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Correlation of a Novel Noninvasive Tissue Oxygen Saturation Monitor to Serum Central Venous Oxygen Saturation in Pediatric Patients with Postoperative Congenital Cyanotic Heart Disease

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Abstract: Using a novel noninvasive, visible-light optical diffusion oximeter (T-Stat VLS Tissue Oximeter; Spectros Corporation, Portola Valley, CA) to measure the tissue oxygen saturation (S_tO_2) of the buccal mucosa, the correlation between S_tO_2 and central venous oxygen saturation ($S_{cv}O_2$) was examined in children with congenital cyanotic heart disease undergoing a cardiac surgical procedure. Paired S_tO_2 and serum $S_{cv}O_2$ measurements were obtained postoperatively and statistically analyzed for agreement and association. Thirteen children (nine male) participated in the study (age range, 4 days to 18 months). Surgeries included Glenn shunt procedures, Norwood procedures, unifocalization procedures with Blalock-Taussig shunt placement, a Kawashima/Glenn shunt procedure, a Blalock-Taussig shunt placement, and a modified Norwood procedure. A total of 45 paired S_tO_2–$S_{cv}O_2$ measurements was obtained. Linear regression demonstrated a Pearson's correlation of .58 (95% confidence interval [CI], .35–.75; $p < .0001$). The regression slope coefficient estimate was .95 (95% CI, .54–1.36) with an interclass correlation coefficient of .48 (95% CI, .22–.68). Below a clinically relevant average $S_{cv}O_2$ value, a receiver operator characteristic analysis yielded an area under the curve of .78. Statistical methods to control for repeatedly measuring the same subjects produced similar results. This study shows a moderate relationship and agreement between S_tO_2 and $S_{cv}O_2$ measurements in pediatric patients with a history of congenital cyanotic heart disease undergoing a cardiac surgical procedure. This real-time monitoring device can act as a valuable adjunct to standard noninvasive monitoring in which serum $S_{cv}O_2$ sampling currently assists in the diagnosis of low cardiac output after pediatric cardiac surgery. **Keywords:** congenital cyanotic heart disease, pediatric, cardiac surgical procedure, tissue oxygen saturation. *JECT. 2013;45:40–45*

Careful postoperative hemodynamic monitoring is essential in children undergoing cardiac surgery for congenital heart defects (1). Maintaining an appropriate balance between oxygen delivery and oxygen consumption is critical. Although pulmonary artery catheters can provide invasive objective monitoring of cardiac output, such real-time measurements can be limited or impractical in pediatric patients. Ideally, given the unpredictable clinical course of postoperative cardiac surgical patients, often marked by abrupt hemodynamic changes, a noninvasive continuous monitor that is able to measure this oxygen delivery–consumption balance would allow for safe, optimal patient management, potentially allowing for the early implementation of life-saving interventions (2,3).

The determination of cardiac output is essential to postoperative cardiovascular care. In the absence of invasive cardiac output monitoring with a pulmonary artery catheter, a common practice among clinicians is to estimate the body's oxygen delivery–consumption balance by measuring the difference between arterial and mixed-venous oxygen (S_vO_2) saturations according to the Fick principle. The ability to evaluate oxygen delivery in pediatric postoperative cardiac surgical patients using superior vena

cava oximetry measurements was found to be associated with increased survival among hypoplastic left ventricle patients after Stage 1 palliation surgery (2).

Noninvasive cardiac output monitoring is particularly desirable in critical care, because invasive line placement, phlebotomy, and laboratory costs are potential obstacles. Others have previously demonstrated the potential clinical applicability of such noninvasive devices (4–6). We report the use of a novel noninvasive, visible-light optical diffusion oximeter in a subpopulation of pediatric cardiac surgical patients. The device, the T-Stat VLS Tissue Oximeter (Spectros Corporation, Portola Valley, CA), can measure the tissue oxygen saturation (S_tO_2) of the buccal mucosa using a specialized probe. The measurement of S_tO_2 has been found to decrease during episodes of hypoxemia and ischemia (7). This study's objective was to assess the correlation of S_tO_2, as measured by the T-Stat VLS Tissue Oximeter, to $S_{cv}O_2$ (surrogate for S_vO_2), as measured by venous blood gas analysis in pediatric patients with congenital cyanotic heart disease undergoing a cardiac surgical procedure. We hypothesized that a correlation exists between the two measurements.

