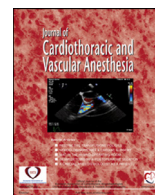


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Original Article

## Accuracy, Precision, and Trending Ability of Perioperative Central Venous Oxygen Saturation Compared to Mixed Venous Oxygen Saturation in Unselected Cardiac Surgical Patients

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**Objective:** To determine whether central venous oxygen saturation (ScvO<sub>2</sub>) measurements could be used interchangeably with mixed venous oxygen saturation (SvO<sub>2</sub>) measurements in adult cardiac surgery patients.

**Design:** A single-center prospective observational study.

**Setting:** A university hospital.

**Participants:** Eighty-five adult patients undergoing cardiac surgery.

**Interventions:** The study authors compared the oxygen saturations in 590 pairs of venous blood samples drawn from the pulmonary artery catheter (PAC) at three different time points during surgery and four different time points in the intensive care unit. They compared samples obtained from the distal pulmonary artery line (SvO<sub>2</sub>) to those drawn from the proximal central venous line of the PAC (ScvO<sub>2</sub>) with the Bland-Altman test and the four-quadrant method.

**Measurements and Main Results:** The mean bias between SvO<sub>2</sub> and ScvO<sub>2</sub> was  $-1.9$  (95% confidence interval [CI],  $-2.3$  to  $-1.5$ ) and the limits of agreement (LOA) were  $-11.5$  to  $7.6$  (95% CI,  $-12.5$  to  $-10.7$  and  $6.8$ - $8.5$ , respectively). The percentage error (PE) was 13.2%. Based on the four-quadrant plot, only 50% of the measurement pairs were in agreement, indicating deficient trending ability.

**Conclusion:** ScvO<sub>2</sub> values showed acceptable accuracy as the mean bias was low. The precision was inadequate; although the PE was acceptable, the LOA were wide. Trending ability was inadequate. The authors cannot recommend the use of ScvO<sub>2</sub> values interchangeably with SvO<sub>2</sub> measurements in the management of adult cardiac surgery patients.

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**Keywords:** Mixed venous oxygen saturation; Central venous oxygen saturation; Goal-directed hemodynamic therapy; Cardiac Surgery

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AS LOW-CARDIAC-OUTPUT syndrome remains the major determinant of adverse outcome after cardiac surgery,<sup>1,2</sup> advanced hemodynamic monitoring commonly is utilized to guide perioperative treatment. Several studies have shown that goal-directed hemodynamic therapy may reduce postoperative complications in cardiac surgical patients and shorten the length of both intensive care unit (ICU) and hospital stays.<sup>3-5</sup>

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The purpose of goal-directed hemodynamic therapy is to improve tissue oxygenation. According to the Fick principle, mixed venous oxygen content of the pulmonary artery, and its surrogate mixed venous saturation (SvO<sub>2</sub>), reflect the balance between oxygen consumption and delivery. Decreases in cardiac output, arterial oxygen saturation, or hemoglobin concentration, or an increase in oxygen consumption, may lead to decreased SvO<sub>2</sub>. Therefore, therapeutic interventions to increase SvO<sub>2</sub> can include intravenous fluids and vasoactive agents, blood transfusion, and patient sedation.

Previously, SvO<sub>2</sub> <60% on admission to the ICU after coronary artery bypass graft (CABG) surgery has been linked with a higher incidence of postoperative complications, prolonged time on mechanical ventilation and ICU stay, as well as increased 30-day mortality.<sup>6</sup> Similarly, in patients undergoing aortic valve surgery, SvO<sub>2</sub> <58% on admission to the ICU was associated with an increase in all-cause postoperative mortality.<sup>7</sup> On the other hand, hemodynamic treatment aiming at SvO<sub>2</sub> >70% during the first eight hours after CABG surgery reduced the number of patients developing complications and shortened the length of hospital stay.<sup>4</sup>

