Predicting blood transfusion using automated analysis of pulse oximetry signals and laboratory values

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BACKGROUND: Identification of hemorrhaging trauma patients and prediction of blood transfusion needs in near real time will expedite care of the critically injured. We hypothesized that automated analysis of pulse oximetry signals in combination with laboratory values and vital signs obtained at the time of triage would predict the need for blood transfusion with accuracy greater than that of triage vital signs or pulse oximetry analysis alone.

METHODS: Continuous pulse oximetry signals were recorded for directly admitted trauma patients with abnormal prehospital shock index (heart rate [HR] / systolic blood pressure) of 0.62 or greater. Predictions of blood transfusion within 24 hours were compared using Delong's method for area under the receiver operating characteristic (AUROC) curves to determine the optimal combination of triage vital signs (prehospital HR + systolic blood pressure), pulse oximetry features (40 waveform features, O_2 saturation, HR), and laboratory values (hematocrit, electrolytes, bicarbonate, prothrombin time, international normalization ratio, lactate) in multivariate logistic regression models.

RESULTS: We enrolled 1,191 patients; 339 were excluded because of incomplete data; 40 received blood within 3 hours; and 14 received massive transfusion. Triage vital signs predicted need for transfusion within 3 hours (AUROC, 0.59) and massive transfusion (AUROC, 0.70). Pulse oximetry for 15 minutes predicted transfusion more accurately than triage vital signs for both time frames (3-hour AUROC, 0.74; $p = 0.004$) (massive transfusion AUROC, 0.88; $p < 0.001$). An algorithm including triage vital signs, pulse oximetry features, and laboratory values improved accuracy of transfusion prediction (3-hour AUROC, 0.84; $p < 0.001$) (massive transfusion AUROC, 0.91; $p < 0.001$).

CONCLUSION: Automated analysis of triage vital signs, 15 minutes of pulse oximetry signals, and laboratory values predicted use of blood transfusion during trauma resuscitation more accurately than triage vital signs or pulse oximetry analysis alone. Results suggest automated calculations from a noninvasive vital sign monitor interfaced with a point-of-care laboratory device may support clinical decisions by recognizing patients with hemorrhage sufficient to need transfusion. (*J Trauma Acute Care Surg*. 2015;79: S175–S180.

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KEY WORDS: Blood transfusion; prediction; massive transfusion; pulse oximetry; point-of-care laboratory testing.

Valid, robust, and reliable methods for diagnosing hemorrhagic shock are urgently needed to reduce delays in transport to surgical care, enhance survival of casualties, and improve planning and resource coordination at multiple points during the chain of survival for seriously injured trauma patients. Although the goal of early identification of hemorrhaging patients has been addressed through the development of numerous predictive scores,[1–8] accurate prediction of ongoing blood transfusion needs for trauma patients in near real time remains an unrealized goal. Hemorrhage remains the most common cause of preventable death among both civilian and military trauma patients,[9–11] and the challenge of identifying the small subset of actively bleeding patients from among the larger population of injured patients is critical to improving survival from traumatic injury.

Existing technology allows for wireless integration of patient physiologic data and the results of point-of-care laboratory data into a single vital signs (VS) monitor.[12,13] We have previously shown that real-time analysis of pulse oximetry signals during initial trauma resuscitation accurately predicts the need for blood product transfusion.[14] We hypothesized that a decision-assist algorithm that incorporates triage VS obtained by emergency medical service (EMS) providers for heart rate (HR) and systolic blood pressure (SBP), pulse oximetry signal analysis, and laboratory values could increase the accuracy of transfusion prediction compared with triage VS, pulse oximetry signal analysis, or laboratory values alone.

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PATIENTS AND METHODS

The method of data collection and pulse oximetry signal analysis has been previously described.[14] In brief, we enrolled adult (≥18 years old) trauma patients who were admitted directly from the scene of injury. Inclusion criteria were shock index of 0.62 or greater based on VS radioed in from the field by the EMS provider, EMS "Priority 1" (denoting a critically ill or injured person requiring immediate attention), or unstable patients with a life-threatening injury without available prehospital VS. A shock index of 0.62 was selected as abnormal[15,16] with an overall intent to ensure that entry criteria did not exclude hemorrhaging patients. Patients surviving less than 15 minutes after admission to the trauma center were excluded. To avoid potential confusion with neurogenic shock, neurologically impaired cervical spine injury patients were excluded. The current analysis includes the population previously reported (n = 557)[14] plus an additional 295 patients.

