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Trends but Not Individual Values of Central Venous Oxygen Saturation Agree with Mixed Venous Oxygen Saturation during Varying Hemodynamic Conditions

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Background: **Previous studies found contradictory results regarding the question whether mixed venous oxygen saturation (Svo_2) and central venous oxygen saturation ($Scvo_2$) are equivalent. The inconsistency of study results may result from different study designs and different, partly questionable, statistical approaches.**

Methods: **The authors performed a prospective clinical trial comparing individual oxygen saturation values as well as the trend of values in blood from the superior vena cava ($Scvo_2$), the right atrium ($Srao_2$), and the pulmonary artery (Svo_2) during varying hemodynamic situations. The subjects were 70 patients scheduled to undergo elective neurosurgical operations in the sitting position. Oxygen saturation was measured photospectrometrically in blood samples simultaneously taken at four different time points during supine and sitting positions. Statistical analysis was performed following the recommendations of Bland and Altman.**

Results: **Five hundred two comparative sets of measurements were obtained. Ninety-five percent limits of agreement ranging from ±6.83 to ±9.30% for single values were interpreted as clinically unacceptable. In contrast, correlations between changes of Svo_2 and $Scvo_2$ as well as of Svo_2 and $Srao_2$ were interpreted as clinically acceptable ($R \geq 0.755$, Pearson correlation coefficient; $P \leq 0.0001$).**

Conclusions: **In this sample of patients, exact numerical values of $Scvo_2$ and $Srao_2$ are not equivalent to those of Svo_2 in varying hemodynamic conditions. However, for clinical purposes, the trend of $Scvo_2$ may be substituted for the trend of Svo_2. In addition, previous studies investigating the agreement between Svo_2 and $Scvo_2$ were found to be lacking in their chosen statistical approaches.**

MIXED venous oxygen saturation (Svo_2) monitoring is used as a surrogate for the balance between systemic oxygen delivery and consumption during the treatment of critically ill patients.[1] However, measurement of Svo_2 requires placement of a pulmonary artery (PA) catheter with a risk-*versus*-benefit relation that is still a matter of controversy.[2–4] On the other hand, a central venous (CV) catheter is routinely inserted in critically ill patients for monitoring of CV pressure and administration of catecholamines and parenteral nutrition. Therefore, measurement of CV oxygen saturation ($Scvo_2$) seems to be an attractive alternative to monitoring of Svo_2 because it can be performed more easily, is less risky, and is less costly.

In a recently published guideline, Svo_2 and $Scvo_2$ were declared as equivalent for the management of severe sepsis,[5] although previous studies found contradictory results.[6–25] It should be noted that the statistical approaches used in most of these investigations (*e.g.*, correlation and regression analysis[7,8,12–14,16]) are questionable regarding the statistical evaluation of the agreement of two different methods.[26,27] Furthermore, one has to differentiate between the analysis of single data points and the analysis of the change in oxygen saturation values over time (trend).

The aim of our study was to compare Svo_2 *versus* $Scvo_2$ in various hemodynamic conditions. Because some previous studies only evaluated the agreement between Svo_2 and right atrial oxygen saturation ($Srao_2$),[10,17,18] we also compared Svo_2 *versus* $Srao_2$. The sitting position, which is used to perform neurosurgical operations in the cerebellum and the cerebellopontine angle, is known to induce hemodynamic changes compared with the supine position.[28–30] Therefore, we prospectively studied the oxygen saturation of blood samples simultaneously taken during both the supine and the sitting position from the superior vena cava (SVC), right atrium (RA), and PA.

Materials and Methods

Subjects

After obtaining approval from the Institutional Review Board at the University of Cologne (Cologne, Germany) and informed consent from each participant, we studied 70 patients scheduled to undergo a neurosurgical procedure in the sitting position.

Anesthesia Protocol and Catheter Placement

Anesthesia was induced and maintained with intravenous fentanyl and midazolam. Monitoring included electrocardiography, intravascular blood pressure measurement, pulse oximetry, CV pressure monitoring, urine output monitoring, precordial Doppler ultrasound for detection of venous air embolism, and arterial blood gas analysis.

