ACCURACY OF CONTINUOUS CENTRAL VENOUS OXYGEN SATURATION MONITORING IN PATIENTS UNDERGOING CARDIAC SURGERY

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ABSTRACT. Objective. Continuous assessment of central venous oxygen saturation ($S_{cevox}O_2$) with the CeVOX device (Pulsion Medical Systems, Munich, Germany) was evaluated against central venous oxygen saturation ($S_{cv}O_2$) determined by co-oximetry. **Methods.** In 20 cardiac surgical patients, a CeVOX fiberoptic probe was introduced into a standard central venous catheter placed in the right internal jugular vein and advanced 2–3 cm beyond the catheter tip. After in vivo calibration of the probe, $S_{cevox}O_2$, $S_{cv}O_2$, mixed venous oxygen saturation ($S_{mv}O_2$) haemoglobin (Hb), body temperature, heart rate, central venous and mean arterial pressure, and cardiac index were assessed simultaneously at 30 min intervals during surgery and at 60 min intervals during recovery in the intensive care unit. Agreement between $S_{cevox}O_2$, and $S_{cv}O_2$ was determined by Bland-Altman analysis. Simple regression analysis was used to assess the correlation of $S_{cevox}O_2$, and $S_{cv}O_2$ to Hb, body temperature and haemodynamic parameters. **Results.** Values of $S_{cevox}O_2$ and $S_{cv}O_2$ (84 data pairs during surgery and 106 in the intensive care unit) ranged between 45–89% and 43–90%, respectively. Mean bias and limits of agreement of $S_{cevox}O_2$ and $S_{cv}O_2$ were −0.9 (−7.9/+6.1)% during surgery and −1.2 (−10.5/+8.1)% in the intensive care unit. In 37.9% of all measured data pairs, the difference between $S_{cevox}O_2$ and $S_{cv}O_2$ was beyond clinically acceptable limits (≥1 s.d.). Mean bias was significantly influenced by cardiac index. Sensitivity and specificity of $S_{cevox}O_2$ to detect substantial (≥1 s.d.) changes in $S_{cv}O_2$ were 89 and 82%, respectively. **Conclusions.** In adult patients during and after cardiac surgery, the current version of the CeVOX device might not be the tool to replace $S_{cv}O_2$ determined by co-oximetry, although sensitivity and specificity of $S_{cevox}O_2$ to predict substantial changes in $S_{cv}O_2$ were acceptable.

KEY WORDS. Central venous oxygen saturation, Continuous monitoring, Mixed venous oxygen saturation, Cardiac surgery.

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INTRODUCTION

Central venous oxygen saturation ($S_{cv}O_2$) is an important parameter for estimating changes in the global oxygen supply-to-demand ratio in various clinical settings [1, 2] and one of the core targets for early goal-directed therapy in the treatment of septic shock [3–6]. Recently, the Collaborative Study Group in Perioperative $S_{cv}O_2$ Monitoring [7] confirmed the importance of low $S_{cv}O_2$ values in predicting an increased risk of perioperative complications in high-risk surgical patients.

Standard means to monitor $S_{cv}O_2$ consist of drawing repeated blood samples from a central venous catheter

placed in the superior vena cava and measuring $S_{cv}O_2$ by co-oximetry [8]. However, this approach is intermittent, increases workload and costs, and results in contamination of stopcocks and iatrogenic blood loss. Therefore, reliable techniques for continuous monitoring of $S_{cv}O_2$ are desirable. One such technique, based on the principle of near-infrared spectroscopy [8], is the recently introduced CeVOX system (Pulsion Medical Systems, Munich, Germany). To our knowledge, only one experimental study [9] and two clinical investigations [10, 11] have been undertaken to evaluate the reliability of the CeVOX system and factors influencing its accuracy.

The aim of this study was to evaluate the accuracy of the CeVOX device for continuous assessment of central venous oxygen saturation ($S_{cevox}O_2$) against $S_{cv}O_2$ determined by co-oximetry during and after cardiac surgery. In addition, agreement between $S_{cevox}O_2$ and mixed venous oxygen saturation ($S_{mv}O_2$) was also documented.

METHODS

The CeVOX system relies on the principle of near-infrared spectroscopy. Tissue chromophores, such as haemoglobin absorb near-infrared light depending on their oxygenation state. Changes in chromophore concentrations and oxygenation states, revealed by comparing emitted and detected near-infrared light, can therefore be quantified using the modified Lambert-Beer law.