The first set of VS (HR and SBP) radioed to the hospital by EMS were designated the "triage vital signs." Pulse oximetry waveforms were recorded at 240 Hz, and numerically monitored trend values of HR and SpO_2 were obtained every 2 seconds (0.5 Hz) for 1 hour beginning at the time of arrival in the trauma resuscitation unit. To ensure that monitoring artifact was not included in the data analysis, the collected data were filtered to reduce noise using a pulse oximetry signal quality index, which excludes signals with more than 5% difference between the pulse oximeter monitor, pulse rate reading, and the automated pulse oximeter measurement of peak-to-peak distance.[14] If at least 5 minutes of the first 15 minutes pulse oximetry signal met signal quality index criteria, the patient was included for analysis.

Laboratory values were obtained from the first venous blood sample collected on arrival to the trauma center within 5 minutes of gaining intravenous access and processed in the central laboratory using standard hospital-based chemistry and hematology analyzers. For the purposes of analysis, the laboratory values were then sorted into data sets based on commercially available cartridges for the iSTAT point-of-care blood analyzer (Abbott Laboratories Inc., Chicago, IL), thereby modeling point-of-care laboratory testing and theoretical data transfer to a patient monitoring device. The cartridges were designated C1, Cartridge 1 (hematocrit, glucose, potassium, chloride, and bicarbonate); C2, Cartridge 2 (prothrombin time [PT], international normalization ratio [INR]); and C3, Cartridge 3 (lactate).

Blood use was tracked by direct observation during resuscitation and by cross-validation with blood bank records tracking individual blood product unit types and time of release from the blood bank. To avoid "prediction" of transfusions that had already occurred, blood transfused within the first 15 minutes while recording the initial pulse oximetry signals was not included; subsequent blood transfusions were included for any patients who received transfusion within the first 15 minutes. Blood use predictions were partitioned into postadmission cohorts of blood transfusion within the first 3 hours. Analysis was also performed for the prediction of rapid transfusion, defined for the purposes of this analysis as 5 U or greater red blood cell transfusion in the first 4 hours after admission, and for the prediction of traditional definition of massive transfusion, that is, 10 or more units of packed red blood cell (pRBC) transfusion in the first 24 hours after admission.

Features of VS signals, laboratory values, and combinations of these features were used to predict transfusion based on stepwise logistic regression, with a $p = 0.05$ used for forward selection and a $p = 0.1$ used for backward selection (SAS, Cary, NC). Area under the receiver operating characteristic (AUROC) curves were calculated for HR + SBP, pulse oximetry signal features, laboratory values grouped as C1, C2, C3, or all laboratory data in combination. AUROC curves were compared using Delong's method, with $p < 0.05$ considered to be statistically significant. Sensitivity and specificity were calculated from the optimal threshold determined by the Youden index.[17] To prevent model overfitting of data, a 10-fold cross-validation repeated 10 times was used to validate the prediction. Models with less than 10% difference in training and testing in AUROC curves were considered not overfitting.[18]

RESULTS

We enrolled 1,191 patients; 293 patients (24.6%) were excluded from the analysis because of incomplete pulse oximetry signal data, and 46 (3.8%) were excluded because of incomplete laboratory availability, leaving a total of 852 patients for analysis. Blood transfusion was recorded for 49 patients (5.6%) within the first 3 hours, 24 patients (2.8%) received rapid transfusion, and 14 patients (1.6%) received massive transfusion. A total of 54 patients were transfused within the first 15 minutes of data collection, of which 12 patients received no further transfusion. Table 1 shows the characteristics of patients included and excluded from the analysis.

