A Comparison of Central and Mixed Venous Oxygen Saturation in Circulatory Failure

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Objective: **The purpose of this study was to evaluate whether central venous oxygen saturation can be used as an alternative to mixed venous oxygen saturation in patients with cardiogenic and septic shock.**

Design: **Prospective clinical study.**

Setting: **A tertiary intensive care unit in a university hospital.**

Participants: **Twenty patients with cardiogenic or septic shock requiring a pulmonary artery catheter and inotropic support.**

Interventions: **None.**

Measurements and Main Results: **The central venous oxygen saturation overestimated the mixed venous oxygen saturation by a mean bias (or an absolute difference) of 6.9%, and the 95% limits of agreement were large (−5.0% to 18.8%). The difference between central and mixed venous oxygen saturation appeared to be more significant when mixed venous oxygen saturation was <70%. The changes in central and mixed venous oxygen saturation did not follow the line of perfect agreement closely in different clinical conditions. The central or mixed venous oxygen saturation had a significant ability to predict the status of cardiac output state, but this ability was reduced when the effect of hyperoxia was not considered.**

Conclusion: **Central and mixed venous oxygen saturation measurements are not interchangeable numerically.**

KEY WORDS: low cardiac output state, shock, monitoring, mixed venous oxygen saturation

CIRCULATORY FAILURE IS associated with significant mortality, and its management involves identification and treatment of the underlying causes and hemodynamic resuscitation to maintain systemic oxygen delivery.[1,2] Inadequate systemic oxygen delivery will result in an increase in tissue fractional oxygen extraction and a decrease in venous oxygen saturation.[3,4] Maintaining central venous oxygen saturation ($ScVO_2$) >70% by an aggressive hemodynamic resuscitation protocol has been shown to reduce mortality in severe sepsis,[5] and as such, either $ScVO_2$ or mixed venous oxygen saturation (SVO_2) has been recommended to guide hemodynamic resuscitation in severe sepsis.[6]

$ScVO_2$ represents an attractive alternative to SVO_2 because central venous catheterization is a less invasive procedure than pulmonary artery catheterization.[7] However, $ScVO_2$ reflects the oxygen saturation of the venous mixture from the upper body, and SVO_2 reflects the oxygen saturation of the venous mixture from both the upper and lower body and also the coronary circulation.

Several studies, both animal and clinical, have investigated the agreement between $ScVO_2$ and SVO_2.[8-11] Reinhart et al[9] showed that $ScVO_2$ correlated closely with SVO_2 during different phases of hypovolemic shock, hypoxia, and hyperoxia. However, in clinical studies of patients with septic shock and cardiogenic shock, the agreement between the 2 measurements has been inconsistent and unsatisfactory.[10,11]

Despite its limitations, $ScVO_2$ may have other useful applications. The authors postulated that it may be possible to predict the global cardiac output state of a patient from the $ScVO_2$ value. Therefore, the authors tested this hypothesis in a group of patients with both cardiogenic and septic shock and also re-evaluated the agreement between $ScVO_2$ and SVO_2 with a different inspired oxygen concentration and cardiac index.

METHODS

After obtaining hospital ethics committee approval and informed consent from the patient's next of kin, 20 mechanically ventilated critically ill patients who had a pulmonary artery catheter in situ and required inotropic support despite adequate fluid resuscitation were recruited. The sample size was determined to give a power of 90% to detect a difference of 5% between $ScVO_2$ and SVO_2 when the standard deviation of $ScVO_2$ and SVO_2 is 2%.[11,12] Some of the characteristics of the cohort were described in a brief report that described the effect of arterial oxygen tension on venous oxygen saturation (Table 1).[13]

After confirming that the central venous catheter was in the lower part of the superior vena cava and the pulmonary artery catheter was in the proximal pulmonary artery on the chest x-ray, samples of arterial blood, central venous blood, and mixed venous blood were simultaneously and slowly drawn from the arterial, central venous, and pulmonary artery catheter, respectively, at baseline and after the patient was ventilated with 100% inspired oxygen for 5 minutes (hyperoxia). The blood samples were also repeated if there was a significant change in cardiac index (≥10%) within 24 hours of study enrollment. During this measurement, the inspired oxygen concentration was left unchanged. In this study, all cardiac output measurements were performed by using an intermittent thermodilution technique, and all blood samples were analyzed by a co-oximeter (ABL 725; Radiometer, Copenhagan, Denmark).