The use of a pulmonary artery catheter (PAC) necessary for SvO<sub>2</sub> sampling has declined markedly in recent decades.<sup>8-11</sup> Central venous oxygen saturation (ScvO<sub>2</sub>) measurements are being used as a substitute for SvO<sub>2</sub>. It has indeed been demonstrated in patients undergoing cardiac surgery that both low (<60%) and supranormal (>77%-80%) ScvO<sub>2</sub> values during the early postoperative period are associated with increased morbidity and mortality.<sup>8,12</sup> However, ScvO<sub>2</sub> is not identical to SvO<sub>2</sub>, as it reflects the upper body instead of a global oxygen balance. Studies comparing ScvO<sub>2</sub> to SvO<sub>2</sub> samples in the cardiac surgical setting still are few and often are limited to either the intraoperative<sup>13</sup> or immediate postoperative period.<sup>14-16</sup> In fact, the authors are aware of only two studies extending over the course of both intraoperative care in the operating room (OR) and postoperative treatment in the ICU.<sup>17,18</sup> Neither of these studies presented any statistical assessment of the trending ability of ScvO<sub>2</sub> compared to SvO<sub>2</sub>.

The study authors performed the present study in an unselected cardiac surgical cohort with the aim to examine the accuracy, precision, and trending ability of ScvO<sub>2</sub> in comparison with SvO<sub>2</sub> pooled over the entire perioperative period. They hypothesized that ScvO<sub>2</sub> is interchangeable with SvO<sub>2</sub>.

## Methods

This single-center prospective observational study was approved by the Ethics Committee of Northern Ostrobothnia Hospital District (17/2020). The authors included 85 consecutive adult patients undergoing cardiac surgery at Oulu University Hospital between March and August 2020. Before obtaining study consent, the patients were properly informed, both orally and in writing, by a cardiac anesthesiologist. The only exclusion criteria were an atrial septal defect with left-to-right shunting and the refusal of the patient to join the study.

The patients were premedicated with oral diazepam and intramuscular morphine one hour before entering the OR. Upon arrival in the OR, a radial artery was cannulated under local anesthesia (BD Arterial Cannula 20G, Becton Dickinson and Company, Franklin Lakes, NJ). In addition, a PAC (Critiath SP5507U TD Catheter, Merit Medical, South Jordan, UT) was introduced via an 8.5F sheath placed in the right internal jugular vein and advanced into the pulmonary artery until a wedge pressure trace was obtained but withdrawn if the central venous pressure tracing indicated ventricular location of the central venous opening. In the authors' hospital, PAC still is routinely used for all patients undergoing cardiac surgery, and SvO<sub>2</sub> values are used in combination with other physical findings and monitoring modalities to guide volume replacement and the administration of inotropes, vasopressors, and vasodilators, both in the OR and in the ICU.

Thereafter, anesthesia was induced with intravenous infusions of propofol and remifentanyl. A single dose of rocuronium was administered to achieve neuromuscular blockade for tracheal intubation. General anesthesia was maintained with sevoflurane, which, in most cases, was combined with a low-dose propofol infusion. Intraoperative analgesia was provided with remifentanyl. All patients underwent transesophageal echocardiography, and significant atrial septal defects were excluded. Postoperatively, the patients were transferred to the ICU under propofol and remifentanyl infusions. In the ICU, remifentanyl soon was replaced with intravenous oxycodone as boluses or an infusion. The patients were awakened and extubated according to local fast-track principles. Hemodynamic management was based on the clinical judgment of experienced cardiac anesthesiologists and intensive care physicians and was not specified in the study protocol.

Blood samples for SvO<sub>2</sub> and ScvO<sub>2</sub> measurements were obtained successively from the distal (yellow) pulmonary artery line and the proximal (blue) central venous line of PAC, respectively. In the OR, the sample pairs were drawn immediately before and after the induction of anesthesia and 15 minutes after protamine administration. In the ICU, the samples were taken immediately after the admission, four hours postoperatively, at midnight, and on the first postoperative morning. Altogether, 590 sample pairs were collected. The samples were analyzed for blood gases and venous saturations with a GEMPremier 4000 (Instrumentation Laboratory, Bedford, MA) blood gas analyzer located in the central laboratory. The instrument calculates oxygen saturations from the spectrophotometrically measured CO-oximetry parameters. Of the venous saturations, only SvO<sub>2</sub> values were used for therapeutic decisions. To assess a proper sample size for the present study, the authors collected preliminary data from 35 patients, yielding 245 samples. From this data, they performed the sample size calculation for an equivalence study, in which the mean SvO<sub>2</sub> was 74.4%, and the mean ScvO<sub>2</sub> was 72.9%. The results were as follows: standard deviation of differences 7.5, noninferiority margin 5, alpha 0.05, and beta 0.10 (power 0.9), giving a sample size of at least 541 measurements.