MATERIALS AND METHODS

Study Design and Patient Population

The study was approved by the University of California, Los Angeles (UCLA) Institutional Review Board. Signed, informed consent was obtained from a parent before subject enrollment in the study. Mattel Children's Hospital UCLA is a university-affiliated, tertiary care children's hospital within UCLA Medical Center. All patients were cared for in the pediatric cardiothoracic intensive care unit after their cardiac surgery.

All patients younger than 21 years of age were eligible for study inclusion if they were identified as having a congenital cyanotic heart defect before their cardiac surgical procedure. Patients were excluded if their cardiac surgical procedure resulted in full correction of their heart defect resulting in completely separated pulmonary and systemic circulations. Further exclusion criteria included the absence of a central venous catheter after surgery. The study team was not permitted to insert or change central venous catheters for purposes of the study after the surgical procedure. No T-Stat VLS Tissue Oximeter readings were obtained for analysis from patients during extracorporeal membrane oxygenation after surgery. Patients were enrolled between July 2010 and April 2011.

After admission to the pediatric cardiothoracic intensive care unit on postoperative Day 0, a T-Stat VLS Tissue Oximeter buccal probe (Spectros Corporation) was inserted into the patient's mouth. A venous blood gas was subsequently drawn from an existing central venous catheter while a T-Stat VLS Tissue Oximeter monitor reading was simultaneously recorded. A second venous blood gas was drawn from an existing central venous catheter at least 24 hours after admission. As before, a simultaneous T-Stat VLS Tissue Oximeter monitor reading was recorded at the time of the blood draw. If a venous blood gas was drawn by the patient's clinician at their discretion during the study, the T-Stat VLS Tissue Oximeter monitor reading was simultaneously recorded at the time of the blood draw. The monitor could stay in place for a maximum of 48 hours. The $S_{cv}O_2$ measurement from each venous blood gas was recorded. In addition, the patient's oxygen saturation (S_pO_2), as measured by pulse oximetry, was simultaneously recorded. The buccal probe could be removed at the time of extubation. A parent could also terminate participation in the study at any time. Demographic information, including patient age, gender, diagnosis, and surgical procedure performed, was also collected. Funding for the study, including the cost of venous blood gas laboratory analyses and buccal probes, was provided by Spectros Corporation.

T-Stat VLS Tissue Oximeter Monitor

The T-Stat VLS Tissue Oximeter emits visible light between wavelengths of 475 and 600 nm. Light between these wavelengths is largely absorbed by hemoglobin within arterioles, arteries, venules, and veins and not detected by the T-Stat sensor. Light between these wavelengths, however, passes more readily through capillaries and can be detected by the sensor to indicate hemoglobin oxygen saturation within these smaller vessels. The T-Stat VLS Tissue Oximeter buccal probe fits within the mouth to monitor the tissue oxygen saturation of the buccal mucosa and does not require pulsatile blood flow (8,9).

Statistical Analysis

S_tO_2 and $S_{cv}O_2$ measurements were assessed for concordance and agreement using a linear regression, the interclass correlation coefficient (ICC), and a Bland-Altman plot. The ICC is a reliability measure ranging from 0–1 and is used to ascertain the level of agreement between two measurement devices. To assess the use of the S_tO_2 reading for predicting when a subject had a clinically low $S_{cv}O_2$ (threshold defined as mean S_pO_2-25 as a surrogate for a clinically acceptable arteriovenous oxygen difference less than 25), a receiver operating characteristic (ROC) curve was constructed using all 45 measurements. For the ROC curve, the $S_{cv}O_2$ readings were dichotomized as either low or clinically acceptable using a threshold of mean S_pO_2-25. The area under the ROC curve was computed by numerical integration. As a result of the repeated measurements from the same subjects, a mixed model was also constructed to examine the correlation of $S_{cv}O_2$ and S_tO_2. This model included a random subject effect to control for variation in

