Prehospital dynamic tissue oxygen saturation response predicts in-hospital lifesaving interventions in trauma patients

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BACKGROUND: Tissue oximetry (StO2) plus a vascular occlusion test is a noninvasive technology that targets indices of oxygen uptake and delivery. We hypothesize that prehospital tissue oximetric values and vascular occlusion test response can predict the need for in-hospital lifesaving interventions (LSI).

METHODS: We conducted a prospective, blinded observational study to evaluate StO2 slopes to predict the need for LSI. We calculated the DeO2 slope using Pearson’s coefficients of regression ($r^2$) for the first 25% of descent and the ReO2 slope using the entire recovery interval. The primary outcome was LSI defined as the need for emergent operation or transfusion in the first 24 hours of hospitalization. We created multivariable logistic regression models using covariates of age, sex, vital signs, lactate, and mental status.

RESULTS: We assessed StO2 in a convenience sample of 150 trauma patients from April to November of 2009. In-hospital mortality was 3% (95% confidence interval [CI], 1.1–7.6); 31% (95% CI, 24–39) were admitted to the intensive care unit, 6% (95% CI, 2.8–11.1) had an emergent operation, and 10% (95% CI, 5.7–15.9) required transfusion. Decreasing DeO2 was associated with a higher proportion of patients requiring LSI. In the multivariate model, the association between the need for LSI and DeO2, Glasgow Coma Scale, and age persists.

CONCLUSION: Prehospital DeO2 is associated with need for LSI in our trauma population. Further study of DeO2 is warranted to determine whether it can be used as an adjunct triage criterion or an endpoint for resuscitation. (J Trauma. 2012;72: 930–935. Copyright © 2012 by Lippincott Williams & Wilkins)

LEVEL OF EVIDENCE: III, observational study.

KEY WORDS: Prehospital; near-infrared spectroscopy; trauma.

Prehospital evaluation of trauma patients relies on evaluating vital signs and mechanism of injury, which often do not predict a need for interventions or outcomes.1,2 Vital signs such as blood pressure and heart rate may not change until patients reach decompensated shock, preventing early recognition and treatment.2–6 Delayed identification of hypoperfusion may lead to triage of some patients away from specialized trauma centers and to inadequate or delayed resuscitation which is strongly associated with an increase in infection, multiorgan dysfunction (MOD), and mortality.3,7,8

Uncontrolled hemorrhage and resultant shock account for up to 82% of early operative deaths after trauma.9 Early aggressive resuscitation of critically ill patients may limit or reverse tissue hypoxia progressing to organ failure.10 Currently used monitoring technology for prehospital evaluation is inadequate for identifying hemorrhage-induced tissue hypoxia. Early identification of tissue hypoxia is necessary to implement timely and corrective lifesaving interventions (LSI).11 These interventions may include blood transfusion and emergent operative intervention (thoracotomy, laparotomy, pelvic fixation, and embolization) and admission to the intensive care unit.

Many patients have compromised regional oxygen delivery despite adequate hemodynamic parameters.7,8 Therefore, prehospital vital signs such as blood pressure, heart rate, and oxygen saturation may not significantly deviate from normal values due to the patient’s physiologic compensatory mechanisms. This may lead to delayed identification of hypoperfusion and inadequate resuscitation in patients with compensated shock.

Tissue oximetry (StO2) is a noninvasive, near-infrared spectroscopy-based monitoring technology that targets both global and regional indices of oxygen uptake and delivery. StO2 allows medical providers to identify critically ill patients with a high risk of developing hemorrhage-induced organ dysfunction.12,13 Evidence suggests that a low tissue
The rate of reoxygenation (ReO₂) reflects the time required to wash out stagnant blood, is thought to be determined by local cardiovascular reserve and microcirculatory flow. These rates of deoxygenation and reoxygenation will be sensitive and specific than vital signs alone for the identification of shock. During the VOT, a pneumatic cuff occludes blood flow proximal to the sensor resulting in deoxygenation of the tissue. The rate of deoxygenation (DeO₂) is thought to reflect the local metabolic rate, which is effected by states of shock. Subsequently, the cuff is released. The rate of reoxygenation (ReO₂), which reflects the time required to wash out stagnant blood, is thought to be determined by local cardiovascular reserve and microcirculatory flow.