For the purpose of $S_{Cevox}O_2$ monitoring, light of three wavelengths (660, 805 and 880 nm) is transmitted through a fiberoptic probe inserted into the distal lumen of a central venous catheter placed in the superior vena cava. The tip of the fiberoptic probe must protrude the distal end of the catheter by 2–3 cm. It is connected to the optical module of the CeVOX system. Light reflected from the haemoglobin in the red blood cells is transmitted back by a second fiberoptic line. The sensor in the optical module analyses the reflected light and determines light extinction. This information is transferred to the CeVOX system and $S_{cevox}O_2$ is calculated and displayed on the screen.

With ethics committee approval and written, informed consent, 20 patients scheduled for cardiac surgery with or without extracorporeal circulation were enrolled in this prospective, non-randomized, open, monocentre study. Exclusion criteria were refusal to participate in the study, hypercoagulation disorders such as factor 5 Leiden disease, contraindications for insertion of a pulmonary artery catheter (e.g., surgery of the tricuspid and/or pulmonary valve, haemoptysis, thrombi within the right heart or pulmonary artery), contraindications against transesophageal echocardiography (e.g., oesophageal varices, gastric

ulcers, history of recent acute gastric bleeding, narrowing or stenosis of the oesophagus, Zenker diverticle), and presence of an open foramen ovale.

Premedication consisted of oral flunitrazepam (1.0–2.0 mg) the evening before surgery and oral midazolam (7.5–15 mg) 45 min before transfer to the operating room. Standard instrumentation included a 2-channel ECG (leads II and V_5) (Hellige SMU 612 monitor, Marquette Hellige Medical Systems, Freiburg i.Br, Germany), pulse oximetry using a finger clip (Nellcor Durasensor, Model DS-100A), and continuous arterial blood pressure monitoring (Hellige SMU 612 monitor, Marquette Hellige Medical Systems, Freiburg i.Br, Germany) via a fluid-filled catheter system (Baxter Healthcare Corporation Cardiovascular Group, Irvine, CA, USA) connected to the non dominant radial artery.

Target-controlled intravenous anaesthesia using propofol (plasma concentration: 1.5–2.5 $\mu g\ ml^{-1}$), supplemented by bolus injections of fentanyl (3–10 $\mu g\ kg^{-1}$) and pancuronium (Organon; 0.1 mg kg^{-1}), was used for induction of anaesthesia in all patients. Anaesthesia was maintained with propofol (1.5–2.0 $\mu g\ ml^{-1}$) and remifentanil (0.1–0.3 $\mu g.kg^{-1}.min^{-1}$). After orotracheal intubation, the patient's lungs were mechanically ventilated (Siemens Servo 900; Erlangen, Germany) using a volume-controlled mode.

A four-lumen central venous catheter (Arrow International, Reading, PA, USA) and a 7.5 FG thermistor-tipped, flow-directed CCO and $S_{mv}O_2$ pulmonary artery catheter (IntelliCath; Baxter Healthcare Corp.), introduced through an 8.5 FG introducer (Arrow International), were inserted in the right jugular vein. The pulmonary artery catheter was connected to a cardiac output computer system (9520A; Baxter Healthcare Corp.). Cardiac index (CI) was determined by injecting 10 ml of iced saline 0.9% with a closed injectate system (CO-set; Baxter Healtcare Corp.) Injections were distributed randomly throughout the respiratory cycle. Thermodilution curves were displayed on a recorder and accepted as correct if the shape of the curve fulfilled the criteria of Levett and Replogle [12] and if the injectate temperature was <10°C.

The CeVOX fiberoptic probe (PV2022-35, Pulsion Medical Systems) was inserted into the distal lumen of the central venous catheter. The correct positions of both, the CeVOX fiberoptic probe tip and the pulmonary artery catheter tip were verified by transesophageal echocardiography before calibration. The CeVOX probe was secured to the distal end of the central venous catheter lumen by the integrated luer lock system and connected to the optical module of the CeVOX system. In vivo calibration was performed according to the reference manual of the manufacturer. Every 30 min during cardiac surgery (t1–t6) and,

after recalibration of the CeVOX system, every 60 min after admission to the intensive care unit (ICU) (t7–t12), central venous and mixed venous blood samples were drawn for assessment of $S_{cv}O_2$, $S_{mv}O_2$ and haemoglobin (Hb) concentration by co-oximetry. Blood samples were analysed using multi-wavelength haemoximetry (ABL 626/620, Radiometer Medical A/S, Akandevey 21, DK-2700 Bronshoj, Denmark). Central venous blood samples were drawn from the distal lumen of the central venous catheter; the mixed venous blood samples were taken from the pulmonary lumen of the pulmonary artery catheter. Simultaneously, $S_{cevox}O_2$ was recorded, and body temperature, heart rate, central venous pressure, mean arterial pressure and CI were documented.

