loss, there was a strong correlation between change in hemoglobin and ST segment with a Pearson coefficient of 0.608 (*P*-value = 0.012). ST segment depression reflects myocardial ischemia and as the myocardium has a higher extraction ratio of oxygen than the other tissues, changes in the ST segment are also reflective of hemoglobin content and may be a sensitive indicator of acute hypovolemic anemia. As ST may be affected by other factors such as HR, linear regression analysis was done, which was also statistically significant (*P* value = 0.012) with a regression coefficient of 0.135. Similar observations have been made by Vallet *et al.*<sup>[9]</sup>

The majority of literature in  $\text{ScvO}_2$  has been in the intensive care setting where  $\text{ScvO}_2$  has been evaluated either as a physiological goal to be achieved or a prognosticator. There is paucity of literature in the role of  $\text{ScvO}_2$  as a transfusion trigger in an intraoperative setting where there is acute ongoing blood loss. This study adds to the available evidence that  $\text{ScvO}_2$ is a definite indicator of a decrease in global oxygenation and thereby a better physiological transfusion trigger thus challenging the role of traditional transfusion triggers based on hemoglobin values alone. Future studies based on continuous, simultaneous monitoring of Hb and  $ScvO_2$ , ST segment changes, lactates, hemodynamics, and computer-based models to evaluate correlations would throw more light on the role of  $ScvO_2$  as a transfusion trigger.

The strengths of our study are that it was a prospective study and followed standard anesthesia management and monitoring protocols and was done in intraoperative setting, unlike most other studies which have been done in critical care settings. To our knowledge, this is the first study to have compared  $\text{ScvO}_2$ values with hemoglobin in patients with ongoing blood loss in an intraoperative setting.

Our study is not without limitations. Our primary limitation is a small sample size and the even smaller fraction of patients who required a transfusion. We expected that at least 50% patients would require an intraoperative blood transfusion but only 22.8% of patients received a transfusion. The sample size that was calculated on this assumption was 84. Power calculation revealed that a sample size of at least 110 patients was required for a power of 80% but we could recruit only 77 patients during the study period as this was a time bound study. A larger sample size would have demonstrated a stronger correlation between ScvO2 and hemoglobin and between ST change and hemoglobin. Technical limitations due to unavailability of intraoperative fluoroscopic guidance to confirm central venous catheter (CVC) placement contributed to a loss of seven patients in the study. Moreover, resuscitation and transfusion were going on simultaneously and hence the blood sample at one point may not be an accurate reflector of the balance between VO2-DO2. Potential measurement errors which are inherent in an observational study design could be overcome by using continuous measurements. To offset the effect of confounders, linear regression analysis has been done.

### Conclusions

In conclusion, the study findings indicate a statistically significant positive correlation between changes in hemoglobin with that of  $\text{ScvO}_2$  and ST segment. Hence, it is recommended that physiologic transfusion triggers such as  $\text{ScvO}_2$  and ST segment changes which are reflective of either global or regional tissue oxygenation should supplement the hemoglobin values in patients with acute blood loss in guiding the anesthesiologists' decisions regarding blood transfusion. However, well-designed trials are required to establish the superiority of physiological transfusion triggers over conventional guidelines based only on hemoglobin values in the intraoperative setting.

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#### **Conflicts of interest**

There are no conflicts of interest.

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