Multiorificed CV catheters (Vygon GmbH, Aachen, Germany) were inserted *via* the right subclavian vein,

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and PA catheters (OptiQ®; Abbott, Chicago, IL) were inserted *via* the right internal jugular vein using a standard aseptic technique. Intravascular electrocardiography (Alphacard®; Sterimed, Puettlingen, Germany) was used to confirm the placement of the CV catheters in the lower SVC directly above the caval–atrial junction. The PA catheters were positioned following standard procedures. When the wedge position was obtained, the catheters were withdrawn to place the proximal injectate port in the RA, which was confirmed by intravascular electrocardiography.

Blood Gas Analysis and Determination of Hemodynamic Variables

Blood samples were drawn simultaneously from the PA, RA, and SVC at four different time points: (1) in the supine position after induction of anesthesia (T1); (2) twice during the neurosurgical operation in the sitting position (T2 and T3); and (3) in the supine position after the neurosurgical procedure was finished (T4). A standard volume of 1.5 ml blood was obtained from each site (QS 50®; Radiometer, Copenhagen, Denmark) and cooled in ice water after withdrawal of dead space blood and flushing fluid. Three consecutive oxygen saturations per blood sample were determined photospectrometrically immediately after each series of blood samples (OSM 3 Hemoximeter; Radiometer). The average of these three measurements was calculated for each site and each time point and used for further statistical analysis. Immediately after a series of blood samples was drawn, mean arterial blood pressure (MAP), heart rate, and cardiac output (CO) were recorded. CO was determined by bolus thermodilution technique using the PA catheter connected to a CO computer (Q-Vue®; Abbott). To quantify the repeatability of the standard oxygen saturation measurement method, in 17 patients, an additional five replicate blood samples were drawn immediately one after the other from the PA.

Statistical Analysis

Based on unpublished data from our institution in a similar neurosurgical population, a power analysis was performed before the study, and it indicated that a sample size of 70 patients was necessary ($\alpha = 0.05$, power = 0.80) to detect a difference of ±2% between Svo_2 and $Scvo_2$, which was defined as the smallest clinically relevant difference. The anticipated SD was set at ±5%.

Repeatability

Each of the resulting five Svo_2 values per patient were subtracted from each other, resulting in $n = 17 \cdot 10$ individual differences. In accordance with the recommendations of Bland and Altman,[27] a one-way analysis of variance with subject as the factor was calculated for these 170 individual differences. The within-subject SD s_w was estimated as the square root of the residual mean square. Furthermore, a 95% repeatability coefficient was calculated as $1.96\sqrt{2}s_w$ ($= 2.77s_w$), which is compared to the 95% limits of agreement between the different methods (see next section).

Statistical Analysis of Individual Values

The systematic error (bias) and the variability (SD of the bias) for Svo_2 *versus* $Scvo_2$ and Svo_2 *versus* $Srao_2$ were calculated. Bias was expressed as the mean of the differences of the individual values. The Student *t* test was used to determine whether the mean differences were significantly different from zero, and Pearson correlation coefficients between Svo_2 and $Scvo_2$ and between Svo_2 and $Srao_2$ were determined. Furthermore, 95% limits of agreement were calculated as bias ± 1.96 SD. The differences between individual values were plotted against their means for each time point (Bland and Altman plot).[26]

Statistical Analysis of Changes in Oxygen Saturation

For evaluating the agreement between the different sites of oxygen saturation measurement (Svo_2 *vs.* $Scvo_2$ and Svo_2 *vs.* $Srao_2$) regarding the trend of values, a Pearson correlation coefficient was calculated for differences of oxygen saturation between sequential time points (T1–T2, T2–T3, T3–T4).

To quantify changes in hemodynamic variables, corresponding to the oxygen saturation measurements, differences between sequential time points were calculated for MAP, heart rate, and CO. Values are presented as mean ± SD unless otherwise stated. For all statistical procedures, a *P* value less than 0.05 was considered significant. The Statistical Package for the Social Sciences (SPSS, release 11.0; SPSS Inc., Chicago, IL) was used for all calculations.

Results

Thirty-two male and 38 female patients with an average height of 170.0 ± 7.9 cm (range, 147–190 cm), weight of 76.1 ± 9.0 kg (40–120 kg), and age of 53.1 ± 8.8 yr (17–78 yr) were enrolled in the study. Five patients had an American Society of Anesthesiologists (ASA) physical status of I, 38 had an ASA physical status of II, 24 had an ASA physical status of III, and 3 had an ASA physical status of IV. Mean changes of hemodynamic variables between time points were as follows: MAP, 14.1 ± 9.6% (range, 2.4–42%); heart rate, 16.1 ± 16.0% (0–69.2%); and CO, 16.4 ± 14.3% (0–70%).