Data analysis

A power calculation revealed that a sample size of 20 patients would have 80% power to detect a difference of ≥1 s. d. between $S_{cv}O_2$ and $S_{cevox}O_2$ using a paired *t*-test with a 0.05 two-sided significance level. Agreement between $S_{cv}O_2$ and $S_{cevox}O_2$ was determined by Bland-Altman analysis [13]. Simple regression analysis was used to correlate mean bias of $S_{cv}O_2$ and $S_{cevox}O_2$ with Hb, body temperature, central venous pressure, mean arterial pressure, and cardiac index. Sensitivity and specificity of changes in $S_{cevox}O_2$ to detect changes in $S_{cv}O_2$ and sensitivity and specificity to detect substantial changes (≥1 s.d.) in $S_{cv}O_2$, were determined. A p value of <0.05 was considered significant. In addition, $S_{cevox}O_2$ and $S_{cv}O_2$ were correlated with $S_{mv}O_2$.

RESULTS

Patients' characteristics and haemodynamic data are shown in Tables 1 and 2. Two hundred twenty-one data pairs of $S_{cevox}O_2$ and $S_{cv}O_2$ (115 during surgery and 106 after admission to the ICU) were recorded. Thirty-one data pairs were excluded because of detection failure of the CeVOX fiberoptic probe due to ambient light when the chest was open. The remaining 190 data pairs (84 during surgery and 106 in the ICU) were analysed. $S_{cevox}O_2$ and $S_{cv}O_2$ values ranged between 45–89% and 43–90%, respectively. Mean bias and limits of agreement of $S_{cevox}O_2$ and $S_{cv}O_2$ for all measurements, for measurements during surgery, and for measurements in the ICU were −1.1 (−9.5/+7.3)%, −0.9 (−7.9/+6.1)% (Figure 1) and −1.2 (−10.5/+8.1)%, respectively (Figure 2, Table 3). In 37.9% of all data pairs, the difference between $S_{cevox}O_2$ and $S_{cv}O_2$ was beyond clinically acceptable limits (≥1 s. d.). A moderate correlation of the first differences between

Table 1. Patients' characteristics

No. of patients	20
Sex (M:F)	12:8
Age (years)	71 (41–84)
Body mass index (kg.m^{-2})	27.8 (18.8–34.4)
Body surface area (m^2)	1.87 (1.5–2.4)
Preoperative LV-EF (%)	60 (10–78)
Surgery, no. of patients	
OPCAB	8
CABG	2
Valve	7
Valve + CABG	3

Values are expressed as number or median (range). LV-EF, left ventricular ejection fraction; OPCAB, off-pump coronary artery bypass; CABG, coronary artery bypass graft; valve + CABG, combined valve and coronary artery bypass graft surgery.

Table 2. Haemodynamic characteristics

$S_{mv}O_2$ (%)	72.15 (50–89)
Blood temperature (°C)	36.6 (31.0–38.6)
Pulse rate (bpm)	83 (40–110)
Mean arterial pressure (mm Hg)	71 (53–95)
Central venous pressure (mm Hg)	9 (0–25)
Cardiac index (l min^{-1} m^{-2})	2.6 (1.0–4.5)

Values are expressed as median (range).

$S_{cevox}O_2$ and $S_{cv}O_2$ was found (Figure 3) and sensitivity and specificity of $S_{cevox}O_2$ to detect changes in $S_{cv}O_2$ (n = 168 data pairs) was 76 and 85%, respectively (Figure 3). When taking into account only substantial changes in $S_{cv}O_2$ (≥1 s. d.), sensitivity increased to 89% with a specificity of 82%.