The summary statistics are presented as medians with 25th- to 75th percentiles or total numbers with percentages. The

mean bias between the measurements and the limits of agreement (LOA) with 95% confidence intervals (CI) were calculated according to Bland and Altman.<sup>19-21</sup> The data structure with multiple independent measurements within the subject was considered while calculating the LOA.<sup>20,21</sup> To evaluate proportional bias, a regression coefficient with 95% CI was calculated to detect whether there is any difference among the techniques dependent on the magnitude of the SvO<sub>2</sub>, thereby making the bias skewed. Squared term was calculated to assess possible nonlinear association (not reported unless significant). The percentage error (PE) with 95% CI was calculated.<sup>22</sup> To assess trending ability, four-quadrant (4Q) plots of two consecutive venous saturation measurements were constructed, with the exclusion zone set at 3%. Based on clinical concordance categories of the 4Q plot, error grids were constructed to create four zones to determine the level of agreement between the changes in SvO<sub>2</sub> and ScvO<sub>2</sub> plotted against each other. In zone 1, SvO<sub>2</sub> and ScvO<sub>2</sub> have changed in the same direction to the same extent, or in other words, both have changed less than 5%, between 5%-to-15%, or more than 15%, leading to uniform treatment decisions. In zone 2, they have changed in the same direction but not to the same extent. In zone 3, only SvO<sub>2</sub> or ScvO<sub>2</sub> has changed, implying that unnecessary treatment may be initiated or necessary treatment withheld. In zone 4, the changes have been opposite, and opposite treatment may have been initiated.<sup>22</sup> Analyses were performed using SPSS for Windows (IBM Corp. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY), MedCalc for Windows, version 20 (MedCalc Software, Ostend, Belgium), and SAS for Windows (version 9.4 SAS Institute Inc., Cary, NC). A two-tailed p value ≤ 0.05 was considered statistically significant.

## Results

The patient characteristics are presented in Table 1. The median age of the patients was 65 years, and 82.4% of them were male. Preoperative ejection fraction was normal in 64 patients (75.3%), while it was <30% only in one patient only. Of the patients, 50.6% underwent coronary artery bypass graft surgery, and approximately one-third of those were off-pump procedures. The others underwent either aortic valvular (17.6%), mitral valvular (10.6%), ascending aortic (4.7%), or combined procedures (14.1%). In addition, one patient underwent aortic arch surgery, while one patient underwent pericardiectomy. Of the procedures, 54.1% were elective. There were no complications associated with the insertion, use, or removal of the PAC. One patient died during the hospital stay due to cardiac arrest during the fourth postoperative day in the ICU.

Figure 1 represents the perioperative course of SvO<sub>2</sub> and ScvO<sub>2</sub> values. In the Bland-Altman analysis of all measurement points, ScvO<sub>2</sub> was associated with a bias of -1.9 (95% CI, -2.3% to -1.5%) and LOA of -11.5 (95% CI, -12.5% to -10.7%) to 7.6 (95% CI, 6.8%-8.5%), in comparison with SvO<sub>2</sub>, as shown in Figure 2. The regression coefficient was -0.05 (95% CI, -0.11% to 0.00%). The PE was 13.2% (95% CI, 12.4%-14.1%). Figure 2 also shows the 4Q method plotting the changes in SvO<sub>2</sub> against the changes in ScvO<sub>2</sub>. In the error

Table 1  
Patients Characteristics (n = 85).