The authors assessed the agreement between $ScVO_2$ and SVO_2 in repeated measurements by the mean bias and 95% limits of agreement (mean bias ± 2 × standard deviation) as described by Bland and Altman.[8] A 5% difference between $ScVO_2$ and SVO_2 was defined as the maximum width for the limits of agreement that would be clinically unacceptable in this study. The coefficient of repeatability of $ScVO_2$ and SVO_2 was not calculated because the measurements were not repeated in identical clinical conditions. Instead, the authors assessed the agreement between the changes in $ScVO_2$ and SVO_2 by observing whether they followed the line of perfect agreement closely and a

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1053-0770/2403-0009$36.00/0

doi:10.1053/j.jvca.2007.10.011

Table 1. Characteristics of the Patients

Age	Diagnosis	Inotrope/Vasopressor	Baseline Cardiac Index (L/min/m²)	Baseline Inspired O_2 Conc./SaO_2 (%)/Hb Conc.
64	Septic shock	Norepinephrine + dobutamine	3.4	0.45/95.6/95
59	Septic shock	Norepinephrine	2.7	0.50/95.3/95
68	Septic shock	Norepinephrine	4.0	0.50/95.5/79
69	Septic shock	Norepinephrine	6.9	0.40/95.8/85
47	Septic shock	Norepinephrine + dobutamine	5.7	0.45/91.2/75
56	Septic shock	Norepinephrine	3.1	0.45/96.9/81
71	Septic shock	Norepinephrine + dobutamine	1.4	0.80/95.4/95
59	Septic shock	Norepinephrine + dobutamine	3.2	0.50/96.9/86
38	Septic shock	Norepinephrine + dobutamine	6.5	0.85/89.6/98
63	Septic shock	Norepinephrine + dobutamine	3.7	0.50/97.7/89
62	Septic shock	Norepinephrine	1.9	1.00/97.6/95
41	Septic shock	Norepinephrine	2.8	0.80/93.3/113
54	Septic shock	Norepinephrine	4.1	0.40/97.0/99
71	Cardiogenic shock	Norepinephrine + dobutamine	2.6	0.40/95.0/99
73	Cardiogenic shock	Norepinephrine + IABP	3.1	0.45/95.0/95
72	Cardiogenic shock	Norepinephrine + dobutamine	3.1	0.50/95.7/126
34	Cardiogenic shock	Norepinephrine + dobutamine	4.2	0.40/95.1/93
35	Cardiogenic shock	Norepinephrine + milrinone	3.0	0.50/96.0/105
43	Cardiogenic shock	Dobutamine + IABP	2.4	0.50/95.1/115
78	Cardiogenic shock	Dobutamine	2.3	0.40/97.4/90

Abbreviations: SaO_2, arterial oxygen saturation; IABP, intra-aortic balloon pump; Hb, hemoglobin (g/L).

separate Bland and Altman plot showing the agreement between the changes in $ScVO_2$ and SVO_2 in different clinical conditions.[14]