Simple regression analyses revealed that the mean bias of $S_{cevox}O_2$ and $S_{cv}O_2$ was not influenced by Hb (P = 0.33), blood temperature (P = 0.23) or mean arterial pressure (P = 0.94), but an association of the bias was found with central venous pressure (P = 0.02) and cardiac index (P = 0.0002). At low cardiac index values, $S_{cevox}O_2$ overestimated $S_{cv}O_2$, whereas in the high cardiac index range, $S_{cevox}O_2$ underestimated $S_{cv}O_2$ (Figure 4). After the CeVOX fiberoptic probe was removed, no probe defect or macroscopic visible clot was observed.

Linear correlation between $S_{cevox}O_2$ and $S_{cv}O_2$ and between $S_{cevox}O_2$ and $S_{mv}O_2$ were r^2 = 0.41 and 0.62, respectively.

DISCUSSION

The main findings of this study are that (i) the agreement between $S_{cevox}O_2$ and $S_{cv}O_2$ was poor; (ii) mean bias of
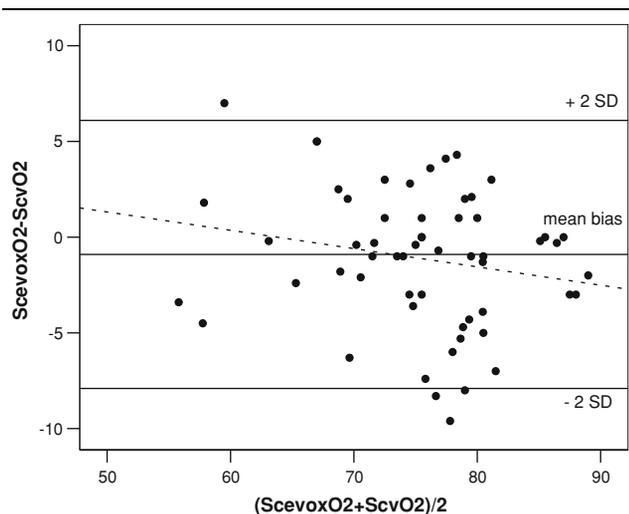
Fig. 1. Agreement between $S_{cevox}O_2$ and $S_{cv}O_2$ of 84 data pairs during surgery. Mean bias, −0.9 %; LOA, −7.9 / + 6.1%.
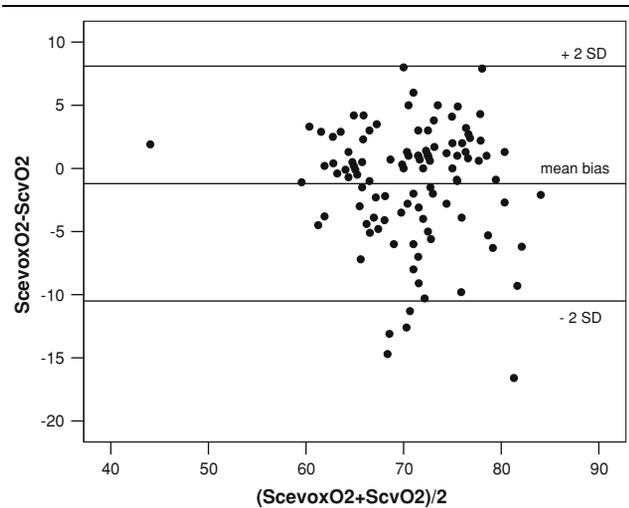

Fig. 3. First differences of $S_{cevox}O_2$ (diff $S_{cevox}O_2$) and $S_{cv}O_2$ (diff $S_{cv}O_2$) [in %] with $R^2 = 0.464$, $P < 0.0001$).

Fig. 2. Agreement between $S_{cevox}O_2$ and $S_{cv}O_2$ of 106 data pairs during recovery in the ICU. Mean bias, −1.2%; LOA, −10.5 / + 8.13%.

Fig. 4. Influence of cardiac index (L min^{-1} m^{-2}) on mean bias of $S_{cevoxO2}$ and $S_{cv}O_2$ (%).

