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Continuous central venous and pulmonary artery oxygen saturation monitoring in the critically ill

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Abstract *Objective:* To compare the course of continuously measured mixed and central venous O_2 saturations in high-risk patients and to evaluate the impact of various factors that might interfere with reflection spectrophotometry. *Design and setting:* Prospective, descriptive study in the interdisciplinary ICU of a university hospital. *Patients:* 32 critically ill patients with triple-lumen central vein catheters, including 29 patients requiring pulmonary artery catheterization. *Interventions:* The accuracy of fiberoptic measurements was assessed by comparison to reference co-oximeter results at regular intervals. We examined the effect on measurement accuracy of physiological variables including hematocrit, hemoglobin, pH, temperature, and the administration of various solutions via central venous catheter. Continuous parallel measurements of SvO_2 and $ScvO_2$ were performed in patients with each type of catheters over a total observation time of 1097 h. *Results:* $ScvO_2$ values were more accurate and stable than in vitro oximeter measurements (r=0.96 from 150 samples, mean difference 0.15%, average drift 0.10%/day) and was not significantly affected by synchronous infusion therapy or by changes in hematocrit, hemoglobin, pH, or temperature. $ScvO_2$ values closely paralleled SvO_2, whether measured in vitro (r=0.88 from 150 samples) or in vivo (r=0.81 from 395,128 samples) but averaged about 7±4 saturation percentage higher. $ScvO_2$ changed in parallel in 90% of the 1,498 instances in which SvO_2 changed more than 5% (over an average of 43 min). *Conclusions:* Continuous fiberoptic measurement of central vein O_2 saturation has potential to be a reliable and convenient tool which could rapidly warn of acute change in the oxygen supply/demand ratio of critically ill patients.

Keywords Central venous oxygen saturation · Mixed venous oxygen saturation · Fiberoptic · Oximetry

Introduction

Measurement of mixed venous oxygen saturation (SvO_2) from the pulmonary artery has been advocated for some time as an indirect index of tissue oxygenation. In myocardial infarction decreased SvO_2 has been found to be indicative of current or imminent cardiac failure [1]. Decreased SvO_2 values predict poor prognosis after cardiovascular surgery [2], in severe cardiopulmonary disease, and in septic or cardiogenic shock [3, 4, 5, 6]. This led to development of the fiberoptic pulmonary artery (PA) catheter for continuous measurement of SvO_2 by reflection spectrophotometry [7, 8].

However, PA catheterization is costly and has inherent risks, and its usefulness in a wide variety of clinical conditions remains under debate for lack of convincing data [9, 10, 11, 12, 13]. In comparison, central venous catheterization using the superior vena cava is part of

standard care for critically ill patients and is easier and safer to perform. Not surprisingly, the monitoring of central venous oxygen saturation ($ScvO_2$) has been advocated as a simple method of assessing changes in the global oxygen supply-to-demand ratio in various clinical settings [1, 14, 15]. Others, however, have questioned the ability of $ScvO_2$ measurements to track SvO_2. For example, in shock the oxygen extraction increases in nonvital organs such as the hepatosplanchnic region, causing a reduced oxygen saturation in the inferior vena cava and thus increasing the difference between SvO_2 and $ScvO_2$ [16, 17, 18].

A recent prospective randomized study comparing two algorithms for early goal-directed therapy in patients with severe sepsis and septic shock showed that maintenance of continuously measured $ScvO_2$ above 70% (in addition to maintaining central venous pressure above 8–12 mmHg, mean arterial pressure above 65 mmHg, and urine output above 0.5 ml/kg per hour) resulted in a 15% absolute reduction in mortality compared to the same treatment without $ScvO_2$ monitoring [19]. These findings have rekindled the interest in central venous oxygen saturation measurements in critically ill patients [20]. We have previously demonstrated in anesthetized dogs that changes in continuously measured $ScvO_2$ closely track SvO_2 across a wide range of changing oxygen supply-to-demand ratios [21]. To date we have found only one study comparing continuous measurement of these two variables in the critically ill [22].