Evaluation of the agreement between different sites of oxygen saturation measurement requires knowledge about the repeatability of the oxygen saturation–measurement method itself.[26] Oxygen saturation values from $17 \cdot 5$ replicate blood samples revealed a within-subject

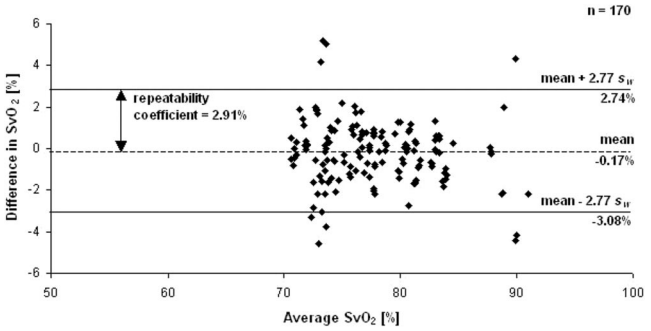

Fig. 1. Bland and Altman plot of the differences between replicate mixed venous oxygen saturation (Svo_2) measurements against their mean values. Five replicate blood samples were drawn in 17 patients. Each of the resulting five Svo_2 values per patient were subtracted from each other, resulting in n = 17 · 10 individual differences. The *broken line* indicates the mean difference, and *unbroken lines* indicate repeatability coefficient (mean ± within-subject SD s_w).

SD s_w of 1.05% and a repeatability coefficient of 2.91% (fig. 1).

Regarding the comparison of different sampling sites, ideally 2 · 280 comparative pairs of measurements from 70 patients at four different time points could be made in our study. However, because of technical (incorrect position of catheter) or organizational reasons (duration of operation), 256 (Svo_2 *vs.* $Scvo_2$) and 246 (Svo_2 *vs.* $Srao_2$) comparative sets of measurements, respectively, were obtained (table 1). The mean Svo_2 was larger than the mean $Scvo_2$ and the mean $Srao_2$ at all time points (T1–T4). Changing from the supine position to the sitting position (from T1 to T2) resulted in an increase in mean differences (bias) in oxygen saturation (Svo_2 *vs.* $Scvo_2$ and Svo_2 *vs.* $Srao_2$), whereas changing from the sitting position to the supine position (from T3 to T4) led to a decrease in bias (Svo_2 *vs.* $Scvo_2$ and Svo_2 *vs.* $Srao_2$) (table 1). Only once did the bias in oxygen saturations exceed 2% (Svo_2 *vs.* $Scvo_2$; bias at T3 = 2.79%), which was defined as a clinically relevant threshold (table 1). Correlation coefficients ranged from 0.688 (Svo_2 *vs.* $Scvo_2$; T4) to 0.851 (Svo_2 *vs.* $Srao_2$; T2) (table 1).

More important are the distributions of differences of individual values from various sites of measurement. Figure 2 depicts the Bland and Altman plot for Svo_2 *versus* $Scvo_2$. Ninety-five percent limits of agreement for Svo_2 *versus* $Srao_2$ are calculated as ±7.12% (T1), ±6.83% (T2), ±7.32% (T3), and ±6.58% (T4). Differences in oxygen saturations of 10% or greater were observed in individual patients at all time points T1–T4 for comparisons Svo_2 *versus* $Srao_2$ and Svo_2 *versus* $Scvo_2$.

Changes in oxygen saturation over time are presented in figure 3. Even when individual values were different, changes in $Scvo_2$ and $Srao_2$ paralleled changes in Svo_2 quantitatively, demonstrated by correlation coefficients of $R = 0.75$ (Svo_2 *vs.* $Scvo_2$) and $R = 0.82$ (Svo_2 *vs.* $Srao_2$), respectively (table 2). Considering more distinct changes in Svo_2 (> 5% and > 10%), correlation coefficients increased (table 2). All values of R are highly significant ($P < 0.0001$).

Discussion

In the current study, the 95% limits of agreement between the standard Svo_2 method and both the $Scvo_2$ method and the $Srao_2$ method were large. In fact, some individual measurements of oxygen saturation of CV blood and RA blood differed more than 10% from corresponding mixed venous blood values. Therefore, an enormous variability was found between absolute values of Svo_2 and $Scvo_2$ and of Svo_2 and $Srao_2$, respectively, suggesting that individual values of $Scvo_2$ and $Srao_2$ cannot substitute true Svo_2 values. However, the trend in $Scvo_2$ values as well as the trend in $Srao_2$ values demonstrated a good correlation with the trend in Svo_2 values.