|   |                  |
|---|------------------|
| Age, y                                    | 65 (59-71)       |
| Sex, male                                 | 70 (82.4)        |
| Weight, kg                                | 82 (71-91)       |
| BMI, kg/m <sup>2</sup>                    | 27 (24-30)       |
| Prior comorbidities                       |                  |
| Hypertension                              | 59 (69.4)        |
| Type 2 diabetes mellitus                  | 23 (27.1)        |
| COPD                                      | 1 (1.2)          |
| Asthma                                    | 1 (1.2)          |
| Left ventricular hypertrophy              | 11 (12.9)        |
| Atrial fibrillation                       | 12 (14.1)        |
| Medication prior to surgery               |                  |
| Acetylsalicylic acid                      | 53 (62.4)        |
| Clopidogrel                               | 8 (9.4)          |
| Low-molecular-weight heparin              | 23 (27.1)        |
| Beta-blocker                              | 50 (58.8)        |
| Statin                                    | 52 (61.2)        |
| ACE inhibitor or AT II receptor inhibitor | 50 (58.8)        |
| Long-acting nitrate                       | 24 (28.2)        |
| Medical state prior to surgery            |                  |
| Ejection fraction, n (%)                  |                  |
| >50%                                      | 64 (75.3)        |
| 31%-50%                                   | 20 (23.5)        |
| 21%-30%                                   | 1 (1.2)          |
| EuroSCORE                                 | 1.6 (1.1-2.6)    |
| Hb, g/L (IQR)                             | 138 (128-148)    |
| INR (IQR)                                 | 1.1 (1.0-1.2)    |
| Tromb E9/I (IQR)                          | 226 (192-262)    |
| NYHA class (IQR)                          | 3 (2-3)          |
| Surgery                                   |                  |
| Urgency, n (%)                            |                  |
| Elective                                  | 46 (54.1)        |
| Urgent                                    | 39 (45.9)        |
| CABG, n (%)                               | 28 (32.9)        |
| OPCAB, n (%)                              | 15 (17.6)        |
| AVR, n (%)                                | 15 (17.6)        |
| MAP/MVR, n (%)                            | 9 (10.6)         |
| Ascending Aorta, n (%)                    | 4 (4.7)          |
| Combined procedures, n (%)                | 12 (14.1)        |
| Aortic arch, n (%)                        | 1 (1.2)          |
| Pericardiectomy, n (%)                    | 1 (1.2)          |
| Levosimendan used, n (%)                  | 17 (20)          |
| Norepinephrine used, n (%)                | 85 (100)         |
| Norepinephrine max dose, µg/kg/min (IQR)  | 0.25 (0.17-0.33) |
| Dobutamine used, n (%)                    | 31 (36.5)        |
| Dobutamine max dose, µg/kg/min (IQR)      | 2.69 (2.13-3.18) |
| OR stay, min (IQR)                        | 375 (322-424)    |
| Time in ventilator, OR and ICU, min (IQR) | 240 (152-360)    |
| ICU length of stay, d (IQR)               | 1 (1-2)          |
| Hospital length of stay, d (IQR)          | 9 (7-9)          |
| Hospital mortality, n (%)                 | 1 (1.2)          |

The values given are medians with 25th and 75th percentiles or number of patients (n) with percentages (%).

Abbreviations: ACE, angiotensin-converting enzyme; AVR, aortic valve replacement; BMI, body mass index; CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; E9/I, 10<sup>9</sup>/l; Hb, hemoglobin; ICU, intensive care unit; INR, international normalized ratio; IQR, interquartile range; MAP, mitral annuloplasty; MVR, mitral valve replacement; NYHA Class, New York Heart Association Classification; OPCAB, off-pump coronary artery bypass; OR, operating room.

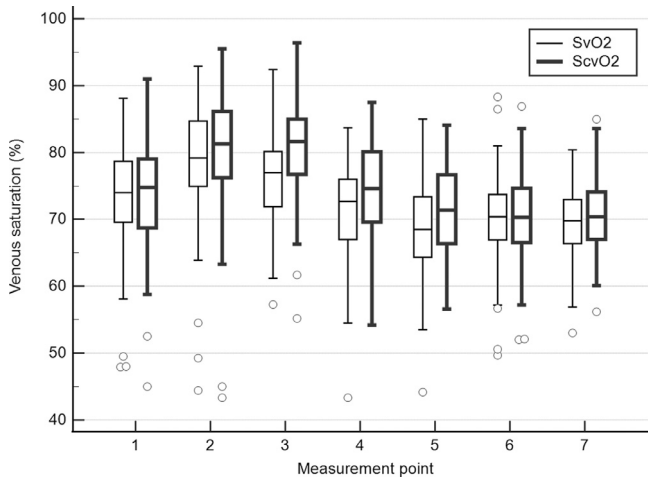


Fig 1. A box-and-whisker plot of SvO<sub>2</sub> and ScvO<sub>2</sub> values in the OR (1-3) and ICU (4-7). Measurement point 1 is before the induction of anesthesia, while 2 is after the induction, 3 after protamine administration, 4 right after ICU admission, 5 four hours after ICU admission, 6 at midnight, and 7 on the first postoperative morning. The horizontal lines indicate median values, the boxes are drawn from the 25th-to-75th percentiles, and the lowest and highest values represent the lower and upper adjacent values, respectively. Circles indicate outlier values. ICU, intensive care unit; OR, operating room.