Thus the purpose of this study was to explore the course of continuous and parallel measurements of SvO_2 and $ScvO_2$ in critically ill patients on an interdisciplinary ICU. Of particular interest was the extent and timing of clinically relevant changes in O_2 saturation, and whether substantial changes in O_2 saturation as measured at one site would be quickly reflected in values at the other site. Also, the reflection spectrophotometry method used in the fiberoptic catheter can be affected by factors such as hematocrit, dysfunctional hemoglobin (e.g., carboxyhemoglobin, COHb; methemoglobin, MetHb), the transparency of blood plasma, blood flow velocity, and the infusion of fluid or parenteral feedings through the same catheter [23, 24]. Another objective of this study was therefore to determine whether such factors affect the accuracy of continuous O_2 saturation measurements.

Materials and methods

The study included 32 patients on an interdisciplinary postoperative ICU with central venous catheters (24 men, 8 women; age range 17–82 years; Table 1). Of these, 29 had calibrated, four-lumen pulmonary artery catheters (Edwards Oximetry TD) to treat hemodynamic instability. Continuous parallel measurement of SvO_2 and $ScvO_2$ was carried out in 26 patients, and measurement accuracy during infusion was studied in 18. Mean Acute Physiology and Chronic Health Evaluation score was 19.16. Fourteen of the patients (44%) died. The local ethics committee approved the study.

Patients were divided into three groups: high-risk surgical patients without sepsis (postop, n=18), patients with severe sepsis and septic shock (sepsis, n=11), and patients with head trauma and clinical signs of increased intracranial pressure (ICP, n=3). The mean observation time per patient with the central venous oximetry catheter was 56 h (3–254), resulting in 1,787 h of total observation time.

The central venous catheter was a standard triple lumen polyvinylchloride tube, 42 cm total and 22 cm insertable length. The distal lumen outlet (16 gauge diameter) was at the catheter tip, the middle and proximal lumen (18 gauge diameter each) ended 2 cm and 5 cm, respectively, from the tip. The catheter was inserted into an internal or external jugular vein in 24 cases and a subclavian vein in 8. Position in the superior vena cava was confirmed by intravascular electrocardiography (System Alphacard, Sterimed) and radiography.

A custom fiberoptic probe consisting of two sheathed monofile plastic optical fibers was inserted under sterile conditions via a special Y-adapter into the distal lumen so that the tip of the fiberoptic catheter ended directly at the tip of the central venous catheter. After connection to an SAT2-Oximeter (Baxter Healthcare, Irvine Calif., USA) the system was calibrated in vivo. The optical fibers and the measurement technology of these fiberoptic probes are essentially identical to the fiberoptic PA catheters commercially available from Baxter. The oximeters employ reflection spectrophotometry using light-emitting diodes that produce two different wavelengths in the red and infrared spectrum. The light is transmitted to the blood through a single optical fiber and reflected back through a separate optical fiber to a photodetector in an optical module. The relative intensities for each wavelength are measured, and O_2 saturation is calculated.

The PA catheter was inserted according to standard procedures. No complications other than transient arrhythmias were observed during the insertion of any catheter. At 2-s intervals the results of in vivo SvO_2 and $ScvO_2$ measurements were transmitted to a portable personal computer via a serial data interface and stored on hard disk. A complete hemodynamic profile was obtained twice daily, including samples from the radial artery and the mixed and central venous sites, measuring blood gases (ABL 300, Radiometer Copenhagen, Denmark) and Hb fractions (Hb, HbO_2, MetHb, COHb; IL-282 Co-oximeter, Instrumentation Laboratories, USA). O_2 saturations were calculated as both the functional (HbO_2/Hb) and fractional (HbO_2/total Hb, which includes the dysfunctional hemoglobins) types. The in vitro O_2 saturation measurements were compared with values obtained by continuous recording. If the difference between the two exceeded 3%, the in vivo oximeter was recalibrated.