The results were compared for triage VS, laboratory values, and pulse oximetry features. Table 2 displays the

TABLE 1. Characteristics of Patients with Complete Versus Incomplete Data Available for Analysis

	Value		
Characteristic	**1,191 cases**	**852 cases**	***p***
Age, mean (SD), y	40.4 (17.7)	40.4 (17.6)	0.94
Admission Glasgow Coma Scale (GCS) score	Minimum, 3; maximum, 15	Minimum, 3; maximum, 15	
Sex, n (%)			
Male	823 (69.1)	593 (69.6)	0.78
Female	368 (30.9)	260 (30.5)	0.84
Injury type, n (%)			
Blunt	955 (80.2)	697 (81.8)	0.25
Penetrating	176 (14.8)	113 (13.3)	0.23
Other	60 (5.0)	42 (4.9)	0.95
Mechanism of injury, n (%)			
Motor vehicle associated	557 (46.8)	402 (47.2)	0.83
Falls	253 (21.2)	192 (22.5)	0.38
Interpersonal violence	230 (19.3)	152 (17.8)	0.30
Other	151 (12.7)	106 (12.4)	0.88
Injury Severity Score (ISS)	11.8 (12.2)	10.7 (11.0)	0.006*

*$p < 0.05$.

TABLE 2. List of Candidate Variables Used for 10 Models

Model Name	Candidate Variables
Model 01	Triage VS (prehospital HR + SBP)
Model 02	40 POF
Model 03	C1
Model 04	C2
Model 05	C3
Model 06	All laboratory values (C1 + C2 + C3)
Model 07	(Triage VS) + C1 + POF
Model 08	(Triage VS) + C2 + POF
Model 09	(Triage VS) + C3 + POF
Model 10	(Triage VS) + (C1 + C2 + C3) + POF

C1, Cartridge 1 (hematocrit, glucose, potassium, chloride, and bicarbonate); C2, Cartridge 2 (PT, INR); C3, Cartridge 3 (lactate); POF, pulse oximetry features.

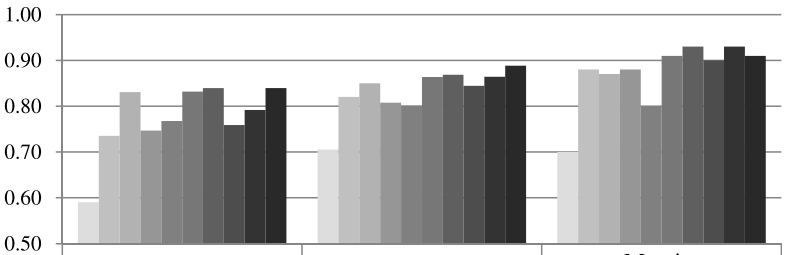
candidate variables organized as 10 models. The AUROC curve for each model with respect to the three outcomes evaluated is displayed in Figure 1. Triage VS (Model 1) predicted blood transfusion within 3 hours with an AUROC curve of 0.59; rapid transfusion was predicted with an AUROC curve of 0.71, and massive transfusion was predicted with an AUROC curve of 0.70. Pulse oximetry signal features (Model 2) predicted transfusion within 3 hours with an AUROC curve of 0.74; rapid transfusion was predicted with an AUROC curve of 0.82, and massive transfusion was predicted with an AUROC curve of 0.88.

The AUROC curve for each laboratory cartridge and combination of all three cartridges is shown in Figure 1. C1 (Model 3), which included hematocrit and electrolytes, predicted transfusion within 3 hours significantly better than the other two cartridges, which analyzed PT/INR ($p = 0.02$) or lactate ($p = 0.04$). The combination of all three cartridges (Model 6) did not predict 3-hour transfusion better than C1 alone ($p = 0.86$). For the predictions of rapid transfusion and massive transfusion, there was no significant difference for any of the three laboratory cartridges. Table 3 shows the summary of coefficients and statistical significance for each laboratory result when all laboratory values were used in a logistic regression model to predict pRBC use within 3 hours. Hematocrit, glucose, and lactate have statistically significant contribution to the prediction. In predicting other outcomes, these three variables are constantly selected by the stepwise logistic regression model, which indicates their importance in predicting those outcomes.

An algorithm based on multivariate logistic regression models combining triage VS, laboratory values, and pulse oximetry features (Model 10) improved the accuracy of prediction, with AUROC curve of 0.84 for transfusion within 3 hours, 0.89 for rapid transfusion, and 0.91 for massive transfusion. The combination of all the measures was significantly better than triage VS alone ($p < 0.05$), better than pulse oximetry signal features alone ($p < 0.05$), but not better than all laboratory values combined (C1 + C2 + C3) ($p > 0.05$) or C1 alone ($p > 0.05$).