grid based on the 4Q plot, clinical concordance was 50.0% in zone 1, 10.9% in zone 2, 36.2% in zone 3, and 2.9% in zone 4. Table 2 shows the Bland-Altman data, the PE, and the regression coefficient separately for each measurement point. A total of 588 samples were included in the analysis. Two out of 590 samples were excluded because they were not taken at the given measurement points.

**Discussion**

This prospective method comparison study in an unselected cardiac surgical cohort was designed to evaluate the accuracy, precision, and trending ability of ScvO<sub>2</sub> compared to SvO<sub>2</sub> during the perioperative period. The authors discovered that ScvO<sub>2</sub> values showed acceptable accuracy as the mean bias was low, but they are not precise enough due to a wide LOA. Furthermore, based on the clinical concordance between the changes in SvO<sub>2</sub> and ScvO<sub>2</sub>, the trending ability of ScvO<sub>2</sub> is inadequate. The results suggested that SvO<sub>2</sub> and ScvO<sub>2</sub> are not interchangeable in the cardiac surgical setting.

The authors’ conclusions were in line with those of earlier studies in patients undergoing cardiac surgery.<sup>14-17,23</sup> However, most of the previous studies were limited to the immediate postoperative period<sup>14-16</sup> and included only patients undergoing elective surgery.<sup>15,17,18,23</sup> Furthermore, only a power analysis was conducted in some studies,<sup>15,23</sup> and the numbers of sample pairs often were insufficient. The statistical methods used especially may be criticized for omitting adequate assessment of trending ability. Therefore, the present study involved many improvements compared to previous works in this field and clearly added to the current evidence.

The study authors assessed the agreement between SvO<sub>2</sub> and ScvO<sub>2</sub> using the Bland-Altman method. However, statistics alone cannot resolve the acceptable level of agreement, and clinical judgment also is required.<sup>21</sup> It previously has been suggested that an acceptable bias should be less than a change in SvO<sub>2</sub> that would induce therapeutic interventions.<sup>18</sup> According to Bendejeld et al,<sup>24</sup> the maximal acceptable difference among SvO<sub>2</sub> values obtained with a fiberoptic PAC and

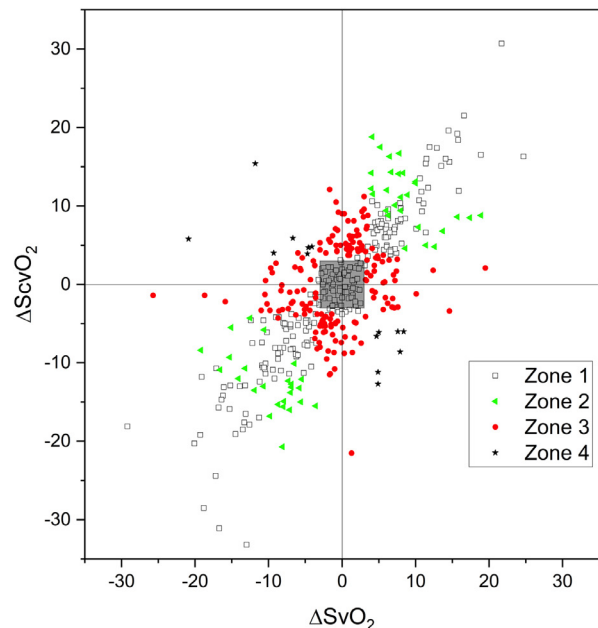
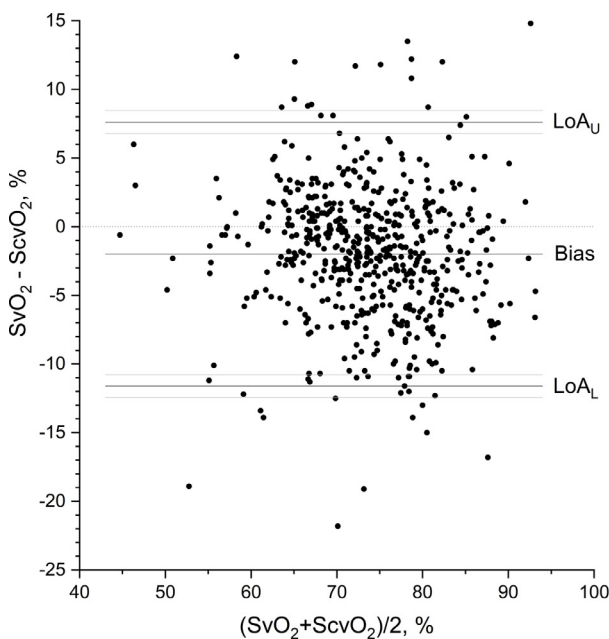