Table 3. Bland-Altman analysis of $S_{cevox}O_2$ and $S_{cv}O_2$ for all data, data pairs during surgery and data in the ICU

Data pairs	n	Mean bias	LOA
$S_{cevox}O_2$–$S_{cv}O_2$ (all data)	190	−1.1	−9.5/+7.3
$S_{cevox}O_2$–$S_{cv}O_2$ (surgery)	83	−0.9	−7.9/+6.1
$S_{cevox}O_2$–$S_{cv}O_2$ (ICU)	107	−1.2	−10.5/+8.1

$S_{cevox}O_2$, continuous measured central venous oxygen saturation by the CeVOX device; $S_{cv}O_2$, central venous oxygen saturation; LOA, limits of agreement.
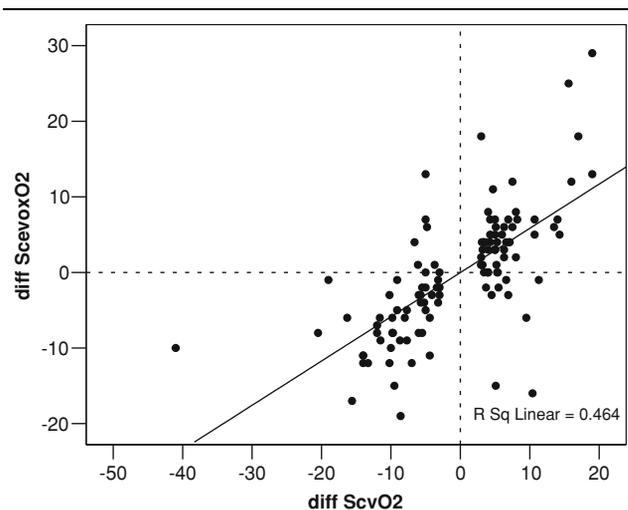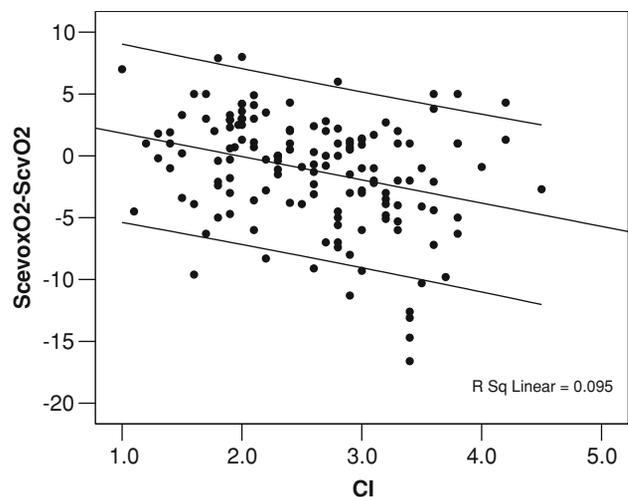
$S_{cevox}O_2$ and $S_{cv}O_2$ was significantly influenced by cardiac index; (iii) correlation of first differences between $S_{cevox}O_2$ and $S_{cv}O_2$ values was only moderate, but sensitivity of $S_{cevox}O_2$ to detect substantial changes in $S_{cv}O_2$ were acceptable; and (iv) only a moderate correlation of $S_{cevox}O_2$ and $S_{cv}O_2$ with $S_{mv}O_2$. was found.

The technical prerequisites for continuous measurements of oxygen saturation in the blood using spectrophotometry have been available for more than 40 years [14]. Multiple clinical and experimental investigations have compared oxygen saturation values derived from fiberoptic catheters with those obtained by co-oximetry. Scuderi and colleagues [15] compared three pulmonary

artery oximetry catheters and reported acceptable agreement with $S_{mv}O_2$ measured by co-oximetry with two of the three catheters (95% confidence limits: 2.47% and 3.36%, respectively). Burchell and colleagues [16], also comparing fiberoptic $S_{mv}O_2$ values with $S_{mv}O_2$ assessed by co-oximetry, interpreted a mean bias of −0.57% and limits of agreement of ±3.76% as acceptable.

The CeVOX system, investigated here is based on three reference light wavelengths and characterised by one transmitting and one detecting fiberoptic filament. Advantages of this system are that it is easy to handle and does not necessitate additional invasive venous access because the disposable 2F fiberoptic catheter can be inserted into a standard central venous line. Various lengths (30–48 cm) of the fiberoptic catheter facilitate its use in connection with a variety of central venous catheters in adults. In the current study the CeVOX monitoring device for continuous assessment of central venous oxygen saturation ($S_{cevox}O_2$) was compared with central venous oxygen saturation ($S_{cv}O_2$) determined by co-oximetry in cardiac surgical patients. This investigation revealed that the bias of all $S_{cevox}O_2$ and $S_{cv}O_2$ values was good, but the limits of agreement were unacceptably high.