measurements between subjects. A repeated-measures Bland-Altman plot was also constructed. All statistical analyses and plots were performed using Rproject.org R Version 2.13.1.
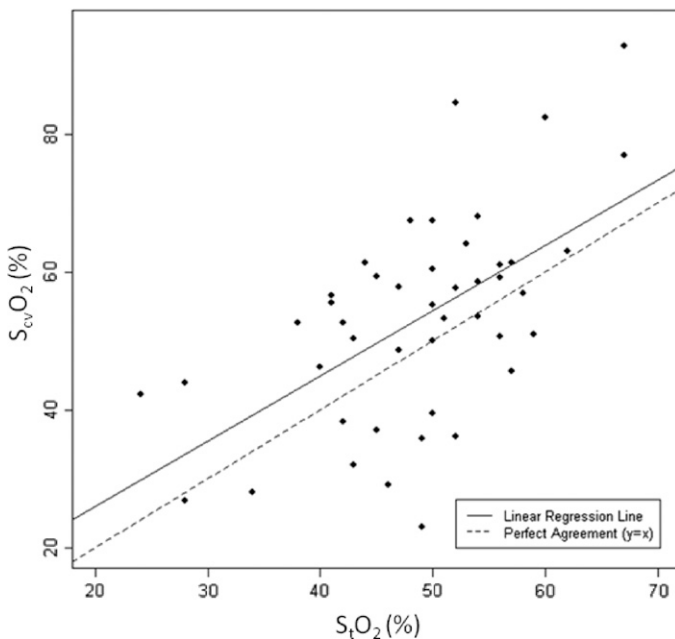
RESULTS

Between July 2010 and April 2011, 13 children with a history of a congenital cyanotic heart defect participated in the study. Each subject had at least one venous blood gas drawn after a cardiac surgical procedure. Subjects ranged in age from 4 days to 18 months (nine male, four female). Cardiac diagnoses included four patients with double-outlet right ventricle, three patients with hypoplastic left heart syndrome, two patients with tricuspid atresia, one patient with an unbalanced atrioventricular canal defect, one patient with Tetralogy of Fallot with discontinuous pulmonary arteries, one patient with a hypoplastic left ventricle and pulmonary atresia, and one patient with a single ventricle and transposition of the great arteries. The cardiac surgical procedures performed included five Glenn shunt procedures, three Norwood procedures, two unifocalization procedures with Blalock-Taussig shunt placement, one Kawashima/Glenn shunt procedure, one Blalock-Taussig shunt placement, and one modified Norwood procedure.

A total of 45 S_tO_2 readings (mean, 49%; median 50%; range, 24–67%) were obtained with paired $S_{cv}O_2$ measure-
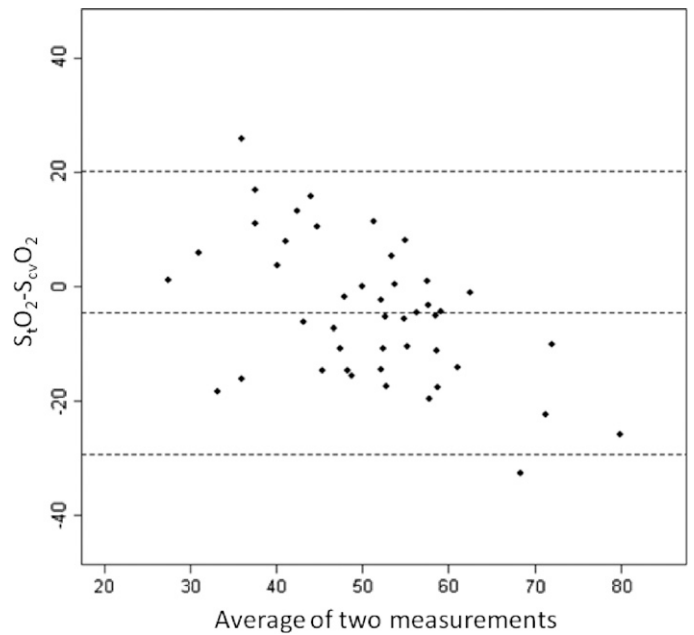