Fig 2. Bland-Altman plot (left) and four-quadrant plot (right) determined from SvO<sub>2</sub> and ScvO<sub>2</sub> values, all measurement points. The lines for bias, LOA and 95% CIs of LOA are shown. See text for exact numbers. The four-quadrant method plots the change in ScvO<sub>2</sub> against the change in SvO<sub>2</sub> showing the trending ability of ScvO<sub>2</sub> at all measurement points and different zones. See text for exact numbers. CI, confidence interval; LOA, limits of agreement.



Table 2  
The Bias, the LOA, the Percentage Error, and the Regression Coefficient for SvO<sub>2</sub> and ScvO<sub>2</sub> Values at Each Measurement Point

| Measurement Point                  | 1n = 85               | 2n = 85               | 3n = 85                | 4n = 84                | 5n = 84                | 6n = 84               | 7n = 81              |
|------------------------------------|-----------------------|-----------------------|------------------------|------------------------|------------------------|-----------------------|----------------------|
| Bias, % (95% CI)                   | -0.3 (-1.2 to 0.5)    | -1.6 (-2.6 to -0.6)   | -4.1 (-5.3 to -3.0)    | -3.1 (-4.3 to -1.9)    | -2.3 (-3.5 to -1.2)    | -0.6 (-1.6 to 0.5)    | -1.4 (-2.3 to -0.5)  |
| LOA lower, % (95% CI)              | -7.9 (-9.3 to -6.5)   | -10.4 (-12.0 to -8.7) | -14.7 (-16.7 to -12.7) | -13.4 (-15.5 to -11.4) | -12.3 (-14.3 to -10.3) | -9.8 (-11.6 to -8.0)  | -8.9 (-10.4 to -7.4) |
| LOA upper, % (95% CI)              | 7.2 (5.8 to 8.7)      | 7.2 (5.5 to 8.8)      | 6.4 (4.4 to 8.4)       | 7.2 (5.2 to 9.2)       | 7.7 (5.7 to 9.7)       | 8.8 (6.9 to 10.5)     | 6.1 (4.6 to 7.6)     |
| Percentage error, % (95% CI)       | 10.5 (8.7 to 12.2)    | 11.2 (9.4 to 13.1)    | 13.7 (11.4 to 15.9)    | 14.5 (12.0 to 17.0)    | 14.6 (12.1 to 17.1)    | 13.4 (11.1 to 15.7)   | 10.9 (9.0 to 12.8)   |
| Regression coefficient, % (95% CI) | -0.02 (-0.13 to 0.09) | -0.04 (-0.15 to 0.07) | -0.0 (-0.19 to 0.19)   | -0.11 (-0.28 to 0.06)  | -0.04 (-0.24 to 0.15)  | -0.05 (-0.21 to 0.11) | -0.0 (-0.19 to 0.19) |

Measurement point 1 is before the induction of anesthesia, 2 is after the induction, 3 after protamine administration, 4 right after ICU admission, 5 four hours after ICU admission, 6 at midnight, and 7 on the first postoperative morning. A total of 588 samples were included in the analysis. Two out of 590 samples were excluded because they were not taken at the given measurement points.  
Abbreviations: CI, confidence interval; LOA, limits of agreement.