DISCUSSION

Our findings will form the basis for a computerized algorithm that can be integrated with patient monitors, allowing ongoing automated transfusion predictions that incorporate available data during trauma resuscitation. For the short span of time analyzed in this study, we found that a combination of



	pRBC15min-3hr	Rapid Transfusion	Massive Transfusion
Model01	0.59	0.71	0.70
Model02	0.74	0.82	0.88
Model03	0.83	0.85	0.87
Model04	0.75	0.81	0.88
Model05	0.77	0.80	0.80
Model06	0.83	0.86	0.91
Model07	0.84	0.87	0.93
Model08	0.76	0.84	0.90
Model09	0.79	0.86	0.93
Model10	0.84	0.89	0.91

Figure 1. AUROC curves for 10 models with respect to outcomes. Rapid transfusion, 5 U or greater pRBC in 4 hours; massive transfusion, 10 U or greater pRBC in 24 hours.

TABLE 3. Summary of a Logistic Regression Model Predicting pRBC Use Within 3 Hours Using Laboratory Results

Coefficients	Estimate	SE	*Z* value	Pr(>|z|)
Intercept	−3.2995	0.2002	−16.483	<2e−16
Bicarbonate	−0.2867	0.1720	−1.667	0.0955
Hematocrit	−0.5438	0.1579	−3.445	0.0006
Glucose	0.4300	0.1131	3.803	0.0001
INR	0.1471	0.1423	1.034	0.3013
Lactate	0.3255	0.1441	2.258	0.0239

The right column shows the statistical significance of each variable contributing to prediction.

triage VS, pulse oximetry signals, and laboratory data was more accurate than triage VS or pulse oximetry signal analysis alone for the prediction of blood transfusion. The addition of pulse oximetry signal analysis and triage VS to laboratory values did not significantly strengthen the prediction based on laboratory values alone. However, it is important to note that the various sources of data input provide complimentary information on the injured patient; pulse oximetry and vital sign measurements are noninvasive and change dynamically over time with an injured patient's changing physiologic status, while laboratory values require processing and represent a static point in time. In addition, variable data may be available for analysis on any given patient, depending on the clinical circumstances and location of care. For instance, in the prehospital environment, automated vital sign and pulse oximetry signal analysis may be feasible, while laboratory data may become available on arrival to the hospital. We propose that this type of data assimilation represents the threshold of a new era of "smart monitoring" whereby all available physiologic and laboratory data can be incorporated into analytic algorithms, compared with an ever expanding database of known patient outcomes, and categorized into accurate predictions.

A secondary finding in our study was that the combination of hematocrit and electrolyte laboratory values outperformed both PT/INR and lactate for prediction of blood transfusion, while the combination of all laboratory values together did not improve prediction compared to the hematocrit + electrolyte cartridge alone. We therefore recommend C1 for the initial evaluation during trauma resuscitation. When individual laboratory values were analyzed separately, hematocrit, glucose, and lactate contributed significantly to the prediction, while INR did not.

Prediction of blood transfusion needs using data available at the time of trauma admission is a surrogate means of identifying an actively bleeding patient. Care of this subset of patients will require mobilization of resources including helicopter transport, blood products, operating room facilities and staff, and interventional radiology. Early identification of the actively bleeding patient will improve resource mobilization and expedite efforts to control bleeding, thereby improving survival.

The challenge of predicting blood transfusion needs has been addressed through numerous methods during the past decade.[8] Multiple transfusion scoring systems have been created using physiologic, laboratory, and injury pattern data available early after admission to quantify the probability of receiving blood transfusion.[1–7] The Assessment of Blood Consumption score uses the admission values of SBP, HR, Focused Assessment with Sonography for Trauma (FAST), and mechanism of injury to calculate a predictive score with an AUROC curve of 0.85,[7] comparable with our results. This score and other similar scores have not achieved widespread acceptance at the bedside and have proven most useful as enrollment criteria for transfusion-related research. Similarly, the Trauma Bleeding Severity Score uses the patient's age, SBP, FAST results, presence of pelvic fracture, and serum lactate to calculate a score, and calculation is facilitated by an application on a handheld device.[1] Although similar predictive power has been demonstrated in previous studies with AUROC curve ranging from 0.78 to 0.99,[1–7] a drawback shared by these scoring systems is that user input and calculations are required, making them cumbersome for field or bedside use. Furthermore, such scoring systems use data from a single time point after hospital admission and do not incorporate dynamic changes that occur during active hemorrhage and resuscitation.