The relation between $Scvo_2$ and Svo_2 has been examined in numerous studies with controversial conclusions.[6–25] The wide range of conclusions might be the result of different study designs and of different statistical approaches (table 3). Some studies used animal models,[12,14,17] whereas other studies examined healthy volunteers[21] or patients with myocardial infarction.[24] The

Table 1. Mean Differences (Bias) and Correlation Coefficients in Oxygen Saturations of Blood Samples Taken from Various Sites

	Difference in Oxygen Saturation at Various Time Points, %			
	T1 (Supine Position)	T2 (Sitting Position)	T3 (Sitting Position)	T4 (Supine Position)
$Svo_2 - Scvo_2$	0.53 ± 4.45 (−10.3 to 14.8)	1.26 ± 4.65 (−9.1 to 12.6)	2.79 ± 3.98 (−6.1 to 10.4)	1.69 ± 4.16 (−6.0 to 11.6)
n	64	67	66	59
P	0.342	0.03	< 0.0001	0.003
r	0.762	0.797	0.758	0.688
$Svo_2 - Srao_2$	0.38 ± 3.56 (−5.5 to 10.4)	0.66 ± 3.42 (−7.7 to 10.0)	1.44 ± 3.66 (−5.9 to 10.5)	1.08 ± 3.29 (−5.2 to 10.6)
n	61	65	63	57
P	0.4	0.124	0.003	0.016
r	0.846	0.851	0.767	0.772

Values are presented as mean ± SD (range).

n = number of comparative pairs of blood samples; *P* = *P* value (Student *t* test); *r* = Pearson correlation coefficient; $Scvo_2$ = central venous oxygen saturation (%); $Srao_2$ = right atrium oxygen saturation (%); Svo_2 = mixed venous oxygen saturation (%).

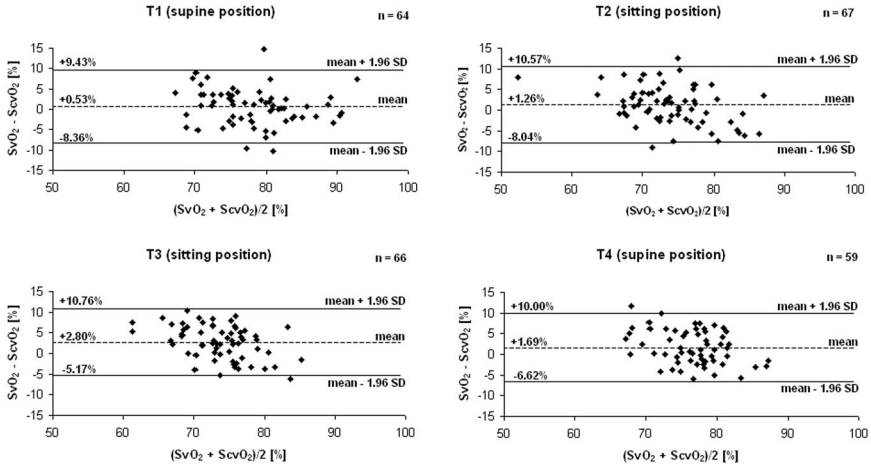

Fig. 2. Bland and Altman plots of the differences between mixed venous oxygen saturation (Svo_2) and central venous oxygen saturation ($Scvo_2$) at different time points. (*T1*) Supine position after induction of anesthesia and insertion of catheters. (*T2* and *T3*) During the neurosurgical procedure in the sitting position, with an interval of at least 1 h between. (*T4*) Supine position after the neurosurgical procedure was completed. The *broken line* indicates the mean difference (bias), and *unbroken lines* indicate 95% limits of agreement (mean ± SD). Note the large 95% limits of agreement.

number of subjects ranged from 7[9] to 61,[7] and the number of comparative pairs of measurements ranged from 27[6] to 580.[9] In most studies, an unequal number of blood samples per subject was drawn,[8–14,16,21,25] potentially resulting in an imbalanced statistical weight of subjects with exceedingly good or bad correspondences of $Scvo_2$ and Svo_2. In addition, in some studies, blood samples were not drawn simultaneously, but sequentially during the advancement of the PA catheter,[6–8,16,21] possibly causing arrhythmia[31] and thus significantly altering hemodynamic variables, which may result in different oxygen saturations at different sites of measurement.