those determined from pulmonary arterial blood samples is 3%. In the light of both these criteria, the mean bias of -1.9% in the present study was acceptable. Furthermore, based on both the small nonsignificant regression coefficient and the visually uniform scatter of the differences between SvO<sub>2</sub> and ScvO<sub>2</sub> in the Bland-Altman plot,<sup>22</sup> significant proportional bias could be excluded. However, as the wide LOA of -11.5%-to-7.6%, confirmed by narrow CIs, clearly exceed the aforementioned criteria, the precision of ScvO<sub>2</sub> measurements was unsatisfactory. Previously, Sander et al performed a Bland-Altman analysis for the pooled perioperative measurements of 300 paired SvO<sub>2</sub> and ScvO<sub>2</sub> samples in 60 patients undergoing elective CABG and reported a mean bias of 0.3%, with LOA of -11.9%-to-12.4%.<sup>17</sup> The lower bias in their findings compared to the authors' data here agreed with a previous finding that the bias between postoperative ScvO<sub>2</sub> and SvO<sub>2</sub> is lower in CABG patients compared to patients undergoing valvular surgery,<sup>16</sup> as only half of the procedures in the present study were mere CABGs. In accordance with the authors' results, the LOA were unacceptably wide.<sup>17</sup> In the study by Lequeux et al, in 15 patients undergoing elective cardiac surgery with cardiopulmonary bypass,<sup>18</sup> SvO<sub>2</sub>, and ScvO<sub>2</sub> continuously were measured using fiberoptic catheters from the induction of anesthesia up to 24 hours postoperatively, totaling 9,267 measurement pairs. The authors found a high mean bias of 4.4% and wide LOA of -13.6%-to-22.5%. Furthermore, the mean bias between SvO<sub>2</sub> and ScvO<sub>2</sub> calculated separately for each patient demonstrated a large interindividual variability. However, their findings have been challenged by previous work suggesting that, during and after cardiac surgery, fiberoptic venous saturations are not interchangeable with values determined from venous blood samples.<sup>24,25</sup>

In addition to the LOA, the PE is a measure of precision and is considered a more appropriate parameter to compare the results from different studies.<sup>22</sup> However, only Sander et al reported the PE, which was 17% compared to 13.2% in this study.<sup>17</sup> It previously has been suggested that a PE <30% is acceptable when comparing two cardiac output monitors to each other.<sup>26</sup> Although this percentage has been used as a reference in some studies assessing fiberoptic ScvO<sub>2</sub> measurements,<sup>27,28</sup> there is no consensus in the literature as to whether the 30% limit is applicable to the comparisons of different methods for measuring venous saturations.

When assessing interchangeability, apart from accuracy and precision, it is important to evaluate the ability of ScvO<sub>2</sub> to reliably track changes in SvO<sub>2</sub>.<sup>29</sup> Some authors even have suggested that the bias is not at all important: irrespective of the bias, ScvO<sub>2</sub> could be used instead of SvO<sub>2</sub> if the trends of the two parameters are similar.<sup>30,31</sup> However, studies comparing ScvO<sub>2</sub> to SvO<sub>2</sub> in patients undergoing cardiac surgery have either ignored this idea<sup>14,16,23</sup> or, at best, evaluated the bias separately for each time period.<sup>15,17,18</sup> Considering other patient groups, the authors here are not aware of a previous study on venous saturations utilizing modern recommended statistical methods, such as the 4Q plot or polar plot, to analyze trending ability. In the present study, the trending ability was assessed using the 4Q method plotting the change in ScvO<sub>2</sub>