To determine the effects of infusion the following standard solutions were administered by an infusion pump through the middle lumen of the catheter (ending approx. 2 cm proximal to the tip of both central venous catheter and fiberoptic probe): Ringer's lactate (Stereofundin, Braun Melsungen, Germany); 10% amino acid solution (Aminoplasmal, Braun); 50% glucose solution (Braun); 20% fat emulsion (Lipofundin, Braun); 20% albumin solution (Behring Werke Marburg, Germany) and 6% hydroxyethyl starch (Fresenius, Bad Homburg, Germany). Each solution was administered to six patients at 30, 60, and 90 ml/h for 5 min, each preceded by 5 min of no infusion, resulting in a total observation period of 35 min for each solution.

Data were analyzed by Wilcoxon nonparametric tests, linear regression, bivariate correlations, and Mann-Whitney U test (SPSS for Windows 7.0). Due to the limited value of correlation coefficients for the comparison of measuring methods we also calculated bias and precision as described by Bland and Altman [25].

Table 1 Patient characteristics (*APACHE II* Acute Physiology and Chronic Health Evaluation, *postop* high-risk surgical patients without sepsis, *sepsis* patients with severe sepsis and septic shock, *ICP* patients with head trauma and clinical signs of increased intracranial pressure)

Case no.	Sex	Age (years)	Height (cm)	Weight (kg)	APACHE II	Dobutamine (μg/kg per min)	Noradrenaline (μg/kg per min)	Survival	Group
1	M	44	175	70	6	7.1	–	Yes	Postop
2	M	33	180	80	12	6.2	0.03	Yes	Sepsis
3	M	64	175	85	14	14.6	–	Yes	Postop
4	M	74	170	64	26	7.8	0.19	No	Postop
5	M	68	175	70	18	–	–	Yes	ICP
6	F	82	170	60	20	–	–	Yes	Postop
7	M	48	185	75	12	–	–	Yes	Postop
8	F	29	175	70	4	7.11	–	Yes	Postop
9	M	37	180	85	20	4.4	–	Yes	Postop
10	F	36	175	70	20	–	–	No	ICP
11	M	41	180	85	22	11.7	0.29	No	Sepsis
12	M	46	180	63	9	–	–	No	Postop
13	M	70	177	83	27	10.0	–	No	Sepsis
14	F	73	170	60	26	13.8	0.07	Yes	Postop
15	M	61	177	80	27	6.2	0.46	No	Sepsis
16	W	69	165	60	12	5.5	–	Yes	Postop
17	W	74	170	65	13	7.7	–	Yes	Postop
18	M	51	187	90	21	1.8	–	No	Postop
19	M	24	180	80	24	–	0.36	No	Sepsis
20	M	19	183	70	5	–	–	Yes	Postop
21	M	68	185	90	20	13.8	0.07	Yes	Sepsis
22	M	25	180	80	13	8.3	–	Yes	Sepsis
23	F	17	175	60	13	5.5	–	Yes	Postop
24	M	50	185	90	23	11.1	0.23	No	Sepsis
25	M	68	180	80	28	6.2	–	No	Sepsis
26	M	69	180	72	30	13.8	0.06	No	Postop
27	M	51	185	95	36	14.0	0.70	No	Sepsis
28	W	74	170	70	28	–	0.12	Yes	Postop
29	M	55	180	65	31	15.3	0.26	Yes	Postop
30	M	26	180	99	18	14.9	0.29	No	ICP
31	M	63	180	90	26	–	–	No	Sepsis
32	M	57	176	70	9	14.2	–	Yes	Postop

Results

Comparison of in vivo to in vitro $ScvO_2$ measurements

The mean difference between $ScvO_2$ values calculated by 150 parallel, twice daily in vivo and in vitro measurements was 0.15±1.93%, with a correlation coefficient of 0.96. Similarly the fiberoptic and bench oximeter measurements of SvO_2 showed a mean difference of −0.17± 2.14% and a correlation coefficient of 0.97. In measurements over time to determine the drift of continuous in vivo $ScvO_2$ measurement the following equation resulted: ΔSO_2=0.0000712 ×*t* (min) +0.0138, corresponding to a minor drift of 0.10% per day. A similar slight drift was noted for the continuous measurement of SvO_2, which was calculated as −0.24% per day (ΔSO_2= −0.0001698 ×*t* (min) +0.136). Recalibration of the in vivo oximeter was necessary in 16 of 150 control measurements (10.7%) due to differences greater than 3% between in vivo and in vitro values.