Figure 2. The Bland-Altman plot shows that $S_{cv}O_2$ values tend to be higher than S_tO_2 as the overall level of saturation increases. $S_{cv}O_2$, central venous oxygen saturation; S_tO_2, tissue oxygen saturation.

ments (mean, 53%; median 53.5%; range, 23–92.9%). S_pO_2 readings (mean, 78%; median 76%; range, 65–98%) were obtained simultaneously by pulse oximetry. The results of the linear regression show a statistically significant

Figure 1. The results of the linear regression show a statistically significant correlation between $S_{cv}O_2$ and S_tO_2 of .58 (95% confidence interval, .35–.75; p < .0001). $S_{cv}O_2$, central venous oxygen saturation; S_tO_2, tissue oxygen saturation.
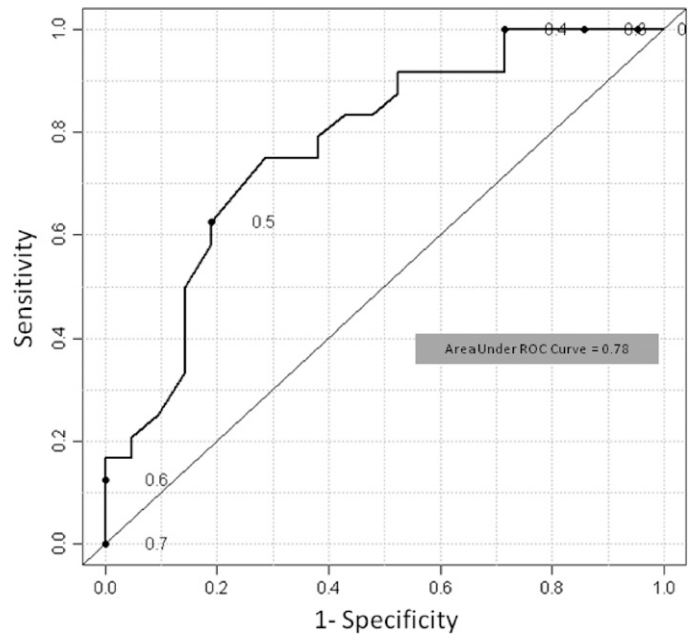
Figure 3. Using a threshold $S_{cv}O_2$ of 53% (mean S_pO_2-25 as a surrogate for a clinically acceptable arteriovenous oxygen difference less than 25), the area under the receiver operating characteristic curve is .78, demonstrating good discrimination between clinically low and acceptable levels of $S_{cv}O_2$ using S_tO_2. $S_{cv}O_2$ = central venous oxygen saturation; S_pO_2, oxygen saturation; S_tO_2, tissue oxygen saturation.
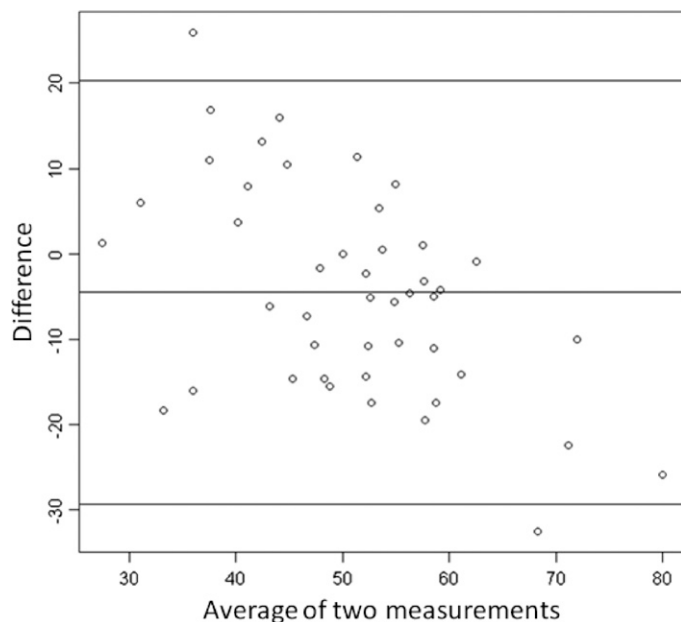
Figure 4. The repeated-measures Bland-Altman plot demonstrated moderate agreement between S_tO_2 and $S_{cv}O_2$ measurements. $S_{cv}O_2$, central venous oxygen saturation; S_tO_2, tissue oxygen saturation.