Additional data can be obtained from a vascular occlusion test (VOT), a regional stress test, which may be more sensitive and specific than vital signs alone for the identification of shock. During the VOT, a pneumatic cuff occludes blood flow proximal to the sensor resulting in deoxygenation of the tissue. The rate of deoxygenation (DeO₂) is thought to reflect the local metabolic rate, which is effected by states of shock. Subsequently, the cuff is released. The rate of reoxygenation (ReO₂), which reflects the time required to wash out stagnant blood, is thought to be determined by local cardiovascular reserve and microcirculatory flow. These rates of deoxygenation and reoxygenation will be referred to as VOT-derived parameters. We hypothesize that prehospital tissue oximetric values and the response to a VOT can predict the need for in-hospital LSI, defined as the need for emergent operation or emergent transfusion in the first 24 hours of hospitalization.

METHODS

Following approval of this study by the University of Pittsburgh Institutional Review Board, we conducted a prospective, blinded, observational study to evaluate the ability of near-infrared spectroscopy StO₂ (InSpectra StO₂; Hutchinson Industries, Hutchinson, MN) in conjunction with a VOT to provide early detection of shock states in trauma patients arriving to a single Level I trauma center in Pittsburgh, Pennsylvania.

We equipped six rotor wing aircraft with StO₂ monitors covering a catchment area of approximately 4 million people. The emergency department, with 50,000 annual visits, serves an urban, academic teaching hospital with 700 beds and is a Level I trauma center with more than 5,000 trauma admissions a year. The study inclusion criteria were age ≥18 years, transport on a StO₂ equipped aircraft, and admission to the trauma service. We excluded prisoners, known pregnant females, and those with bilateral forearm injuries. We instructed crews not to perform the VOT on an injured extremity. The study period encompassed 9 months, during which StO₂ measurements were obtained during the critical care transport.

Flight crews applied the StO₂ monitor to the thenar eminence of eligible trauma patients in flight to a Level I Trauma Center and performed a VOT. Data recorded during the VOT were used to generate DeO₂ and ReO₂. Providers were blinded to DeO₂ and ReO₂ results, as the evaluation of these parameters required post hoc computer analysis and was not available in real time. No change in clinical care was initiated during the flight based on these observational data.

All trauma patients had automated and continuous monitoring with LIFEPAK 12 monitors (Physio-Control, Redmond, WA) sampling vital signs every 5 minutes of transport. A single point of care lactate (Arkay Lactate Pro, Kyoto, Japan) was obtained upon patient contact. After each patient transport, prehospital providers transcribed vital signs into an electronic medical record (EMS Charts, West Mifflin, PA). A narrative of injury, medications administered, point of care prehospital lactate, and changes in patient condition were recorded on the prehospital record.

From the prehospital database, the patient’s demographics, date of service, vital signs, and treatment were downloaded, and probabilistic linkage was used to identify the in-hospital record using time and date of service. In-hospital medical records were used to record outcome information. Medical record number was linked to in-hospital record using date of service. Three investigators (H.G., J.M., and J.O.) used a standardized data collection sheet to record all de-identified prehospital and outcome data.

Injury severity score (ISS) was calculated as previously described. Emergent operation was defined as any of the following procedures performed for hemorrhage control in the first 24 hours of hospitalization: thoracotomy, laparotomy, pelvic fixation, and embolization. Emergent transfusion was defined as a patient receiving blood in the first 24 hours of hospitalization. The trigger for transfusion is hypotension (systolic blood pressure (SBP) <90 mm Hg) not responsive to 2 L of crystalloid or at the discretion of the command physician (prehospital) or trauma surgeon (trauma bay). The primary outcome was the ability to predict these LSI.