Effect of Hb, pH, hematocrit, and temperature on the accuracy of central venous O_2 saturation

To evaluate the effect of Hb, pH, hematocrit, and temperature on two-wavelength fiberoptic spectrophotometry the patients were divided into two groups using the mean value of each variable as the cutoff point. For each variable in turn the above-average and below-average groups were compared by calculating the difference in mean values between the fiberoptic and reference measurements [$ScvO_2$ (SAT2)−$ScvO_2$ (IL282)]. The values in the above-average and below average groups (parentheses: cutoff value) were as follows:

- Hb (10.2 g/dl): 0.43%, 0.40%
- MetHb (1.39%): 0.65%, 0.21%
- COHb (1.05%): 0.47%, 0.40%
- Hematocrit (0.30): 0.13%, 0.36%
- Cardiac index (5.22 l min^{-1} m^{-2}): 0.50%, 0.40%
- pH (7.33) −0.11%, 0.93%
- Temperature (37.68°C): 0.11%, 0.62

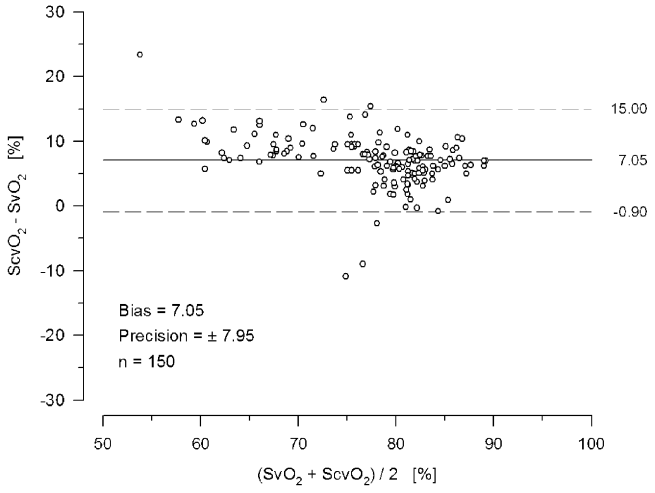

Fig. 1 Comparison of in vitro SvO_2 and $ScvO_2$ measurements using the method of Bland and Altman. *Middle line* Bias; *upper and lower lines* precision (2 SD)

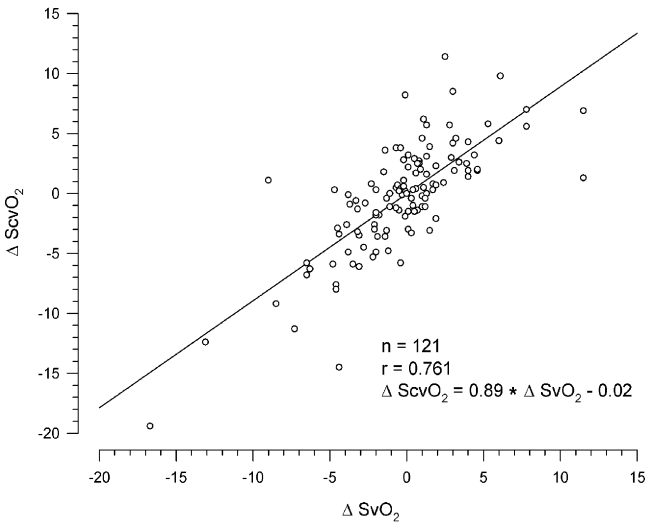

Fig. 2 Relative changes in mixed and central venous O_2 saturations between two in vitro measurements (n=121, r=0.761). Equation of the regression line: Δ $ScvO_2$=0.89 ×Δ SvO_2–0.02, SEE=3.0%

No significant statistical difference was found between the groups for any of these variables.