Recently, Muller and colleagues [10] investigated the CeVOX system in three cyanotic infants undergoing modifications of the stage 1 Norwood procedure. They reported that the technique is feasible in infants, although the number of measured data pairs was small and, at $S_{cv}O_2$ values ≤ 50%, the mean bias and limits of agreement of $S_{cevox}O_2$ and $S_{cv}O_2$ were unacceptable.

Most recently, Molnar and colleagues [11] performed a multicentre study and reported good comparability of $S_{cevox}O_2$ and $S_{cv}O_2$ in a heterogeneous group of critically ill patients, although the limits of agreement were high (−13.2 and 12.5%). Furthermore, in 12 of 53 patients (>20%) they found a difference of ≥10% at any time point between $S_{cevox}O_2$ and $S_{cv}O_2$ values determined by co-oximetry. This was confirmed in the current study, were the difference between $S_{cevox}O_2$ and $S_{cv}O_2$ was beyond clinically acceptable limits in 37.9% of all data pairs.

Hofer and colleagues [17] investigated the CeVOX device in ASA III patients undergoing elective off-pump coronary artery bypass surgery. They reported that continuous $S_{cv}O_2$ assessment using CeVOX was reliable. In their study, the mean bias of $S_{cevox}O_2$ and $S_{cv}O_2$ was good, but the limits of agreement during surgery and in the ICU were as high as in the present study (±8% and ±12%, respectively). Similar to our results, they also found less agreement between $S_{cevox}O_2$ and $S_{cv}O_2$ after surgery than during surgery. It could be hypothesized that the probability of inadequate volume load and consecutive vein wall artefacts of the fiberoptic probe is higher in the

ICU. Indeed, in our study the mean central venous pressure found in the ICU was lower than during surgery at constant positive end-expiratory pressure. Another possible explanation for the reduced agreement of the two methods after surgery may be the time-related higher probability of clot formations at the tip of the fiberoptic catheter during recovery in the ICU. Hypercoagulation states after cardiac surgery with or without cardiopulmonary bypass are well known [18, 19]. We cannot definitively exclude this explanation, although no visible clots were found at the tips of the CeVOX fiberoptic probes after removal.

Interestingly, the Bland-Altman analysis of the data pairs collected during and after surgery suggests a nearly linear dependence of the mean bias of $S_{cevox}O_2$ and $S_{cv}O_2$ on $S_{cv}O_2$, possibly indicating a systematic error in the CeVOX algorithm. Most recently Huber and colleagues [9] compared oxygen saturation values obtained with a 2 French CeVOX fiberoptic probe and a 4 French Edwards oximetry catheter against values measured by co-oximetry in an in vitro setting and demonstrated overestimation at low and underestimation at high oxygen saturations. They recommended repeated recalibration to reduce the drift of fiberoptic oximetry values. In an own most recently published in vitro study [20] these findings were confirmed. One possible reason for the suggested linear dependency may be a systematic error in the calibration factor (Cal-Value) of the CeVOX system, recommended by the manufacturer. But this hypothesis remains to be determined.

Additionally, the mean bias of $S_{cevox}O_2$ and $S_{cv}O_2$ in the present study was significantly influenced by the Cardiac index: $S_{cevox}O_2$ overestimated $S_{cv}O_2$ at low CI values and underestimated it at high values.

First differences between $S_{cevox}O_2$ and $S_{cv}O_2$ found in the current investigation showed only a moderate correlation, indicating a considerable number of significant changes in opposite direction. Only sensitivity and specificity of $S_{cevox}O_2$ to detect substantial changes in $S_{cv}O_2$ were acceptable (85 and 82%, respectively).

In agreement with previous investigations [21–23], neither $S_{cevox}O_2$ nor $S_{cv}O_2$ reliably reflected $S_{mv}O_2$. The first differences between $S_{cv}O_2$ and $S_{mv}O_2$ were only moderately correlated, and changes in $S_{cv}O_2$ only roughly tracked changes in $S_{mv}O_2$ (data not shown). Correlation of the first differences between $S_{cevox}O_2$ and $S_{mv}O_2$ was even worse.

In conclusion, the current version of the CeVOX device might not be the tool to replace $S_{cv}O_2$ determined by co-oximetry. Even though the sensitivity and specificity of $S_{cevox}O_2$ to detect substantial changes in $S_{cv}O_2$ are acceptable, the current version of the CeVOX device cannot be recommended for clinical application in high

risk surgery. Considering the importance of continuous central venous oxygen saturation monitoring, efforts should be made to improve the reliability of the CeVOX device.

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