Neither a power analysis nor an analysis of method repeatability was presented in previous investigations. A power analysis has to be calculated on the basis of a difference between Svo_2 and $Scvo_2$ that is defined as clinically relevant before the study. Furthermore, this Δ (Svo_2 − $Scvo_2$) value serves as an *a priori* standard, which is necessary to discuss the variability found in the actual study data. Evaluation of the repeatability of single measurements is a very important issue because the repeatability of methods limits the amount of agreement that is possible.[27] Therefore, repeatability represents a baseline (within-method variability) to which the between-method variability can be compared.

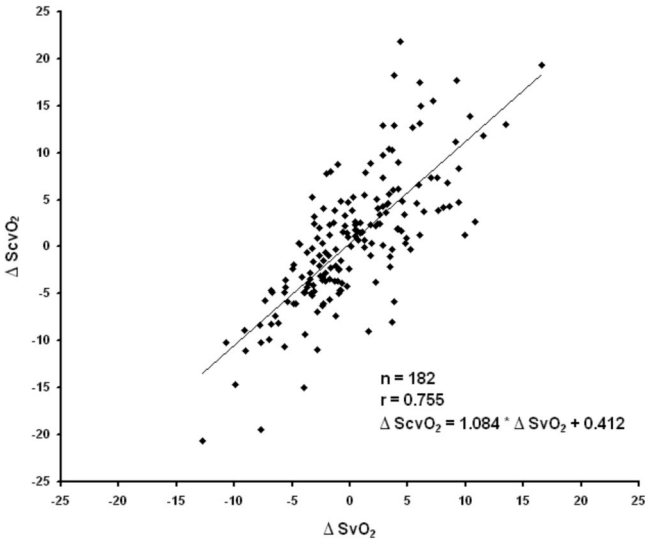

Fig. 3. Changes in mixed venous (ΔSvo_2) and central venous oxygen saturation ($\Delta Scvo_2$) between two measurements. n = 182; r = 0.755; equation of the regression line: $\Delta Scvo_2 = 1.084 \times \Delta Svo_2 + 0.412$.

Most studies present the bias[6–8,10,11,13,15–20] as well as correlation coefficients between the measurements.[7–20,25] However, calculating bias and correlation coefficients for individual values is not enough for evaluating the agreement of two different methods.[26,27] Despite large differences between individual values, the bias (*i.e.*, mean of the differences between individual values) might be zero, and the correlation coefficient measures proportionality, not agreement. In 1986, Bland and Altman[26] recommended the calculation of 95% limits of agreement of individual values for method comparison studies. However, only 5 of 10 investigations studying the equivalence of Svo_2 and $Scvo_2$ have presented these limits of agreement since then.[9–11,14,18] Furthermore, only 8 of 17 studies analyzed the agreement of the trend of oxygen saturations measured at different sites in addition to the agreement of absolute values.[8–13,15,17]

Table 2. Correlation of Changes in Oxygen Saturation of Blood Samples Taken from Different Sites

	Changes in Oxygen Saturation between Different Time Points		
Site	n	*R*	*P*
PA *vs.* SVC			
|Diff| > 0%	182	0.755	< 0.0001
|Diff| > 5%	71	0.849	< 0.0001
|Diff| > 10%	23	0.930	< 0.0001
PA *vs.* RA			
|Diff| > 0%	176	0.821	< 0.0001
|Diff| > 5%	70	0.916	< 0.0001
|Diff| > 10%	24	0.928	< 0.0001

\|Diff\| = absolute value of the change in oxygen saturation between sequential time points; n = number of analyzed differences in oxygen saturation between different time points; *P* = *P* value; PA = pulmonary artery; *R* = Pearson correlation coefficient; RA = right atrium; SVC = superior vena cava.