Infusions via central venous and accuracy of continuous $ScvO_2$ measurement

Only the administration of 6% hydroxyethyl starch at the rate of 90 ml/h resulted in a slight increase in $ScvO_2$ (0.2%); turning the infusion off resulted in a decrease of 0.5%. Infusion of the other solutions did not result in statistically significant changes in the in vivo $ScvO_2$ measurements.

Agreement between SvO_2 and $ScvO_2$ measurements

The 29 patients who had both types of indwelling catheters, provided the data for the evaluation of the in vitro and in vivo SvO_2 and $ScvO_2$ measurement techniques. For the in vitro comparisons 150 samples of the twice-daily control measurements were analyzed. The average value (bias) for $ScvO_2$ was 7.05±3.98% higher than the SvO_2 (precision 7.95%). The correlation coefficient between in vitro SvO_2 and $ScvO_2$ measurements was 0.88 (p<0.01; $ScvO_2$=0.714 ±SvO_2 +28.164). Figure 1 presents the Bland-Altman plot of the distribution of these in vitro measurements. To eliminate the individual bias between the saturations for each patient we also examined the relative changes between two in vitro controls. Figure 2 depicts the delta of saturation changes for each site with a regression line through the origin and a slope close to 1. The standard error of the estimate was 3.0%.

For the continuous in vivo comparisons SvO_2 and $ScvO_2$ values were recorded every 2 s from each oximeter. For calculation 10-s periods were averaged, resulting in a total of 395,128 comparisons over an observation period of 1,097 h. The average duration of continuous parallel measurement was 42 h/patient. Mean SvO_2 was 74.5±8.99% and mean $ScvO_2$ 82.26.95%). The mean difference (bias) was 7.75.32% (precision 10.6%). The bias tended to be smaller when O_2 saturations were in the upper range. The correlation coefficient for continuous measurement of SvO_2 and $ScvO_2$ was 0.81 (p<0.01). The Bland-Altman plot for in vivo SvO_2 and $ScvO_2$ is presented in the Electronic Supplementary Material (F.S1). To examine the agreement between subjects we compared mean SvO_2 and $ScvO_2$ values for each patient (Fig. 4) and found a correlation coefficient of r=0.866 (bias 7.37%, precision 10.21%). Among patients in the sepsis group the agreement was similar, with a higher precision (r=0.833, bias 8.56%, precision 5.91%) than in the other groups (r=0.859, bias 6.63%, precision 12.13%). Bias and precision for each patient with continuous measurement are presented in the Electronic Supplementary Material (S.T1).

Differences between $ScvO_2$ and SvO_2 (ΔSO_2) in respective patient groups

The difference between central and mixed venous O_2 saturation was highest in patients with elevated ICP (mean ΔSO_2=10.7±4.0%, p<0.001) and lowest in the postop group (7.25±5.92%, p<0.001). Among sepsis patients the mean ΔSO_2 was 7.90±4.27% (p<0.001). These group ΔSO_2 values were themselves significantly different from each other; the difference between postop ΔSO_2