Data are presented as mean ± standard deviation or median (25–75 interquartile range [IQR]) for non-Gaussian variables. Comparison of the two groups was performed using Kruskal-Wallis test or one-way analysis of variance for continuous variables and the χ² statistics for comparing categorical variables. We calculated DeO₂ and ReO₂ slopes using linear regression. We determined the DeO₂ slope using Pearson’s coefficients of regression (r²) for the first 25% of descent and the reoxygenation slopes using the entire recovery interval to baseline values as previously described. We used univariate logistic regression models to determine the association of demographics; prehospital vital signs; baseline StO₂, DeO₂, and ReO₂ curves; and outcomes (LSI). From these results, we created a multivariate model to account for age, Glasgow Coma Scale (GCS), and vital signs as covariates in predicting LSI. A parametric receiver operating characteristic curve was generated and the area under the curve was calculated. The Hosmer-Lemeshow statistic is reported to assess the performance of the model. Analysis was performed using STATA software (version 10; STATA Inc, College Station, TX).

RESULTS

The StO₂ device was applied in a convenience sample of 150 trauma patients transported by a single critical care transport service from April to November of 2009. The age range of the patients was 18 years to 98 years (mean, 47 years) and 60% were men. In-hospital mortality was 3%
(95% confidence interval [CI], 1.1–7.6); 31% (95% CI, 24–39) were admitted to the intensive care unit, 6% (95% CI, 2.8–11.1) had an emergent operation, 10% (95% CI, 5.7–15.9) required transfusion, 3% required both transfusion and emergent operation, 10% were treated with prehospital intubation, and 19% required mechanical ventilation. The median length of mechanical ventilation was 2.5 days (IQR, 1–6 days).

StO2 measurements were obtained a median of 48 minutes (IQR, 40–64) from the time of injury. When the time of injury was not available, the time of EMS dispatch was used as a surrogate. Among those patients requiring LSI, 31 arrived directly from the scene whereas 21 were transported from other hospitals. The initial mean StO2 level was 78 % (IQR, 8–78), median DeO2 was 0.17%/s (IQR, 0.12–0.21), and median ReO2 was 2.4%/s (IQR, 1.3–3.6). DeO2 and ReO2 are poorly associated with field lactate measurements ($r = 0.13$ and $r = 0.17$, respectively). As detailed in Table 1, differences were apparent in the distribution of injury among those requiring LSI: less extremity trauma, more head, chest, and abdominal trauma. Initial prehospital vital signs did not differ between the LSI group versus those that did not require LSI (Table 1). The median ISS for patients requiring an LSI was 16 (IQR, 9–25) while those who did not need LSI had a median ISS of 5 (IQR, 1–10). Only 8 of 52 (15%) patients with the combined outcome had an episode of prehospital hypotension below 90 mm Hg. An abnormal DeO2 slope would have identified 29 of 52 (56%) patients requiring LSI and 7 of 8 (88%) hypotensive patients requiring LSI. A higher proportion of patients with abnormal mental status exist in the LSI cohort.

Decreasing DeO2 and ReO2 are associated with increasing ISS. As ReO2 values decreased, the proportion of survivors decreased. Neither DeO2 nor ReO2 (Fig. 1) correlated with SBP. Decreasing DeO2 was associated with a higher proportion of patients requiring LSI. The fitted receiver operating characteristic for DeO2 as a predictor of LSI is shown in Figure 2. The time from StO2 VOT to LSI procedure was a median of 237 minutes (IQR, 154–858). Intervention occurred within 2 hours in 3 of 12 cases and 6 of 12 within 2 hours to 12 hours with only three requiring >12 hours. Univariate relationships were identified between death and ReO2, GCS, and age; however, the small number of deaths precluded any attempt at performing a multivariate analysis. The need for LSI has a univariate association with DeO2, lowest SBP, and GCS. In the multivariate model, the association between the need for LSI and DeO2, GCS, and age persists (Table 2). Other than lowest SBP, there is no association between prehospital vital signs and outcomes.