against the change in SvO<sub>2</sub>. Additionally, the study authors applied the clinical concordance method with four error grid zones for therapeutic consequences as recommended in the literature.<sup>22</sup> They discovered that only 50.0% of the data points were in zone 1, indicating that only half of the ScvO<sub>2</sub> measurements would have yielded a similar treatment decision as compared to SvO<sub>2</sub>. Furthermore, 36.2% of the data points were in zone 3, implying that compared to SvO<sub>2</sub>, more than one-third of ScvO<sub>2</sub> measurements might have resulted in initiating unnecessary or withholding necessary treatment.<sup>22</sup> This insufficient clinical concordance indicates a deficient trending ability. It previously has been suggested by Dueck et al, using correlation coefficients for changes of ScvO<sub>2</sub> between sequential time points and the corresponding changes in SvO<sub>2</sub>, that the trends of ScvO<sub>2</sub> and SvO<sub>2</sub> in patients undergoing a neurosurgical procedure in the sitting position were comparable.<sup>31</sup> Several authors investigating venous saturations in critically ill patients have used the same statistical approach and drawn a similar conclusion.<sup>29,32,33</sup> In addition to different study designs in divergent clinical settings, the inconsistency among earlier results and the data here plausibly is due to the statistical methods chosen. It has been argued that correlation coefficients are inadequate in providing sufficient statistical accuracy in method comparison studies.<sup>21</sup> In cardiac output monitoring studies, the 4Q plot with error grids is the method currently recommended to examine the trending ability of different cardiac output monitors.<sup>22,29</sup> As ScvO<sub>2</sub> and SvO<sub>2</sub> values are used comparably to assess hemodynamics, the same approach should be applied.

The present study had several weaknesses. The authors calculated their sample size by collecting a set of pilot data, which they utilized to calculate the final sample size. This approach can be considered a *post hoc* analysis. However, the study authors also performed another *post hoc* sample size calculation according to Bland, with an expected 95% CI for LOA of  $\pm 1\%$ , producing a sample size of at least 270 samples.<sup>19</sup> Therefore, the sample size of the present study seemed to be large enough and was justified. The median EuroSCORE II was 1.6%, and 75% of the patients had an ejection fraction of more than 50%, which may limit the generalization of these results to a higher-risk population.

As it would have been unethical to expose these patients to the risks of additional central venous cannulation for study purposes only, the authors collected the blood samples for ScvO<sub>2</sub> analyses from the central venous line of the PAC. Although this approach previously has been used by others,<sup>34,35</sup> it may be criticized because it is reasonable to believe that at least some, if not most, of the blood samples for ScvO<sub>2</sub> measurements actually were drawn from the right atrium.<sup>35</sup> Although complete mixing of venous blood only occurs during right ventricular contraction, the blood collected from the right atrium is a various mixture of venous drainage from the superior and inferior caval veins and the coronary sinus. In experimental conditions in healthy awake individuals breathing room air, the oxygen saturation of inferior vena caval blood is higher than that in the superior vena cava, and, hence, the right atrial oxygen saturation and SvO<sub>2</sub> are slightly

higher than ScvO<sub>2</sub>.<sup>36</sup> However, unstable hemodynamics may modify this dynamic relationship, as the oxygen content of blood in the inferior vena cava will decrease, while that of the superior vena cava is maintained if the cardiac output is redistributed from the kidneys and the splanchnic region toward the brain and the heart. Thus, in critically ill patients, as well as in patients undergoing major surgical procedures, the absolute values of ScvO<sub>2</sub> generally exceed those of SvO<sub>2</sub>.<sup>37</sup> Under all circumstances, the oxygen saturation of right atrial blood is supposed to be closer to SvO<sub>2</sub> than is ScvO<sub>2</sub>. Indeed, it has been suggested previously that compared to ScvO<sub>2</sub>, the right atrial saturation may be a better estimate of SvO<sub>2</sub>.<sup>23,33</sup> Accordingly, using atrial saturations instead of ScvO<sub>2</sub> increases the agreement between ScvO<sub>2</sub> and SvO<sub>2</sub>. In other words, the authors' conclusions would not have changed even if they had inserted a separate catheter in the superior vena cava for blood sampling. Furthermore, in the clinical setting, the tip of the central venous catheter actually may be located in the right atrium as often as in 15% of patients.<sup>38</sup> Some authors have suggested that, in terms of blood sampling for venous saturations, the catheter tip location is not important provided that it remains constant.<sup>32</sup>

In conclusion, the mean bias of the ScvO<sub>2</sub> measurements was low, and the PE was reasonable, while the LOA were wide, indicating acceptable accuracy but insufficient precision. In addition, the trending ability of ScvO<sub>2</sub> measurements was inadequate. The authors' hypothesis about equivalence was not supported by the results. Therefore, they cannot recommend the use of ScvO<sub>2</sub> measurements interchangeably with SvO<sub>2</sub> samples for the hemodynamic assessment of adult cardiac surgery patients.

## Conflict of Interest

None.

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