Table 3. Studies Comparing Mixed Venous Oxygen Saturation and Central Venous Oxygen Saturation

Author	Subjects	No. of Pairs of Comparative Measurements ($Scvo_2 - Svo_2$)	Equal No. of Samples per Subject	Power Analysis	Blood Samples Drawn Simultaneously	Repeatability of Measurements
Animal studies						
Davies *et al.,*[17] 1988	10 pigs, circulatory shock or lung damage	464, only $Sra o_2$ *vs.* Svo_2	No	No	Yes, fiberoptic sensors	No
Reinhart *et al.,*[12] 1989	38 dogs, hypoxia, hemorrhage, or resuscitation	179	No	No	Yes	No
Schou *et al.,*[14] 1998	20 pigs, hemodilution	92	No	No	Yes	No
Clinical studies						
Barratt-Boyes and Wood,[21] 1957	26 healthy subjects	49?*	No	No	No, consecutive samples	No
Scheinman *et al.,*[13] 1969	24 critically ill patients	52	No	No	Yes	No
Lee *et al.,*[8] 1972	44 critically ill patients	54	No	No	No, consecutive samples	No
Tahvanainen *et al.,*[15] 1982	42 critically ill patients	44	No	No	Yes	No
Wendt *et al.,*[25] 1990	19 critically ill patients	44	No	No	Yes	No
Berridge,[20] 1992	51 patients, ICU and cardiovascular surgery	76	No	No	No comment	No
Martin *et al.,*[9] 1992	7 critically ill patients	580	No	No	Yes, fiberoptic sensors	No
Herrera *et al.,*[19] 1993	23 patients, single-lung ventilation	283, seven measurement time points	Yes	No	Yes, blood samples and fiberoptic sensors	No
Pieri *et al.,*[10] 1995	39 critically ill patients after major surgery	296, only $Sra o_2$ *vs.* Svo_2	No	No	Yes	No
Edwards and Mavall,[6] 1998	30 critically ill patients	27	Yes	No	No, consecutive samples	No
Turnaoglu *et al.,*[16] 2001	41 critically ill patients, 32 patients for cardiovascular surgery	73	Yes	No	No, consecutive samples	No
Ladakis *et al.,*[7] 2001	61 critically ill patients	61	Yes	No	No, consecutive fiberoptic measurements	No
Reinhart *et al.,*[11] 2004	29 critically ill patients	150†	No	No	No comment	No‡
Chawla *et al.,*[18] 2004	32 postoperative patients, 21 critically ill patients	53, only $Sra o_2$ *vs.* Svo_2	Yes	No	Rapid succession	No
Current study	70 neurosurgical patients	256, four measurement time points	Yes	Yes	Yes	Yes

(*Table continues*)

Table 3. Continued

Author	Mean of Individual Differences ($Scvo_2 - Svo_2$) (Bias)	Correlation Coefficient of $Scvo_2$ and Svo_2	95% Limits of Agreement	Change of Oxygen Saturation over Time (Trend)	Authors' Conclusion
Animal studies					
Davies *et al.,*[17] 1988	Yes	Yes	No	Yes	Animal model, fiberoptic measurement: $Sra o_2 = Svo_2$
Reinhart *et al.,*[12] 1989	No	Yes	No	Yes	Animal model: Individual $Scvo_2$ values are not sufficiently identical to Svo_2 Trend: Close tracking of $Scvo_2$ and Svo_2
Schou *et al.,*[14] 1998	No	Yes	Yes	No	Animal model: During hemodilution, monitoring of $Scvo_2$ is as useful as monitoring of Svo_2
Clinical studies					
Barratt-Boyes and Wood,[21] 1957	No	No	(Yes)§	No	Only mean values are presented; $Scvo_2 - Svo_2$ is not calculated for individual pairs of measurements
Scheinman *et al.,*[13] 1969	Yes	Yes	No	Yes	Patients in heart failure or shock: Individual values: $Scvo_2 =/ Svo_2$ Trend: $Scvo_2 = Svo_2$
Lee *et al.,*[8] 1972	Yes	Yes	No	Yes	Patients in shock: Individual values: $Scvo_2 < Svo_2$ Trend: Svo_2 must be interpreted cautiously
Tahvanainen *et al.,*[15]1982	Yes	Yes	No	Yes	Individual values: $Scvo_2 = Svo_2$ for clinical use but not for exact values Trend: $Scvo_2 = Svo_2$
Wendt *et al.,*[25] 1990	No	Yes	No	No	Individual values: $Scvo_2$ yields adequate information on Svo_2
Berridge[20] 1992	Yes	Yes	No	No	Individual values: $Scvo_2$ is a useful estimate of Svo_2
Martin *et al.,*[9] 1992	No	Yes	Yes‖	Yes	Monitoring of $Scvo_2$ and Svo_2 is not interchangeable
Herrera *et al.,*[19] 1993	Yes	Yes	No#	No	Thoracic anesthesia: Svo_2 may be substituted by $Scvo_2$
Pieri *et al.,*[10] 1995	Yes	Yes	Yes	Yes	Individual values: $Scvo_2 =/ Svo_2$ Trend: $Scvo_2 =/ Svo_2$
Edwards and Mavall,[6] 1998	Yes	No	No**	No	Patients in shock: $Scvo_2 =/ Svo_2$
Turnaoglu *et al.,*[16] 2001	Yes	Yes	No	No	Svo_2 should not be replaced by $Scvo_2$