Because the relationship between venous oxygen saturation and cardiac index is likely to be curvilinear (ie, $ScVO_2$ or SVO_2 reaches a plateau or even decreases when cardiac index reaches a very high level),[15,16] the authors used polynomial regression with a quadratic equation instead of linear regression to assess the relationship between cardiac index and $ScVO_2$ or SVO_2. The R^2 in the regression model is the coefficient of determination and represents the variability in the $ScVO_2$ and SVO_2 that is accounted for by cardiac indexes. A receiver operating characteristic (ROC) curve was used to assess the ability of the $ScVO_2$ and SVO_2 to predict a low cardiac output state. The difference between the areas under the ROC curve was analyzed by the method suggested by Hanley and McNeil.[17] In this study, a low cardiac output state was defined as cardiac index <2.5 L/min/m^2, a low $ScVO_2$ as $<70\%$, and a low SVO_2 as $<65\%$.[5,18] All statistical tests were two-tailed and performed by SPSS 13.0 software (SPSS Inc, Chicago, IL). The confidence intervals of the sensitivity, specificity, and predictive values were calculated by Confidence Interval Analysis (version 2.0.0; BMJ Books 2000, Bristol, UK). A p value <0.05 was regarded as significant.

RESULTS

The mean age of the patients was 57.8 years old (standard deviation, 13.7). Thirteen patients had septic shock, and 7 patients had cardiogenic shock. None of the patients had a significant element of hemorrhagic shock or received blood transfusions during the study period. All 20 patients had 2 sets of blood samples taken at different inspired oxygen concentrations, but only 19 patients had a significant change ($\geq 10\%$) in their cardiac index within 24 hours of enrollment in the study.

The $ScVO_2$ overestimated the SVO_2 by a mean bias (or an absolute difference) of 6.9%, and the 95% limits of agreement between the $ScVO_2$ and SVO_2 were large (-5.0% to 18.8%) (Fig 1). The difference between $ScVO_2$ and SVO_2 appeared to be more significant when SVO_2 was $<70\%$. The changes in $ScVO_2$ and SVO_2 did not follow the line of perfect agreement closely after a change in cardiac index or inspired oxygen concentration (Fig 2). The bias between the changes in $ScVO_2$ and SVO_2, after a change in inspired oxygen concentration or cardiac index, was -1.1%, and the 95% limits of agreement between these changes were large (-9.3% to 7.1%) (Fig 3).

Considering the data of $ScVO_2$ and SVO_2 at different cardiac indexes when the inspired oxygen concentration was not varied from baseline (ie, no hyperoxia); both $ScVO_2$ ($R^2 = 0.416$, $ScVO_2 = 38.977 + 14.655 \times$ cardiac index $- 1.272 \times$ (cardiac index)^2, $p = 0.0001$) and SVO_2 ($R^2 = 0.344$, $SVO_2 = 24.723 + 18.120 \times$ cardiac index $- 1.668 \times$ (cardiac index)^2, $p = 0.001$) were correlated with the cardiac index, with the cardiac index accounting for about 42% and 34 of the variability of the $ScVO_2$ and SVO_2, respectively (Figs 4 and 5). The ability of the $ScVO_2$ (area under ROC 0.88; 95% confidence interval [CI], 0.74-0.99, $p = 0.004$) to predict a low cardiac output state (cardiac index <2.5 L/min/m^2) was not worse than the SVO_2 (area under ROC 0.84; 95% CI, 0.63-0.99, $p = 0.009$) (z statistic of the difference in area under ROC curve $= 5.9$, $p = 0.001$), and the negative predictive values of $ScVO_2$ (93%) and SVO_2 (96%) to exclude a low cardiac output state were also comparable (Table 2).

When the data of $ScVO_2$ and SVO_2 at 100% inspired oxygen concentration were also included, the area under the ROC curve of $ScVO_2$ and SVO_2 to predict a low cardiac output state reduced to 0.67 (95% CI, 0.47-0.87; $p = 0.100$) and 0.68 (95% CI, 0.48-0.88; $p = 0.075$), respectively. Similarly, the negative predictive value of $ScVO_2$ and SVO_2 to exclude a low cardiac output state decreased to 87% and 88%, respectively, when the data of $ScVO_2$ and SVO_2 at 100% inspired oxygen concentration were included (Table 3).

DISCUSSION

The present results show that $ScVO_2$ and SVO_2 are not interchangeable numerically for clinical monitoring purposes.