correlation between $S_{cv}O_2$ and S_tO_2 of .58 (95% confidence interval [CI], .35–.75; $p < .0001$) (Figure 1). The regression slope coefficient estimate is .95 (95% CI, .54–1.36) indicating a moderate linear relationship between S_tO_2 and $S_{cv}O_2$ measurement methods and an approximate 1:1 relationship between their values. The ICC was .48 (95% CI, .22–.68), indicating some level of agreement. The Bland-Altman plot shows that $S_{cv}O_2$ values tend to be higher than S_tO_2 as the overall level of saturation increases (Figure 2). Using a threshold $S_{cv}O_2$ of 53% (mean S_pO_2-25), the area under the ROC curve is .78, demonstrating good discrimination between clinically low and acceptable levels of $S_{cv}O_2$ using S_tO_2 (Figure 3).

The results of the mixed model show a significant association between S_tO_2 readings and $S_{cv}O_2$ measurements ($p < .001$) with a slope coefficient of .92 (95% CI, .39–1.45; $p < .001$). The repeated-measures Bland-Altman plot demonstrated moderate agreement between S_tO_2 and $S_{cv}O_2$ measurements (Figure 4). No adverse events related to the study occurred.

DISCUSSION

Survival after pediatric cardiac surgery depends heavily on the quality of postoperative care delivered in the intensive care unit. The ability to determine early compromise of cardiac output is essential to directing this care (2). To our knowledge, this is the first published case series to demonstrate an association between $S_{cv}O_2$ measurements and S_tO_2 readings using a novel noninvasive, visible-light

optical diffusion oximeter in a cohort of pediatric patients with congenital cyanotic heart disease undergoing a cardiac surgical procedure.

Traditionally, cardiac output measurements have been derived from the thermodilution technique established by Forrester and colleagues using objective data obtained from an indwelling pulmonary artery catheter (10). Although the use of pulmonary artery catheters has not been shown to improve survival in adult studies (11,12), valuable hemodynamic information can nonetheless be obtained. In children, the use of pulmonary artery catheters is often complicated by patient size and the fear of arrhythmia induction and thrombosis. Furthermore, the optimal placement of pulmonary artery catheters in pediatric patients with congenital cyanotic heart disease, either before or after cardiac surgery, can be complicated by the patient's cardiac and vascular anatomy. Often, $S_{cv}O_2$, obtained from a central venous line, is used as a surrogate for S_vO_2 in the absence of a pulmonary artery catheter.

The measurement of S_vO_2 is used as surrogate measurement of cardiac output and, more specifically, the adequacy of oxygen delivery according to the Fick principle. The use of S_vO_2 monitoring in using the Fick principle closely mirrors the thermodilution technique of measuring cardiac output (13). In states of poor cardiac output or increased oxygen consumption, a patient's S_vO_2 will fall, leading to a larger difference between arterial and venous oxygen saturations. A fall in S_vO_2 below a critical value coincides with the development of predominantly anaerobic metabolism and the resultant increased production of lactic acid, indicating an imbalance between oxygen delivery and oxygen consumption (14,15). Serum lactate levels from patients with compromised cardiac output, however, may not rise until a certain threshold of S_vO_2 is reached or a patient can no longer compensate for such a derangement in oxygen delivery and consumption (16). Elevated lactate levels, therefore, may be a late sign of impaired oxygen delivery. Furthermore, serum lactate monitoring requires blood sampling. These limitations, therefore, affect the use of lactate measurement in minute-to-minute patient management. The ability, therefore, to continuously measure S_vO_2 would allow for monitoring and provide the potential for early intervention to improve cardiac output.