We describe a promising method for predicting transfusion based on analysis of noninvasive pulse oximetry signals recorded by a standard pulse oximeter, both alone and in combination with laboratory analysis. The pulse oximetry waveform has been shown in many studies to detect hypovolemia,[19–21] and emerging data have demonstrated usefulness for transfusion prediction in unstable trauma patients during resuscitation.[14] Pulse oximetry signal analysis overcomes limitations of other methods of predicting transfusion because it requires no user input and can be automated through computerized calculations that are continually updated with trend analysis during ongoing resuscitation. Although the AUROC curve reported in our study is similar to previous results, we believe that a computerized algorithm incorporating automated analysis of data trends as described in this study will represent a radical departure from trauma scoring systems that will bring real-time decision assistance to the bedside. This study lays the foundation for our future research that will focus on bringing this algorithm online as a real-time data analysis tool that is integrated into patient monitors, continuously analyzing data as they become available, and providing a continuously updated quantification of bleeding risk.

Point-of-care laboratory testing is increasingly available, facilitated by advances in technology. In particular, lactate, INR, hemoglobin or hematocrit, and base deficit have all been found to be independent predictors of massive transfusion, and each of these laboratory values has been identified through logistic regression to be important components of massive transfusion prediction scores.[1–6,22] Because of required reagents, these laboratory analyses currently use three separate point-of-care testing cartridges to complete the battery of tests, each cartridge requiring a separate blood sample and up to 5 minutes to complete. In our model, we grouped the laboratory analyses based on commercially available cartridges for the iStat device, although the blood analyses were completed in the central hospital laboratory using venous blood drawn during initial trauma patient resuscitation. We theorized that the three cartridges could in the future be combined to perform simultaneous analyses with one blood sample. Running more than

one cartridge during initial trauma resuscitation would be cumbersome in a field environment; however, we also recognized that various laboratory data would become available as resuscitation progressed and could then be incorporated into analysis.

An existing commercially available advanced vital sign monitoring system (Tempus Pro, Remote Diagnostics Technology, Ltd., England) allows recording of continuous high frequency VS, programming of automated computer algorithms, and rapid transfer of iStat laboratory data via Wi-Fi or infrared data link, making incorporation of these data into a decision-assist algorithm imminently possible.

A limitation of our study is the exclusion of nearly one quarter of patients because of inadequate PPG waveform quality. This occurred for two reasons: (1) competing priorities during the initial minutes of resuscitation may have delayed optimal positioning of the pulse oximetry monitor, and (2) pulse oximetry waveforms may be difficult to obtain in patients who are vasoconstricted because of hypothermia or hypovolemia. Future investigations will focus on improving PPG waveform quality as well as incorporating alternate input such as the electrocardiogram waveform into the algorithm.

It is likely that our predictions would have been slightly different with the use of actual point-of-care testing results rather than central laboratory results; however, point-of-care and central laboratory results have been shown to correlate closely for the specific laboratory tests used in our study.[23–25] We anticipate that prehospital data collection, including automated analysis of continuous vital sign waveforms as well as point-of-care laboratory testing,[26–28] will become more common in the future and will further improve decision assistance for prehospital triage and blood transfusion. Such an increase in the accuracy of triage may improve the safety of long-range evacuation or even transport with an autonomous critical care system using an unmanned vehicle of the future as envisioned by the military. Further prospective study is required to validate this approach.

CONCLUSION

Triage VS of HR and SBP with continuous automated analysis of 15 minutes of pulse oximetry signals and laboratory values predicted the need for early blood transfusion during trauma resuscitation more accurately than the triage VS or pulse oximetry signal analysis alone. Clinical decision support for rapid recognition of hemorrhage sufficient to need transfusion may lead to improved triage, targeted blood transfusion, and earlier hemorrhage control. Automated calculations incorporating numerous data points can bring near real-time, clinically useful, and continuously updated decision support to bedside and field monitors.

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AUTHORSHIP

S.S., S.Y., P.H., and C.Ma. were involved in designing the study, analyzing the data, and writing the article. C.Mi. and S.G. were involved in designing the study and contributing critical revisions to the article. A.A. and L.H. were involved in the data acquisition. Y.W. was involved in analyzing the data. R.F. was involved in designing the study.

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