### DISCUSSION

In a large convenience sample of prehospital patients being transported to a Level I trauma center, a measure-
ment of near-infrared tissue oximetry using an adjunctive VOT provided useful risk-stratification information about in-hospital morbidity. First, this study demonstrated that the noninvasive measurement of StO2 and VOT-derived variables (DeO2 and ReO2) can be performed successfully during medical air transport. Second, ReO2 and DeO2 were found to be associated with injury severity and the need for LSI. More importantly, the relationship between DeO2 and need for LSI is independent of the presence of other available prehospital information, including vital signs and mental status.

The VOT requires approximately 3 minutes to perform using an automated tourniquet. Graphical data produced by the VOT can be viewed in real time; however, additional education of the flight crews would be necessary to teach them how to interpret the data. Currently, the slope calculations are done post hoc after extracting the raw data from the machine. Modifications of the current software could perform the slope calculations and produce an actionable value forprehospital providers.

The DeO2 slope may be decreased as a consequence of impaired oxygen metabolism among tissue either with impaired regional perfusion distribution or owning to a lower metabolic rate. Previous studies of the prognostic utility of tissue oximetry have shown that it is predictive of poor outcomes when measured in the hospital setting.14,15 Furthermore, StO2 and VOT-derived parameters are predictive of multisystem organ failure,12,14,15 suggesting that these dynamic parameters may be able to discriminate altered perfusion states. In particular, a decrement in the DeO2 slope may be explained by different pathophysiologic mechanisms including a reduction in oxygen metabolism (lower metabolic rate) within the monitored tissue, an impaired regional blood flow distribution, or an impairment in oxygen utilization by the mitochondria. Tissue oximetry and VOT-derived parameters may provide a real-time, semicontinuous measurement of regional tissue perfusion in occult shock states. Software modifications could allow for contemporaneous analysis potentially creating a tool to assess the effectiveness of ongoing resuscitation.

Patients in need of LSI did not differ from those not requiring LSI with respect to age, sex, and frequency of penetrating injury. Conventional prehospital variables such as heart and respiratory rate could not differentiate patients requiring LSI from those who did not. The lowest SBP did discriminate between these two groups of patients; however, it did so at levels that would not be actionable by a prehospital provider (122 ± 27 vs. 134 ± 20 mm Hg). Two other parameters predicted the requirement for LSI: GCS, a well-known triage and prognostic indicator and the VOT-derived parameters. Interestingly, baseline oximetric values also do not differ significantly between the groups. Previous studies have noted changes in baseline StO2 associated with MOD.

<table>
<thead>
<tr>
<th>Predictor for LSI</th>
<th>Univariate Odds Ratio (95% CI)</th>
<th>P</th>
<th>Multivariate Odds Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lowest SBP</td>
<td>0.97 (0.95–0.99)</td>
<td>0.001</td>
<td>0.97 (0.93–0.99)</td>
<td>0.002</td>
</tr>
<tr>
<td>DeO2</td>
<td>2.3 (1.3–4.1)</td>
<td>0.003</td>
<td>2.5 (1.3–4.9)</td>
<td>0.007</td>
</tr>
<tr>
<td>ReO2</td>
<td>0.78 (0.6–1.0)</td>
<td>0.07</td>
<td>0.8 (0.6–1.1)</td>
<td>0.2</td>
</tr>
<tr>
<td>Abnormal GCS</td>
<td>2.7 (1.3–5.6)</td>
<td>0.006</td>
<td>3.3 (1.2–8.9)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Univariate and multivariate odds ratios are described with 95% CI.
scale and mortality but may not address compensated or occult shock states. This is an inherent limitation of the technology in that peripheral vasoconstriction associated with compensated shock states may be accompanied by a reduction in regional tissue oxygen demand and compromised supply. However, stressing the system by producing a vascular occlusion yields parameters such as the ReO₂ and DeO₂ slopes which differentiate those patients requiring LSI from those that did not (Table 1).