The data show that the T-Stat VLS Tissue Oximeter provides a surrogate measurement (S_tO_2) for $S_{cv}O_2$ that is linearly associated across a broad spectrum of pediatric postoperative patients with cyanotic heart disease. The advantages of such an association compared with traditional central venous blood sampling are numerous. First, venous blood sampling may lead to an increased risk of central line infection, the prevention of which has become a prominent Centers for Disease Control and Prevention quality initiative estimated to have resulted in significant cost savings (17). Second, venous blood sampling may

compound blood loss in patients undergoing cardiac surgery, possibly leading to the development of anemia, especially pertinent among younger children who have a lower total blood volume. Third, venous blood gas sampling is impractical for minute-to-minute patient evaluation and management. Fourth, central venous catheters in the jugular and subclavian veins are associated with a high incidence of thrombosis (18), potentially catastrophic to postoperative pediatric patients undergoing cardiac surgery (19). Simple venous blood gas sampling from central venous catheters has been recently replaced by a commercially available catheter that can display continuous S_vO_2 readings using an embedded sensor (PediaSat; Edwards Lifesciences, Irvine, CA). Despite this potential use, central venous catheters, given their associated risks of infection, bleeding, and thrombosis, remain problematic for patients. Furthermore, given the smallest embedded sensor catheter size available (4.5-French PediaSat catheter), the size of some pediatric cardiac surgical patients may preclude safe placement.

Additional advantages of the T-Stat VLS Tissue Oximeter include the ability to monitor a surrogate marker of cardiac output in real-time as an additional vital sign. We report no adverse events during our study. The buccal probe was well tolerated. The insertion and removal of the probe is noninvasive, leaving open the possibility of intermittent monitoring in extubated patients as well. In addition, the T-Stat VLS Tissue Oximeter has been used in infants in whom the placement of large venous catheters may not be safe or possible.

There are potential limitations to this study. This study only enrolled 13 patients from a single institution. Caution should be used when generalizing these results to all pediatric postoperative patients with congenital cyanotic heart disease without further validation. In addition, the precise location from which central venous blood gas sampling occurred was not obtained for all samples. As discussed previously, however, measurement of S_vO_2 can be challenging as a result of vascular and cardiac anatomy, specifically in terms of the location of venous blood gas sampling. This consideration may be more pronounced in this population as streaming, shunting, and mixing of blood is common in patients with cyanotic heart disease after cardiac surgical procedures. Given these limitations, the precise location of central venous blood gas sampling would likely be misleading when attempting to generalize the correlation reported here to other patients with similar cardiac lesions. Furthermore, venous blood gas sampling was limited in this study to existing central venous catheters. The study team was not permitted to insert or change central venous catheters for purposes of the study after the surgical procedure. As a result, this cohort is representative of common limitations encountered in a pediatric cardiothoracic intensive care unit.

Although this cohort of patients includes a representative sampling of congenital cyanotic heart defects, the study did not evaluate the T-Stat VLS Tissue Oximeter among all possible cyanotic heart defects, potentially limiting generalizability. Lastly, the Bland-Altman plot appears to show that the differences between S_tO_2 and $S_{cv}O_2$ may depend on the level of oxygen saturation. However, the ROC curve indicates that the S_tO_2 values provide a moderately high level (area under the curve = .78) of prediction ability for identifying those patients with clinically low $S_{cv}O_2$ values.

In summary, there is a linear association between $S_{cv}O_2$ measurements and S_tO_2 readings using a novel noninvasive, visible-light optical diffusion oximeter in pediatric patients with congenital cyanotic heart disease who have undergone a cardiac surgical procedure. This device can act as a valuable adjunct to standard noninvasive monitoring in which $S_{cv}O_2$ measurements currently assist in the diagnosis of low cardiac output syndrome after pediatric cardiac surgery. The ability to monitor a surrogate marker of cardiac output in real-time as an additional vital sign would likely enable clinicians to adjust medications or intervene surgically in a timelier manner. Further study is needed to determine whether the ability to monitor S_tO_2 improves patient outcomes after a pediatric cardiac surgical procedure.

ACKNOWLEDGMENTS

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