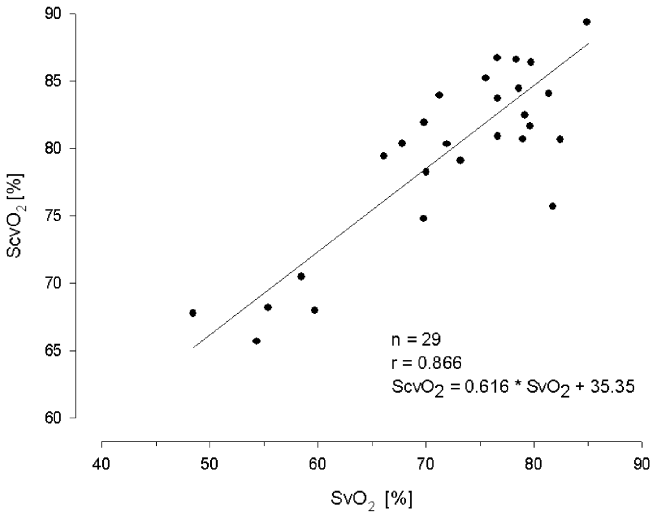

Fig. 3 Plot of mean SvO_2 and $ScvO_2$ values for each subject

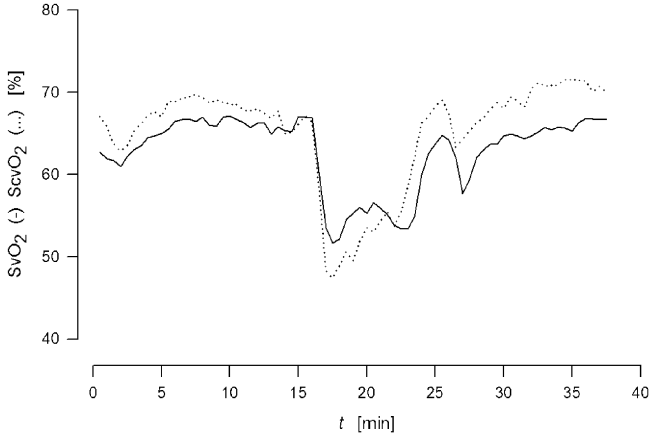

Fig. 4 Time course of continuously measured SvO_2 and $ScvO_2$ in a patient with acute respiratory distress syndrome who developed tension pneumothorax that was treated by insertion of a chest tube

and sepsis ΔSO_2 was 0.6% ($p<0.01$), that between ICP ΔSO_2 and sepsis ΔSO_2 was 2.1% ($p<0.1$), and that between postop ΔSO_2 and ICP ΔSO_2 was 2.8% ($p<0.01$).

Differences in $ScvO_2$ values between survivors and nonsurvivors

As $ScvO_2$ of 70% has recently been used as a target for guiding therapy with regards to outcome of critically ill patients [19], we evaluated the occurrence of saturations above and below this value with respect to survival. Only 4.3% of $ScvO_2$ measurements among survivors fell below 70%; the corresponding figure among nonsurvivors was 12.6% ($p<0.001$). Expressed as average time per patient below the cutoff value, the corresponding results were approximately 1.7 h per survivor compared to 3.5 h per nonsurvivor.

Parallelism of continuous SvO_2 and $ScvO_2$ measurements

A total of 1,498 episodes of mixed venous oxygen saturation changes greater than 5% O_2 saturation occurred during the observation period. The average time, over which such change took place, was 43 min, but over one-half the changes occurred within 15 min, and 80% of changes were observed within 1 h. SvO_2 increased in 764 cases and decreased in 734. $ScvO_2$ changed in the same direction in 1351 cases (90.2%) and in the opposite direction in 147 (9.8%). The mean increase in SvO_2 was 5.6±1.4 saturation percentage, which was accompanied by a mean increase of 3.4±3.2 saturation percentage in $ScvO_2$. The mean decrease in SvO_2 was 5.8±1.2 saturation percentage, which was accompanied by a mean decrease of 3.5±3.6 saturation percentage in $ScvO_2$. Likewise, changes in $ScvO_2$ of more than 5% were noted 1,286 times. In 1,135 cases (88.3%) these were followed by SvO_2 changes in the same direction and in 151 (11.7%) in the opposite direction. An average increase of 5.6±1.2% in $ScvO_2$ resulted in an increase of 3.3±3.4% in SvO_2. An average drop of 5.9±1.3% in $ScvO_2$ was followed by a 3.4±3.6% decrease in SvO_2. Figures 3 and 4 demonstrate the rapidity, with which changes in both $ScvO_2$ and SvO_2 can occur, and the close tracking of these two sites.

Discussion

The findings of this study show that continuous fiberoptic measurement of $ScvO_2$ in an ICU using two wavelength reflection photometry is a reliable method that yields values closely corresponding to in vitro oximeter measurements (r=0.96, bias=0.15%, precision= ±3.6%). Throughout the period of observation continuous $ScvO_2$ measurements remained accurate with an average drift of only 0.1 saturation percentage per day, when calibration was checked by the in vitro comparison twice daily and recalibration performed when the difference between in vivo and in vitro saturation was more than 3 saturation percentage. The relatively infrequent need to recalibrate (<11% of the control measurements for the central venous catheter and <18% for the PA catheter) and the small drift is consistent with previous studies using these techniques [8, 26].