To further evaluate the VOT-derived parameters, we constructed a model that incorporates data elements that are available to prehospital providers and differ between the LSI and control cohorts. Using multiple logistic regression, we demonstrate that DeO₂ impairment is associated with LSI irrespective of GCS and blood pressure. Furthermore, DeO₂ slope did not correlate with SBP (Fig. 1, A), despite SBP being an accepted indicator of hypoperfusion. This may be explained by the fact that SBP and DeO₂ assess hypoperfusion at different levels. SBP, just as central venous oxygen saturation is a global indicator of hypoperfusion, whereas DeO₂ is a more regional marker of perfusion deficits. Decreasing DeO₂ slope is associated with an increase in ISS. Our findings are supported by previous published data showing that there is no association between global parameters of perfusion and StO₂, or VOT-derived parameters. These data suggest that DeO₂ may be used as a prehospital triage tool to identify a group of patients in need of LSI.

Lactate is also used as a surrogate to assess prehospital hypoperfusion. In-flight lactate levels did not discriminate between patients requiring LSI from those who did not. Furthermore, there was no association between lactate levels and DeO₂ as expected. This may be explained by the fact that lactate accumulation usually lags behind the initial insult. Moreover, this discrepancy between DeO₂ and lactate may indicate that DeO₂ is capable of detecting occult shock, defined as persistent occult hypoperfusion in the setting of normal vital signs and lactate levels.

We think that DeO₂ has several advantages for prehospital trauma risk stratification of patients that require LSI and intensive in-hospital therapy. Patients with a low DeO₂ slope may benefit from earlier triage to Level I trauma centers, even when they have no apparent vital sign abnormality, respiratory distress, or altered sensorium. This study does not address titration of prehospital resuscitation and its impact on both DeO₂ and the subsequent need for LSI. Additional data are required to establish whether a tool such as tissue oximetry may be used to guide prehospital resuscitative therapy. If such application would be successful, then it might help in decreasing indiscriminate use of crystalloid solutions that are known to worsen dilutional coagulopathy and hemorrhage. In conjunction with vital signs and neurologic assessment, tissue oximetry may allow for the selection of a patient population that would benefit from early resuscitation while minimizing patient exposure to isotonic fluids. Furthermore, tissue oximetry using serial VOT may be able to guide therapy providing both feedback on the efficacy of treatment and an endpoint for resuscitation.

Our study indicates that tissue oximetry measured during patient transport provides additional prognostic information about LSI in the absence of clinically apparent shock, respiratory distress, and altered sensorium. A prospective validation in unselected trauma patients is necessary before widespread adoption of tissue oxygenation by prehospital providers. Future implementation might include using DeO₂ as part of a decision aid to identify and direct the need for aggressive prehospital and emergency department resuscitation.

LIMITATIONS

The patient populations transported by our air medical service are predominantly blunt trauma victims, of higher acuity, and may not be broadly generalizable to trauma patients at large. We collected data from April to September and thus did not evaluate the performance of the device in cold weather. A bias for high acuity patients likely exists, as minor trauma patients would be sent by ground to local facilities. Despite the high acuity of these patients, mortality was low (3%), perhaps indicating a selection bias. This cohort of patients may not include some patients with short flight times or patients who were in extremis. In these cases, tissue oximetry is not necessary to identify severe illness or initiate early resuscitation.

CONCLUSION

Prehospital DeO₂ is associated with need for LSI in our trauma population. Further study of DeO₂ is warranted to determine whether it can be used as an adjunct triage criterion or an endpoint for resuscitation.

AUTHORSHIP

F.X.G., D.H., J.-C.P. and M.R.P. designed this study. F.X.G., H.G., J.Q., J.M., and H.K.K. acquired the data, which were analyzed by F.X.G., H.G., B.S., D.H., and J.-C.P. All authors participated in preparing and editing the manuscript.

DISCLOSURE

Michael R. Pinsky, MD, received an honorarium for lecturing from Hutchinson Industries.

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