(*Table continues*)

Table 3. Continued

Author	Mean of Individual Differences ($Scvo_2 - Svo_2$) (Bias)	Correlation Coefficient of $Scvo_2$ and Svo_2	95% Limits of Agreement	Change of Oxygen Saturation over Time (Trend)	Authors' Conclusion
Ladakis *et al.,*[7] 2001	Yes	Yes	No	No	Individual Svo_2 and $Scvo_2$ values are interchangeable
Reinhart *et al.,*[11] 2004	Yes	Yes	Yes	Yes	Individual values: Svo_2 =/ $Scvo_2$ Trend: $Scvo_2$ has potential to guide therapy
Chawla *et al.,*[18] 2004	Yes	Yes	Yes	No	Individual values: Svo_2 =/ $Scvo_2$ The difference between Svo_2 and $Scvo_2$ may be a marker of myocardial O_2 consumption
Current study	Yes	Yes	Yes	Yes	Neurosurgical patients: Individual values: $Scvo_2$ =/ Svo_2 Trend: $Scvo_2$ = Svo_2 for clinical decisions

* The authors calculate mean central venous oxygen saturation ($Scvo_2$) and mixed venous oxygen saturation (Svo_2) values from 49 (superior vena cava) and 59 samples (pulmonary artery), respectively. However, no differences of comparative measurements are presented. † The authors also report on agreement between (1) *in vivo* (fiberoptic sensors) and *in vitro* $Scvo_2$ measurements (150 pairs of comparative measurements) and on agreement between (2) continuous *in vivo* measurements (fiberoptic sensors) of Svo_2 and $Scvo_2$ (395,128 pairs of comparative measurements). ‡ The authors evaluated the effect of different variables (hemoglobin, pH, hematocrit, temperature) on the accuracy of the continuous *in vivo* measurement (fiberoptic sensors) of $Scvo_2$. § In this study from 1957, the authors discuss their data using the mean as well as twice the SD of the differences of comparative measurements. These variables are introduced by Bland and Altman to define their concept of the 95% limits of agreement almost 20 years later. ‖ The 95% limits of agreement are discussed in the Discussion section but not depicted in the Bland and Altman plots. # The authors present SD of the mean difference between individual values (bias). ** The authors present confidence limits instead of 95% limits of agreement.

The wide range of 95% limits of agreement regarding individual values of Svo_2 and $Scvo_2$ found in our study indicates a large between-method variability. Because the 95% repeatability coefficient was 2.91% in our study, this considerable lack of agreement between the methods is not solely explained by a lack of repeatability. Our finding parallels the results of previous studies, demonstrating an enormous variability of absolute values.[6,8–13,16,18] In contrast, some studies found that individual $Scvo_2$ values can adequately replace Svo_2 values,[7,15,17,20,24,25] but these studies do not present a statistical analysis that includes more than the evaluation of bias and correlation coefficients. In addition, none of these studies performed a power analysis before the investigation. Therefore, it remains unclear whether a number of 44[15,25] or 76[20] comparative measurements is enough to detect statistically significant differences. Schou *et al.* [14] concluded from their data that Svo_2 and $Scvo_2$ are interchangeable, although the 95% limits of agreement plotted in their figures equaled or exceeded ±10%. Because of these controversial results regarding absolute values, there has been a considerable debate on the question of the clinical utility of $Scvo_2$.[1,32]