The accuracy of continuous $ScvO_2$ measurement was not impaired by simultaneous administration of various solutions through the same central venous catheter. Furthermore, the measurements were not affected by any of the variables that might influence reflection spectropho-

tometry such as dysfunctional hemoglobins, abnormal pH, and blood temperature [24]. It should be noted, however, that although our subjects were critically ill, the deviation of these variables from normal values was not extreme. These findings are similar to those found in other investigations [8].

The present data confirm the findings of others that in critically ill patients with circulatory failure from various causes $ScvO_2$ is generally higher than SvO_2 measured in the pulmonary artery. In healthy individuals $ScvO_2$ is typically slightly lower than SvO_2 [27, 28]. This, however, is not true in heart failure, cardiac shock [16, 17], and severe sepsis [29, 30]. In circulatory shock and heart failure blood flow is redistributed away from the hepatosplanchnic region to the coronary and cerebral circulation, and in sepsis there is a marked increase in O_2 consumption in the hepatosplanchnic region [30, 31]. This results in greater O_2 desaturation from venous blood that drains into the hepatic vein and inferior vena cava, respectively. Studies carried out in cardiac and shock patients have observed differences between 5% and 18% [16, 17]. In our study the difference between $ScvO_2$ and SvO_2 was greatest in the patients with elevated intracranial pressure, followed by the patients with septic shock. This is likely due to the fact that these patients may have decreased cerebral metabolism induced by head injury as well as by therapeutic barbiturate coma. Taken together then, the data suggest that the presence of a pathologically low $ScvO_2$ very likely indicates an even lower SvO_2.

Because of this difference between SvO_2 and $ScvO_2$ values some authors have concluded that $ScvO_2$ measurements are not reliable for the monitoring of critically ill patients, whether measured in vitro [32] or with fiberoptics [22]. We agree that precise determination of absolute values for SvO_2 from $ScvO_2$ is not possible, despite the reasonable correlations that have been reported in several clinical studies (r=0.78–0.95) [16, 17, 33, 34, 35]. Our correlations of 0.88 for single in vitro measurements and 0.81 for continuous measurements also lie within this range. However, for therapeutic decision making, more important than correlations or the precise prediction of SvO_2 from $ScvO_2$, is the parallel tracking of the values, and the ability to graphically monitor venous saturation in real time. We collected data every 2 s over an average of 42 h for each of the 26 patients. Our current data confirm earlier animal studies in which we showed close parallelism of the two curves over a wide range of changing cardiorespiratory conditions [21]. Also supporting the advantage of real time monitoring of $ScvO_2$ is our finding that changes that might be clinically relevant (>5% saturation) typically occur so quickly that might very well be delayed in the absence of continuous monitoring treatment. More detailed analysis of our data, however, shows that this parallelism is not perfect. In approximately 90% of the occasions when changes in either $ScvO_2$ or SvO_2 greater than 5% occurred in an individual, they were paralleled by changes in the other monitor in the same direction.

The success of goal-oriented therapy in the recent study by Rivers et al. [19] suggests that maintaining $ScvO_2$ values higher than 70% may be a reasonable target for patients early in sepsis [20]. It is interesting to note that our eventual nonsurvivors showed values below that point for twice as long as our survivors. Other studies have also shown that $ScvO_2$, which is easily obtainable in both ICU and non-ICU settings, is superior to conventional hemodynamic parameters to detect tissue hypoxia [36].

In conclusion, our data suggest that for those who believe that SvO_2 can be used for early detection and rapid treatment of tissue hypoxia, consideration of $ScvO_2$ may be appropriate, especially if it is continuously monitored. It has the potential for time and cost savings and has fewer risks than PA catheterization. These advantages offset the lack of exact matching of O_2 saturation values. The fiberoptic $ScvO_2$ measurements were stable, in agreement with in vitro oximeter values, and not adversely affected by factors which might interfere with reflection spectrophotometry.

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