Clinical decisions are rarely based on single measurements but always reflect various variables as well as the trend of these variables. In the early stage of a disease, $Scvo_2$ values are often found to be less than 50%, with Svo_2 values even lower.[1] Consequently, these low $Scvo_2$ values, although they do not exactly equal Svo_2 values, may serve as a representative variable guiding therapeutical interventions. Furthermore, not the individual value but the trend of $Scvo_2$ may detect an imbalance of oxygen delivery and oxygen consumption. Our study reveals a good correlation between the trends of Svo_2 and $Scvo_2$, which is in accordance with previous studies.[11–13,15] Scheinman *et al.* [13] found a poor correlation between absolute values in patients with severe heart failure or shock but a better correlation between changes of Svo_2 and $Scvo_2$. In an animal model, Reinhart *et al.*[12] demonstrated a close tracking of the oxygen saturations continuously measured in the PA and the SVC across a wide range of hemodynamic conditions. In a recent study, the same group could confirm these findings in critically ill patients.[11] Tahvanainen *et al.* [15] found a significant correlation between PA blood samples and both SVC and RA blood samples during subsequent changes of oxygen saturation in critically ill patients. These data suggest that $Scvo_2$ is equivalent to Svo_2 in the course of clinical decisions as long as absolute values are not required. This is supported by our data, because the degree of correlation between the trend of $Scvo_2$ and Svo_2 is better with larger changes in oxygen saturation. In a recent study, Rivers *et al.*[33] significantly reduced mortality and organ dysfunction in patients with severe sepsis or septic shock using an early goal-directed

therapy approach. The early goal-directed algorithm of the treatment of the first 6 h included the continuous measurement of $Scvo_2$ defining an $Scvo_2$ value greater than 70% as an endpoint of therapy.[33] Although some variables of the algorithm, including $Scvo_2$, have been criticized,[34] monitoring $Scvo_2$ has recently been declared as appropriate for the management of severe sepsis.[5]

In addition, in our study, a comparison between Svo_2 and $Srao_2$ could be performed using the proximal port of the PA catheter for withdrawal of blood samples from the RA. However, 95% limits of agreement were too large to accept individual $Srao_2$ values as equivalent to Svo_2. The trend of $Srao_2$ correlated better with Svo_2 than those of $Scvo_2$. However, because of potential dangerous complications (*e.g.*, arrhythmia, perforation), placing the catheter tip in the RA is not recommended[35] or at least debatable.[36]

Limitations of the Study

Monitoring Svo_2 is used as a clinical marker of systemic oxygen utilization in critically ill patients.[1] During sepsis, a redistribution of blood flow associated with a proportionally greater reduction in splenic, renal, and mesenteric blood flow may occur,[1,32] and in heart failure or circulatory shock, blood flow is relatively increased in cerebral and coronary circulation,[8,13] thus altering the relation between Svo_2 and $Scvo_2$, with Svo_2 generally lower than $Scvo_2$. However, our study was performed in patients scheduled to undergo elective neurosurgical operations in the sitting position during general anesthesia, resulting in a mean Svo_2 higher than $Scvo_2$. This study design was chosen because, in our neuroanesthesia department, these patients are routinely monitored with both a PA catheter and a CV catheter (for aspiration of entrained air), whereas critically ill patients are rarely provided with both catheters. Second, this setting, in contrast to the clinical situation of critically ill patients, allows withdrawal of blood samples at different time points that are clearly defined. Third, positioning the patient from the supine position to the sitting position and *vice versa* was reported to induce a clear change of hemodynamic variables[28,29] due to a change in blood volume distribution from the intrathoracic to the extrathoracic compartment,[30] which is demonstrated for the current study. A mean change of 14% in MAP, with ΔMAP greater than 40% in some patients, and a mean difference in CO of 16%, with a maximum ΔCO of 70%, were detected. This might partly mimic the situation of patients in hypovolemic shock and resulted in an increase in bias between Svo_2 and $Scvo_2$ after changing the position from supine to sitting and *vice versa* in a decrease in bias after changing the position from sitting to supine. Anesthesia was induced and maintained with intravenous fentanyl and midazolam in all patients. Because both drugs are often used as a sedative or an analgesic on the intensive care unit,[37,38] the anesthesia regimen used in our study is not significantly different from sedation regimens used in critically ill patients. Furthermore, fentanyl and midazolam are reported to produce only modest hemodynamic effects.[39,40] Therefore, it is unlikely that our findings are significantly affected by the specific anesthesia regimen.

In summary, our study demonstrates that despite some large differences between absolute values, in patients with varying hemodynamic situations, the trend in $Scvo_2$ may be used as a surrogate variable for the trend in Svo_2.

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